A measurement method that can be applied to the calibration of a wide range of working RMs must satisfy the following conditions:

1) It must satisfy market demands regarding uncertainty, while also provide speed and simplicity of use.

2) It must be highly versatile and applicable to a wide variety of chemical compounds (general organic compounds for the purposes of this study).

Quantitative NMR is the most feasible candidate that can satisfy both conditions 1) and 2), although the answer is not yet fully established. Accordingly, in this study, we endeavored to establish quantitative NMR as a universal calibration technology for working RMs in organic compounds.

### *4.2 Principles of quantitative NMR*

NMR is one of the main methods for determining the molecular structure of a chemical compound. It has an extensive track record in unraveling molecular structures, including the analysis of complex molecules such as proteins. Information obtained using NMR, such as chemical shift (the resonance peak position dependent on atomic bonding and the ambient environment) and spin-spin coupling (a split of the peak due to bonded nearby nuclei), provide hints about the chemical species and ambient environment of a molecule. In addition, the area ratio of various peaks, which resonates according to different chemical shifts, generally indicates the ratio of the number of atomic nuclei contributing to the peaks. As Figure 2 shows, the area ratio of $^1$H NMR signals can easily be used to confirm the relative number of protons for the resonances, which is vital for the qualitative analysis of organic compounds.

Conventionally, this aspect of NMR was used exclusively to determine the chemical structure, solely by expressing the number of protons as a ratio in a molecule. However, the concept can be applied differently. If the molecular structure of an organic compound is already known and assignments of its $^1$H NMR spectrum has been set, the number of protons contributing to each resonance peak is known, and this information can be applied to the quantitative analysis of chemical compounds. Thus, when the $^1$H NMR measurement is performed by adding a reference chemical compound to a sample solution separately in an analyte (substance to be analyzed) solution, the spectra of the two chemical compounds overlay each other, as shown in Fig. 3. At this point, if the mass (weight), molecular weight, and purity of the added reference chemical compound (hereinafter, will be called the Primary Standard: PS) are known, the amount-of-substance (number of molecules) corresponding to peak I in Fig. 3 will also be known, and can be used as the criterion for finding the number of molecules in the analyte. To illustrate with a specific example, if the number of protons in PS (I) is the same as the number of protons in analyte (D) (the number is 6 for both), the ratio of the areas for peak I and peak D indicates the relative number of molecules. As such, the relationship can be expressed as follows:

(Peak area I)/(Number of molecules of PS) = (Peak area of D)/(Number of molecules in analyte)

Since the number of molecules in PS is already known, the

**Table 1 Types of primary methods of measurement and their characteristics.**

| Analytical method | Primary direct method | | | Primary ratio method | | |
|---|---|---|---|---|---|---|
| | Coulometry | Gravimetry | Freezing point depression method | Titrimetry | Isotope dilution mass spectrometry | Quantitative NMR |
| Outline of analytical method | Amount of electricity used in electrysis of specified substances is measured. | Settling quantity of specified substances in solution is measured. | Relationship between fraction melted and temperature around the melting point is measured. | The specified substance is measured using chemical reactions. | Mass spectrometry is performed using a stable isotope. | The ratio of areas of $^1$H peaks with different chemical shifts is measured. |
| Main target substance | Metallic elements | Inorganic salts | High purity organic compounds | Acid, base, elements | Trace metals trace organic compounds | Organic compounds |
| Reference standard | Not required | Not required | Not required | Reference standards based on the principles of titration are required. | Required for each analyte | A reference standard for $^1$H is required. |
| Uncertainty (less than 1 %) | ○ | ○ | ○ | ○ | ○ | △(Unknown value) |
| Rapid analysis | × | × | × | × | ○ | ○ |
| General applicability | × | × | × | × | × | ○ |

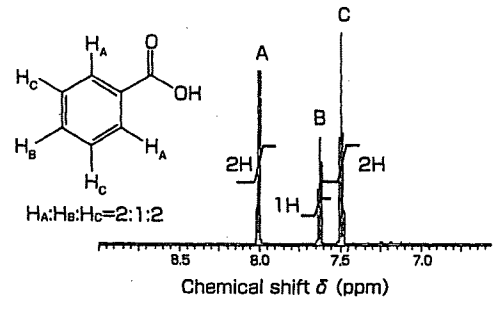


**Fig. 2 Qualitative analysis of chemical compounds using $^1$H NMR.**

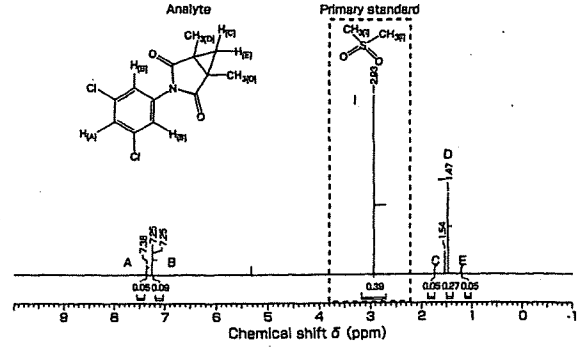


**Fig. 3 Quantitative analysis of chemical compounds using $^1$H NMR.**

number of molecules in the analyte can be obtained. The mass (weight) and molecular weight of the target substance can then be used to determine the purity of the analyte[3]. Therefore, quantitative NMR is, in principle, a primary ratio method which can be used to obtain traceable measurement values for the number of protons — that is, amounts of substance in a sample.

In the example in Fig. 3, both the analyte and the PS are pure substances. After weighing the two substances individually, they are dissolved in a deuterated solvent, and quantitative NMR is used to measure the purity of the analyte using the mass ratio of the two substances. Working RMs, in contrast, are often supplied in the form of solution. If supplied at a certain concentration (about 0.1 %), quantitative NMR can be applied by dissolving the working RM in an appropriate deuterated solvent. The concentration of working RM can be found from the number of molecules obtained for the analyte, the mass of sample solution added, and the number of molecules in the analyte.

### *4.3 Feasibility of quantitative NMR*

National metrology institutes in several countries (including AIST), which are members of the Consultative Committee for Amount of Substance (CCQM)[Term 12], have shown interest in the possibility of applying quantitative NMR as a primary ratio method, which was first suggested by Germany's Federal Institute for Material Research and Testing (BAM). In 2001, the Laboratory of the Government Chemist (LGC) in the United Kingdom and BAM served as pilot laboratories to conduct an international comparison[Term 13] for the quantitative analysis of ethanol in aqueous solution, with the participation by 10 institutes in key countries. On this occasion, measurements were conducted on the same sample using conventional analytical approaches such as gas chromatography (GC) as well as quantitative NMR[4]. The sample was precisely

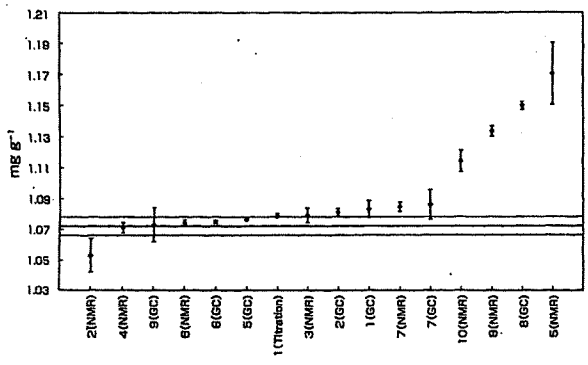


**Fig. 4 Results of international comparison on quantitative analysis of ethanol in aqueous solution.**

The solid line indicates the preparation value; the dotted line indicates uncertainty for the preparation value. No. 6 is the result for NMIJ/AIST. Participants: BAM (Germany), KRISS (Korea), LGC (UK), LNE (France), NIST (USA), NMi (Netherlands), NMIJ (Japan), NRC (Canada), NRCCRM (China), and VNIM(Russia).

produced by LGC, one of the pilot laboratories. The ethanol concentration was 1.072 mg/g ± 0.006 mg/g, but this value was not disclosed to the participants. Also, BAM separately supplied a deuterated water solution of PS (3-trimethylsilyl sodium propionate-$d_4$) of known concentration to the participating institutions that declared to conduct the quantitative NMR measurement.

The measurement results were reported individually to the pilot laboratory. Figure 4 is a summary of the results. Each data point represents a reported result. The adjacent error bar is the measurement uncertainty estimated by each participating institution (95 % confidence interval). The uncertainty of the quantitative NMR results from most institutions was in the range that could be described as percentage, and some of the results deviated significantly from the preparation values. In short, it was found that the quantitative NMR lacked accuracy compared to the conventional analytical methods such as GC. From the result of this international comparison, it was determined that the quantitative NMR did not offer sufficient technical accuracy. This view remains essentially unchallenged in the international scientific community today.

At the same time, Fig. 4 shows that the value reported by AIST closely matched the preparation value and its uncertainty was considerably smaller than the quantitative NMR findings of other participating institutions. This is why AIST takes a different stance on quantitative NMR. The uncertainty AIST reported to the pilot laboratory for quantitative NMR in the international comparison is illustrated in Fig. 5. Upon evaluating the relative standard uncertainties of each component, we found that the greatest factor was the uncertainty of the concentration of $^1$H PS supplied by the pilot laboratory. Because the uncertainty of AIST's quantitative NMR measurement was much smaller, it became clear that a much smaller measurement uncertainty would have resulted if AIST had supplied its own more accurate PS.

It should be emphasized that the quantitative NMR offers a major advance in versatility. Whereas GC and other

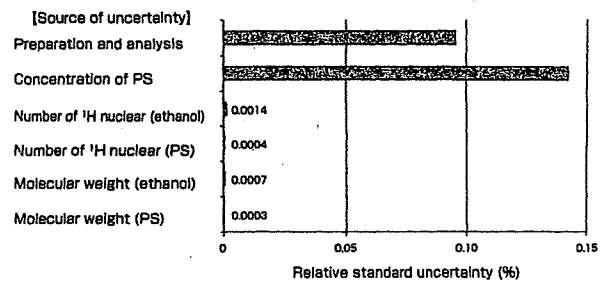


**Fig. 5 Uncertainty for $^1$H NMR in the international comparison on quantitative analysis of ethanol in aqueous solution.**

conventional analytical calibration technologies applied in the international comparison can only be used to compare the concentrations of like chemical compounds (PS must be the same chemical compound as the measured substance), quantitative NMR can compare quantities of chemical compounds of different types (that is, PS does not have to be the same type of chemical compound as the measured substance). As such, although quantitative NMR requires at least one substance including $^1$H, it can be used to measure any organic compound that includes proton, and a wide range of applications can be expected accordingly. The Authors believe that quantitative NMR can be applied in the calibration of working RMs by developing and integrating certain elemental technologies. These are discussed below.

## 5 Development and integration of elemental technologies to realize the quantitative NMR

### *5.1 Core elemental technologies*

Figure 6 illustrates the elemental technologies developed by the authors, and the combination necessary to realize the potential of quantitative NMR as a universal calibration technology for working RMs. The features required of NMR differ greatly depending on whether the technology is optimized for qualitative analysis or for quantitative analysis, as in our case. With quantitative NMR, the highest priority is to observe the signal in accurate proportion to the number of atomic nuclei in the analysis, rather than improving measurement speed or improving the signal-to-noise ratio (S/N). We therefore revised the conditions for selecting the core elemental technologies.

The first elemental technology corrects a signal amplification issue. Generally speaking, NMR signals relax throughout its lifetime called the spin lattice relaxation time ($T_1$), which is the time taken for the atomic nuclei to settle from their excited state to their ground state. This period varies according to the environment of protons (such as bonding with other atoms). When NMR is performed for qualitative analysis, the sample is irradiated with microwave pulses with short cycle to increase the signal and to improve S/N. In such case, the delay time may be shorter than $T_1$, where excitation pulse is applied before all protons settled to their ground state. As result, differences in $T_1$ among the protons of analyte and PS make it impossible to obtain the peak area in correct proportion for the number of protons in each proton. We resolved this problem by measuring the relationship between repetition time and peak area. By taking delay time six times or greater than $T_1$ for the analyzed protons, it was demonstrated by experiment that 99.9 % or more of original signal intensity could be obtained, providing a stable peak-area ratio[5]. By ensuring that the delay time was sufficiently longer than the longest $T_1$ for all protons in the analyte, it was possible to obtain accurate peak-area ratio that was unaffected by the $T_1$ of the protons (though the measurement time increased several times longer than the conventional method).

The second elemental technology also concerns the S/N. Normally, S/N in the NMR signal is further improved by using an audio filter to narrow the bandwidth. However, this filter is not "flat" in sensitivity throughout the bandwidth, but exhibits severe loss of sensitivity at both ends of the filter bandwidth. Depending on the chemical shift, this loss of sensitivity can be in the range of several percents. Greater the chemical shift in the protons observed in the analyte and PS, more difficult it is to obtain an accurate peak-area ratio. To obtain flat sensitivity, we set the audio filter to cover 60 %~70 % of bandwidth and also widened the spectral width for data acquisition to 100 ppm, compared to less than 20 ppm in the conventional setting. This setting allowed the resulting spectrum to remain unaffected by sensitivity loss caused by filter for all chemical shifts. While such filter settings are not practical for ordinary NMR that involves handling of large volume data, we were able to solve several issues by taking an unconventional

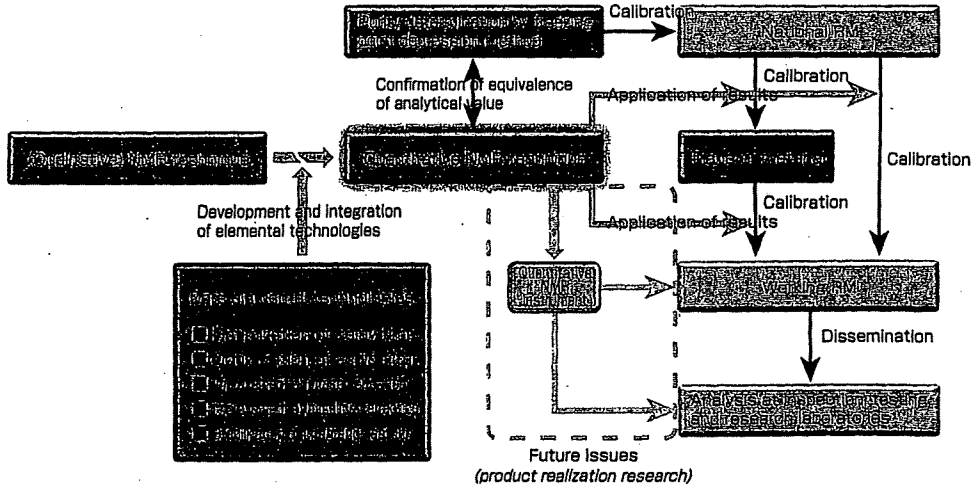


**Fig. 6 Development of elemental technologies for the construction of universal calibration technology and the process of integration.**

approach with priority on measurement accuracy[5].

In addition to the two elemental technologies described above, the Authors found that to improve the reproducibility of measurement results, phase correction, baseline correction, and peak area integration setting (range) were more important compared to other minor factors.

### 5.2 Use of transfer materials

Although quantitative NMR requires $^1$H as the PS, the analyte does not have to be the same substance. The PS (limited to pure substances in this discussion) must satisfy the following conditions:

1) It must have as little impurities as possible, to keep the uncertainty for its purity value small.
2) It must dissolve easily in wide range of solvents, and must be stable in solution.
3) It must have low volatility (sublimability) and absorbency, so its mass (weight) can be measured easily.
4) Its chemical shift must not overlap with that of the target substance.

Although some national RMs satisfy these conditions for PS, many national RMs do not satisfy requirement 2), because a suitable solvent for dissolving both the PS and the analyte has not been found. Also, some national RMs do not satisfy 4), as the PS used depends on the analyte, and different PSs must be used with certain analytes.

The number of national RMs cannot be reduced if different PSs must be prepared according to various analytes. The Authors solved this problem using the calibration methods illustrated in Fig. 7, marshaling the advantages of quantitative NMR. We achieved this by selecting the transfer materials or chemical compounds whose chemical shifts do not overlap with either the PSs or the analytes. In Step 1, the PS (national RM) is used to calibrate the characteristic peak of the transfer material using quantitative NMR. In Step 2, the characteristic peak of the calibrated transfer material is adopted as the standard for calibration of the analyte. By adopting this two-step calibration method, the number of national RMs, which anchor the traceability system, can be minimized. Moreover, the transfer material does not need to be homogeneous or long-term stable like the RMs, so a wide range of materials is available for selection according to their match with a given analyte. The introduction of transfer materials to quantitative NMR was an important technological development in the process of synthesizing the elemental technologies.

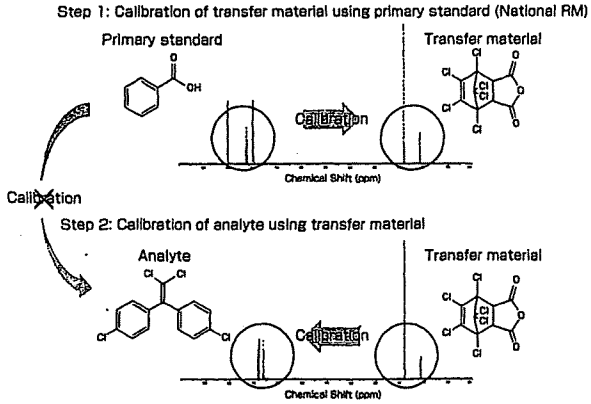


**Fig. 7 Use of transfer material in quantitative NMR.**

### 5.3 Evaluating the integrated technologies

In sections 5.1 and 5.2, we described how several elemental technologies were integrated to construct a calibration technology using quantitative NMR. Next, we demonstrated the reliability of the technologies by comparing them with long-established techniques. To do this, we first selected several target substances from commercially available, high-purity compounds. Their purity values were determined using the freezing point depression method, a well-established primary direct method that AIST has been using for the valuation of national RMs (see Table 1). Then we measured the same samples with the newly developed quantitative NMR to find the purity value, and checked whether the two values matched in the range of their respective uncertainties.

As the PS for measurements using quantitative NMR, we used benzoic acid (NIST SRM 350a, 99.9958 % ± 0.0027 %), a national RM distributed by the National Institute of Standards and Technology (NIST) of the United States. We performed the two-step calibration process described above using dimethyl sulfone or 1,4-bis-trimethylsilylbenzene-$d_4$ (1,4-BTMSB-$d_4$) as the transfer material, as the peak of the chemical shift for several substances overlaps the peak for benzoic acid. To dissolve the PS and the analyte, solvents were selected from a number of deuterated solvents, to minimize skewing of results from the protons of any impurities in the solvent. The solubility and other characteristics of the PS and analyte were also taken into consideration, and a solution with a concentration of about 1000 mg/L was prepared.

The analytical results are summarized in Table 2. Although in many cases the uncertainty was larger for the purity values by quantitative NMR compared to freezing point depression method, the values for the two methods matched within the uncertainty ranges, demonstrating that our calibration technology using quantitative NMR was sufficiently reliable[6]. The uncertainty for quantitative NMR was between 0.3 % and 1.2 % ($k$=2, 95 % confidence interval). Although this accuracy as a purity measurement technology is somewhat inferior to the freezing point depression method, quantitative NMR can be used to calibrate substances to which the freezing point depression method cannot be applied, including a wide range of organic compounds, and

it satisfies the market demand for the uncertainty levels in working RMs.

## 6 Issues for further study

We envision a transfer from the current one-to-one traceability system based on separate national RMs for each substance, to one-to-many traceability system in which several substances can be traced to just a few national RMs. So far, we made advancement for the development of universal calibration technology, a core technology applicable to numerous organic compounds. After establishing an ideal scenario for this project, we began by developing elemental technologies, using irradiation pulse delay time and optimization of audio filters. We then demonstrated that these calibration technologies could satisfy market requirements for uncertainty. We learned that the transfer materials could be used to minimize the number of national RMs required as standards for amount-of-substance. Finally, we plotted a roadmap toward an efficient traceability system, as illustrated in Fig. 8.

The system we outlined represents a quantum leap in the efficiency of traceability systems, since it removes the need to maintain one-to-one traceability chain from national RMs to working RMs for individual substances. It is an entirely new approach to RMs, unseen elsewhere in the world. The novelty of this technology, however, means that it is necessary to conduct numerous proving tests and to publish the results. The quantitative NMR technique must be standardized as an analytical method, and new international comparisons will be required at national metrology institutes

**Table 2 Purity analysis results for organic compounds using quantitative NMR.**

| Terget substance | Freezing point depression method | | Quantitative NMR | | | | |
|---|---|---|---|---|---|---|---|
| | Reference value (%) | Uncertainty (%, $k$=2) | Analytical value (%) | Uncertainty (%, $k$=2) | Primary standard | Transfer material | Solvent |
| *trans*-Nonachlor | 99.6 | 0.2 | 99.5 | 0.6 | Benzoic acid | — | Acetone-$d_6$ |
| *cis*-Nonachlor | 99.8 | 0.2 | 99.9 | 0.5 | Benzoic acid | — | Dichloromethane-$d_2$ |
| Oxychlordane | 99.9 | 0.1 | 99.3 | 0.5 | Benzoic acid | — | Dichloromethane-$d_2$ |
| Endrin | 99.7 | 0.2 | 99.2 | 0.8 | Benzoic acid | — | Dichloromethane-$d_2$ |
| *trans*-Chlordane | 99.8 | 0.3 | 99.5 | 0.6 | Benzoic acid | — | Dichloromethane-$d_2$ |
| *cis*-Chlordane | 99.7 | 0.4 | 99.1 | 0.5 | Benzoic acid | — | Dichloromethane-$d_2$ |
| Trichlorfon (DEP) | 99.7 | 0.3 | 99.6 | 0.5 | Benzoic acid | — | Dichloromethane-$d_2$ |
| Heptachlor | 99.7 | 0.3 | 99.3 | 0.3 | Benzoic acid | — | Dichloromethane-$d_2$ |
| 4,4'-DDT | 99.6 | 0.3 | 99.9 | 1.2 | Benzoic acid | Dimethyl sulfone | Acetonitrile-$d_3$ |
| 4,4'-DDE | 99.7 | 0.3 | 99.8 | 0.7 | Benzoic acid | Dimethyl sulfone | Acetonitrile-$d_3$ |
| 4,4'-DDD | 99.8 | 0.2 | 99.9 | 0.6 | Benzoic acid | Dimethyl sulfone | Acetonitrile-$d_3$ |
| Procymidone | 99.9 | 0.2 | 99.3 | 0.5 | Benzoic acid | Dimethyl sulfone | Dichloromethane-$d_2$ |
| Fenobucarb (BPMC) | 99.8 | 0.2 | 99.8 | 0.7 | Benzoic acid | 1,4-BTMSB-$d_4$ | Dichloromethane-$d_2$ |
| Fenitrothion (MEP) | 99.8 | 0.3 | 99.6 | 0.6 | Benzoic acid | 1,4-BTMSB-$d_4$ | Dichloromethane-$d_2$ |
| $\alpha$-HCH | 99.6 | 0.3 | 99.2 | 0.6 | Benzoic acid | — | Dichloromethane-$d_2$ |
| $\beta$-HCH | Inapplicable (thermal decomposition) | | 99.5 | 0.3 | Benzoic acid | — | Dichloromethane-$d_2$ |
| Atrazine | Inapplicable (thermal decomposition) | | 99.7 | 0.7 | Benzoic acid | 1,4-BTMSB-$d_4$ | Dichloromethane-$d_2$ |
| EPN | Inapplicable (Uncrystallized) | | 99.4 | 0.7 | Benzoic acid | 1,4-BTMSB-$d_4$ | Dichloromethane-$d_2$ |
| Diazinon | Inapplicable (Uncrystallized) | | 99.8 | 0.7 | Benzoic acid | 1,4-BTMSB-$d_4$ | Dichloromethane-$d_2$ |
| Malathion | Inapplicable (Uncrystallized) | | 99.5 | 0.7 | Benzoic acid | — | Dichloromethane-$d_2$ |
| Etofenprox | Inapplicable (Uncrystallized) | | 99.5 | 0.5 | Benzoic acid | Dimethyl sulfone | Dichloromethane-$d_2$ |

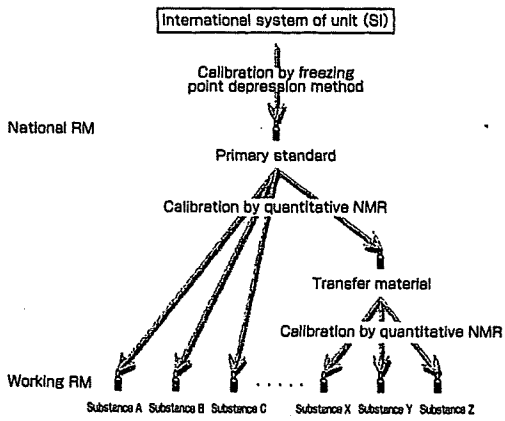


**Fig. 8 Efficient traceability system with quantitative NMR.**

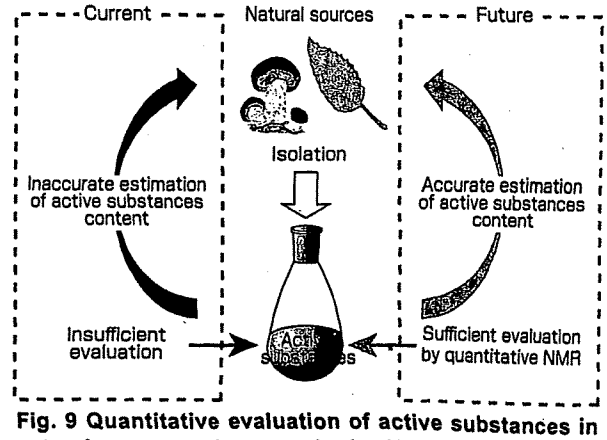


**Fig. 9 Quantitative evaluation of active substances in natural sources using quantitative NMR.**

around the world. More work must be done before one-to-many traceability can be firmly established.

At the same time, it is necessary to build the infrastructure that allows the industrial community to perform calibration of the wide range of working RMs that are in demand by the society. For this purpose, national RMs that are easy to use with quantitative NMR must be supplied along with sample applications. Automation tools are also necessary, covering all processes from measurement parameter sets using quantitative NMR to data analysis.

## 7 Future directions

Quantitative NMR has great potential marketability, as the necessary analytical equipment are commercialized (Fig. 6: Future issues). As reasonably priced, easy-to-use equipment, which are optimized for quantitative NMR, become available, and applications for nuclei other than $^{1}H$ are developed, they will find use not only in calibration technologies for working RMs, but also in quantitative analysis of several organic compounds occurring in numerous fields conducted at a wide variety of proving, testing, and research laboratories.

Many de facto commercial calibration standards are in use today, even though evaluation of their purity or concentration remains inadequate. For example, for active substances in *natural sources*, such as bioactive constituents and herbal medicines, quantitative analysis often depends on the samples of isolated constituents or the commercially available reagents. Quantitative NMR can offer highly reliable and effective quantitative analysis in such cases (see Fig. 9)[7], where the discovery of appropriate standard would normally be difficult.

Perhaps most exciting of all, an efficient traceability system based on this calibration technology for organic compounds may provide an effective scheme for responding flexibly to today's proliferating demand for RMs. Although core technologies other than quantitative NMR have not yet been demonstrated, universal calibration technologies that can be used similarly in the construction of a rational traceability system may be developed. The Authors hope that this paper will serve as a starting point for the development of such universal calibration technology.

## Acknowledgments

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Finally, Dr. Shinichi Kinugasa (AIST) provided valuable assistance in writing this paper, for which we thank him sincerely.

## Terminology

Term 1. Positive List System: Established in 2006 based on a revision of Japan's Food Sanitation Law, this system prohibits the sales of foods that contain agricultural chemical residues above a certain quantity. In cases where the safe (not harmful to human) quantity has been specified (called the residue level), the agricultural chemical must be below that quantity. In case where the safe quantity has not been specified, a uniform limit of 0.01 ppm is applied.

Term 2. Official Method of Analysis: A set of analytical procedures officially published and recognized in accordance with laws governing chemical compounds, to enable comparison of analytical results among different testing laboratories and samples. An official method of analysis must be robust and universally applicable. Examples used in Japan are Japanese Industrial Standard (JIS), Japanese Agricultural Standard (JAS), and Japanese Pharmacopoeia (JP).

Term 3. Certified reference material (CRM): In ISO Guide 35, which provides the international guidelines for RMs, this is defined as "reference material, characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability."

Term 4. Traceability: The characteristic of a measurement result, where the result can be linked to a known reference standard (usually a national standard) through an unbroken chain. In the 3rd version of

the *International Vocabulary of Metrology* (VIM), this term is amended to "metrological traceability" to distinguish from the term used to manage the shipping histories of foods and other goods.

Term 5. National metrology institute: A research institute that sets a country's official measurement standards. In Japan, it is the National Metrology Institute of Japan within the National Institute of Advanced Industrial Science and Technology.

Term 6. Primary method of measurement: The method used to define national RMs. It is defined as follows: "primary method of measurement is a method having the highest metrological qualities, whose operation can be completely described and understood, for which a complete uncertainty statement can be expressed in terms of SI units."

Term 7. Coulometry: The method of measuring the amount-of-substance of an analyte from measurements of current and time when electrolysis is applied to a specific substance based on Faraday's Law. It is used in the analyses of inorganic ions of metallic elements as well as of trace amounts of moisture.

Term 8. Gravimetry: An analytical technique in which the quantity of an analyte in a sample is found by separating the analyte from the rest of sample using a reagent that reacts specifically to that component. The resulting mass is used to determine the quantity of the analyte. Generally, mass is found by precipitating the selected component out of the solution, but it can also be found by separating the selected component from the sample as gas, adsorbing the component using an adsorbent, and then calculating the mass from the amount adsorbed.

Term 9. Freezing point depression method: An analytical technique that finds the amount-of-substance fraction of impurities in a sample as a proportion of its amount-of-substance by measuring the temperature and enthalpy of impurities in a sample, as its freezing point decreases. It is generally used to determine the purity of high-purity organic compounds.

Term 10. Titrimetry: This is volumetric measurement in a limited sense. A solution that includes an RM that reacts with the sample is dropped into a sample solution, and the quantity of RM consumed before the equilibrium is reached is measured to find the quantity of the analyte in the solution. Depending on the chemical reaction used, the method includes neutralization (acid-base) titration, oxidation-reduction titration, complex formation titration, or precipitation titration.

Term 11. Isotope dilution mass spectrometry: A method of finding the quantity of an analyte in a sample using substance labeled with a stable isotope. The labeled substance is added to the sample, and the signal ratio of the mass spectrums of the analyte and the labeled substance are obtained. Because the chemical properties of the analyte and the labeled substance are roughly identical, the effect of the process of sample preparations with significant impurities can be cancelled (the signal ratio of the analyte and its labeled substance is maintained). In this technique, the concentration of the labeled substance for the RM must be known in advance.

Term 12. Consultative Committee for Amount of Substance (Comité Consultatif pour la Quantité de Matière: CCQM): One of the consultative committees formed under the aegis of the International Committee of Weights and Measures (Bureau International des Poids et Mésures: BIPM)) that consists of the Meter Convention member institutions. Established in 1993, this consultative committee discusses issues on metrology in chemistry.

Term 13. International comparison (CCQM inter-comparison): Comparison among calibration laboratories to confirm the degree of equivalence in the calibration and measurement capabilities and values assigned to RMs between various national metrology institutes. Normally, this process begins with an international comparison for research purposes, called a pilot study. After the technical groundwork has been established to a certain degree, an official international comparison, called a key comparison, is performed.

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## Authors

**Toshihide Ihara**
Completed the doctoral course in engineering at Tokyo Metropolitan University in 1994. In 1996, he joined the National Institute of Materials and Chemical Research of the Agency of Industrial Science and Technology, where he worked on the development of RMs for volatile organic compounds and other organic compounds. At the National Institute of Standards and Technology in the United States from 2002 to 2003, he pursued development of RMs related to health foods. Moving to BIPM from 2005 to 2006, he worked on purity evaluation techniques for organic compounds. In 2006, he was assigned to his current position at the RMs Systems Division of the National Metrology Institute of Japan of AIST (now the Measurement Standards Systems Division), where he conducts research on standards dissemination systems in the fields of environmental science, foods, and clinical testing. In this paper, he conceived the idea for a new traceability system in chemical metrology and designed specific approaches.

**Takeshi Saito**
Joined the National Institute of Materials and Chemical Research of the Agency of Industrial Science and Technology, where he engaged in research in advancing Spectral Database (SDBS) for Organic Compounds, which is now publicly available on the Internet. He is now in charge of this project. Since joining the Institute, he has made extensive use of NMR in research. In a contract work with the New Energy and Industrial Technology Development Organization (NEDO), he worked on a platform for measurement at nanoscale, focusing on the measurement of particle diameter in liquid using NMR. Currently he is working to improve the precision and accuracy of quantitative analytical techniques using NMR. He also works on the general application of quantitative analytical methods. In this paper, he constructed the basic technology for quantitative NMR.

**Naoki Sugimoto**
After completing the doctoral course in Natural Sciences and Technology at Kanazawa University in 1997, he joined the National Institute of Health Sciences (NIHS) in the same year. There, he worked on setting standards for food additives and other substances. From 2005 to 2006, at the Food and Drug Administration (FDA) and Center for Food Safety and Applied Nutrition (CFSAN) in the United States, he developed methods for analyzing food additives, to promote international standardization. Since 2008, he became the chief of 3rd Section, Division of Environmental Chemistry at NIHS, where he currently works on setting criteria and developing guidelines of analytical methods for chemical substances related to water quality. In this paper, he contributed to the application technologies for quantitative NMR and to the proposal of automation tools to make the technology accessible to the general public.

## Discussion with Reviewers

### 1 General evaluation

**Comment (Akira Ono)**

Today the society is facing difficulties as the development of techniques for accurate analysis of harmful organic compounds in foods and environment cannot keep up with the ever-diversifying demands. The quantitative NMR developed in this research project, along with the new, more efficient traceability system, strike at the heart of this problem. They hold the potential for a revolution in the metrological traceability.

I believe your approach represents the first use of NMR equipment for quantitative analysis that was originally developed for qualitative analysis. What makes this project a particularly outstanding *Type 2 Basic Research* is that you returned to the development of elemental technologies to complete the core technology of quantitative NMR.

**Comment (Hisao Ichijo)**

Your writing shows clearly how you steadily pursued your program of research and development, by drawing scenarios along the way toward the ambitious goal of switching to a new, more efficient traceability system based on calibration technology.

### 2 Focus on specific descriptions

**Question and comment (Akira Ono)**

You advocate a new traceability system using quantitative NMR. Since that alone is a remarkable accomplishment, I think you should describe this system in a more understandable way. Perhaps you could provide a simple description of the freezing point depression method and how it is used to measure the purity of pure substances.

**Question and comment (Hisao Ichijo)**

Your paper clearly describes the objectives, how they relate to the demands of society, the elements of technology, and so forth. You determined that the quantitative NMR is appropriate (because it can be applied to a wide range of substances within the uncertainty range the market demands), and that the freezing point depression method is inappropriate (because of crystallization problems). I think your paper will be easier to understand if you explain more fully the research processes by which you came to your conclusions (crystallization is difficult, number of applicable substances is limited, and so on).

**Answer (Toshihide Ihara)**

We rewrote the paper to change the rationale behind the comparison with freezing point depression method and to focus more closely on the technical structure of quantitative NMR. The freezing point depression method is a well-established technique. We described it only to demonstrate the appropriateness of quantitative NMR.

### 3 Illustration of research scenarios and integration of elemental technologies

**Question and comment (Akira Ono)**

Please add some figures illustrating your research scenarios for *Type 2 Basic Research* and the integration of elemental technologies, to make your paper more accessible to a general readership.

**Answer (Toshihide Ihara)**

We added Fig. 6 to illustrate the process of integrating the elemental technologies to construct the universal calibration technology.

### 4 Selection of primary standards

**Question and comment (Akira Ono)**

In the purity determinations of organic compounds in Table 2, benzoic acid, a national RM from NIST of the United States, is used as a primary standard for quantitative NMR. Why didn't you use one of the national RMs as high-purity organic compounds available from AIST?

**Answer (Toshihide Ihara)**

Benzoic acid (NIST SRM 350a), the NIST national RM used in our study, satisfies the conditions 1) to 3) as outlined in section

5.2. We therefore determined that it is the ideal RM among the national RMs currently available for quantitative NMR. Certain national RMs at AIST, such as potassium hydrogen phthalate (NMIJ CRM 3001-a) and 1,4-dichlorobenzene (NMIJ CRM 4039-a), qualify for condition 1), but potassium hydrogen phthalate does not dissolve easily in organic solvents, and therefore, fails to satisfy condition 2) in our view. Similarly, 1,4-dichlorobenzene is highly sublimable and does not meet condition 3). At present, no national RMs have been developed specifically for quantitative NMR. We are currently in the process of developing the AIST national RMs that satisfy condition 4) as well as 1) to 3).

## 5 Final status of primary standards

**Question and comment (Akira Ono)**

You assert that, in principle, the ideal outcome of the application of quantitative NMR would be the development of a single primary standard that serves as the national RM for all organic compounds. Realistically, how many national RMs do you expect are required when this future traceability system is completed? Do you have any specific candidates in mind as organic compounds for the national RMs?

**Answer (Toshihide Ihara)**

In this study, our priority was to minimize the number of national RMs required, thus reducing development time and expense. That is why we proposed the use of transfer materials in the multi-stage calibration process. Benzoic acid has served as the primary standard for all organic compounds we have measured so far. This success gives us confidence that a traceability system based on a single national RM can be constructed for all organic compounds for which $^1$H NMR measurement can be performed.

On the other hand, such a traceability system has its disadvantages. Multi-stage calibration is time-consuming and increases uncertainty. If the accuracy or swiftness of analysis becomes more important for users, it is necessary to develop multiple national RMs with different polarities and chemical shifts. We are looking at ways of restricting calibration to single stage. To handle organic compounds that do not have protons, it is necessary to develop quantitative NMR for other nuclei, such as phosphorus and fluorine, along with the corresponding national RMs.

## 6 Preparation and use of transfer materials

**Question and comment (Akira Ono)**

I ask about how the transfer materials are used. When this new, efficient traceability system is completed in the future, will AIST produce, store, and disseminate these transfer materials as needed? Or can the reagent manufacturers that produce working RMs make the transfer material when needed, and dispose it when they are done?

**Answer (Toshihide Ihara)**

In our paper, we envisioned the transfer material to be prepared by the developers or suppliers of the working RMs (RM producers) according to their objectives. To ensure appropriate evaluations, the transfer materials will not be prepared for each batch, but the RM producers will be responsible for producing and storing them for a certain period.

Also, as described in chapter 7, if quantitative NMR becomes widely used as a quantitative analytical method for organic compounds, prepared transfer materials can be used. Moreover, AIST or RM producers may supply easy-to-use transfer materials as RMs.

## 7 Comparison of quantitative NMR and freezing point depression method

**Question and comment (Akira Ono)**

My question concerns the analytical results in Table 2. In the freezing point depression method, uncertainty for purity determinations rarely exceeds the upper limit of 100 %, whereas in many cases using quantitative NMR, the upper limit for analytical result exceeds 100 %. Such results are unreasonable. Since the freezing point depression method directly measures impurities in pure substance, the upper limit for analytical result over 100 % is rare. Using quantitative NMR, on the other hand, measurement of the main components is performed when the concentration of the pure substance is diluted to about 1000 mg/L. Isn't this one reason why the upper limit for analytical result can rise above 100 %? Isn't this the case where quantitative NMR is fine for measuring components in a solution but is inappropriate for measuring the purity of pure substances? If so, quantitative NMR seems to be most promising for *Product Realization Research* surrounded by the dotted line in Fig. 6. I'd like to hear the authors' views on this.

**Answer (Toshihide Ihara)**

Although the factors contributing to the uncertainty of quantitative NMR are not separated in Fig. 5 between preparation uncertainty and measurement uncertainty, preparation uncertainty is not relatively small. Thus, when applied to purity determination, quantitative NMR is undeniably inferior to the freezing point depression method in terms of uncertainty for preparation of solutions, and purity determination higher than the upper limit for analytical result exceeding 100 % is obtained as a result, as you pointed out (however, this does not indicate any bias in the purity determinations).

The freezing point depression method cannot be applied to measure concentrations of components in solution, but there are many examples where the characteristics of quantitative NMR can be applied, as you also pointed out. Because many organic solvents contain hydrogen, we must find ways of reducing these effects so NMR can be applied to protons. In *Product Realization Research*, including the development of quantitative NMR equipment, solving the issue of protons in solution and enabling measurement of concentrations of components in solution are keys to establishing the use of quantitative NMR.

## 8 Other candidates for universal calibration technologies

**Question and comment (Akira Ono)**

In chapter 7, "Future Directions," you raised the possibility that universal calibration technologies other than quantitative NMR may be found in the future. Are there any candidate calibration technologies at this time?

**Answer (Toshihide Ihara)**

In section 4.1, we stated that a universal calibration technology should theoretically be an analytical method qualified as a primary ratio method (measures the value of a ratio of an unknown to a standard of the same quantity; its operation must be completely described by a measurement equation).

Although not yet established as an analytical technique, one candidate the Authors are examining is a combination of chromatography and atomic emission spectrometry. In this process, the analytes are separated from the sample by chromatography. Then each analyte is introduced into high-temperature plasma and atomized into constituent carbon, hydrogen, oxygen, and other atoms. These atoms can then be measured to find the emission of spectrally separated (for example) carbon atoms. By adding a primary standard containing a known quantity of carbon to the sample, the quantity can be combined with the emission of carbon to find the quantity of analyte, as the primary standard itself is also atomized. The point here is that the efficiency of atomization is not dependent on the molecular species. Currently, the combination of gas chromatography and helium-plasma atomic emission spectrometry can obtain uncertainty of 5 % (95 % confidence interval). Further

improvements are needed for the commercialization of this technique.

### 9 Reason for using deuterated solvents

**Question and comment (Akira Ono)**

You noted in section 4.2 that you used a deuterated solvent. Can you explain why you used deuterated solvents for quantitative NMR? Should we infer that using $^1H$ (proton) solvents disable quantitative NMR?

**Answer (Toshihide Ihara)**

In our study, $^1H$ was used as the measurement nucleus. When solvents contain $^1H$ or protonated solvents are used, the $^1H$ signals from the solvents become much stronger than those from the compounds intended to be observed. As a result, the dynamic range of an instrument may prevent the accurate measurement of the analyte signal. Deuterated solvents are used to minimize the $^1H$ from the solvents to resolve this problem. This is, in general, not just for quantitative NMR, but is also for conventional $^1H$ NMR measurements.

On the other hand, in the international comparison of ethanol, aqueous solution was used, and the solvent in this case was protonated water ($H_2O$) rather than deuterated water ($D_2O$). Therefore, the problem of dynamic range may occur. In such case, the resonance frequency of the solvent (water) signal is irradiated selectively with low power radio frequency pulse to saturate this signal. This saturation pulse is immediately followed by a normal pulse. This approach, called the pre-saturation method, cancels the interference of a strong $H_2O$ peak. Although power applied to this saturation pulse is low, peaks resonating at nearby frequencies are influenced by the pulse. This may compromise the accuracy of the analytical value obtained in this method. In other cases, irradiation strength, duration, and other factors must be set correctly to obtain the accurate analytical values. For these reasons, it is simple and safe to use a deuterated solvent.

Additionally, to maintain the stability of the magnetic field, resonance frequency of the deuterium signal from the solvent is monitored to adjust the strength of the magnetic field from time to time to maintain constancy of the signal frequency. This process is called a "deuterium lock." Since NMR measurements, including quantitative NMR, tend to take relatively long time, deuterium lock is indispensable to obtain spectra of high resolution. If the sample solvent is not deuterated, deuterated solvent must be added.

論　　文
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# qNMRに基づく有機リン系農薬イソキサチオンオキソンの品質管理

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# Quality control of organophosphorus pesticide isoxathion oxon based on qNMR

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## Abstract

On the quantitative analysis of pesticide residues by LC/MS or GC/MS, the standard samples of pesticides are essential. But most of their purities are not traceable to the International System of Units (SI) and it results in degrading the reliability of analysis data. Therefore, the SI-traceable quality control of pesticide standard samples will be most important. We are developing quantitative nuclear magnetic resonance (qNMR) as one of simple quality control methods that is able to determine the purities or contents with SI traceability. We demonstrated that qNMR was used for the purity determination of two standard samples of isoxathion oxon (IXO), an organophosphorus pesticide. The purities of the two samples were certificated by the manufacture as 96.9 % and 98.9 % which were calculated from the peak area percentages using GC/FID. On the qNMR spectrum, IXO showed the proton signals in the range of δ 1.0-8.0 ppm, and the quantitation was performed by calculating the relative peak area ratios of selected proton signals of the target compound to the known purity and amount of the internal standard, hexadimethylsilane which was calibrated with SI-traceable diethyl phthalate. For this method no reference compound of IXO is needed. The purities of two IXO samples showed 75.4 % and 98.5 % by qNMR. The relative ratio of the two purities was equivalent to the ratio of IXO peak areas in the two samples observed by GC/MS. This result shows that qNMR does not only lead to SI-traceable purity, but it also will be a rapid and simple SI-traceable quality control method of any pesticides with overall analysis time of only 20 min.

Keywords：イソキサチオンオキソン、定量NMR、有機リン系農薬、品質管理
isoxathion oxon, qNMR, organophosphorus pesticide, quality control

## I　緒言

有機化合物の定量分析として、LCおよびGC等を用いた方法（クロマトグラフ法）が広く採用されている。クロマトグラフ法では、分析値の信頼性の確保のために測定対象物の検量線作成用標準品が不可欠である。しかし、分析対象と

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なる有機化合物は無限にあるため、すべての標準品の供給体制を整えることは現実的に不可能である。さらに、既に市販されている標準品の多くは各試薬メーカーが独自に純度を値付けしたものであり、国際単位系 (SI) に基づく計量トレーサビリティが確保されているものではない。また、標準品の安定性は物質毎に異なり、保存期間や保存状態によっては分解し純度が低下していく可能性もあり、たとえ同一の標準品を用いたとしても室間誤差を与えるなど、結果として、分析値の信頼性の低下を引き起こしていると考えられる。したがって、分析精度の更なる向上のために、有機化合物の純度を計量学的に正確に測定する方法が必要とされている。

SI に基づく計量学的な分析法を一次標準測定法といい、本法は一次標準直接法と一次標準比率法に分類される。一次標準直接法は、「物質量の基準となる他の化学物質を用いずに、自分自身で目的の化学物質の物質量を測れる方法（絶対測定法）」であり、電量分析法、重量分析法及び凝固点降下法がある。一方、一次標準比率法は、「物質量の基準となる別の化学物質を用い、それとの比較において目的の化学物質の物質量を測れる方法」であり、すでに実用化されているものに滴定法及び同位体希釈質量分析法がある。これらの方法は、一般に分析の迅速性に欠け、また分析できる物質の種類に制限がある。そこで我々は、簡便且つ応用範囲の広い分析法または校正法として、一次標準比率法の資格を原理的に有する核磁気共鳴に基づく定量分析法 (quantitative NMR (qNMR)) の開発を行っている[1]。qNMR は、純度値が明らかな他の化合物を基準物質（内標準）として測定対象の有機化合物の純度を求めることが可能な方法である。すなわち、$^1$H-NMR スペクトル上に観察される異なる化合物のシグナル強度の比は化合物のモル比に対応することから、一方の化合物の純度が明らかであれば、得られたモル比と溶液の調製値の関係から測定対象の化合物の純度（あるいは濃度）を決定できる。測定対象化合物の標準品を参照せずに純度値を決定できる点で従来法より優れている。

食品残留農薬のポジティブリスト制度[2]の導入により、国内外で流通する農薬が規制の対象となり、食品の安全性と直結する残留農薬試験の精度管理が要求されている。我々は、有機リン系農薬のチオノ型 (P=S) が環境中や浄水工程の間に塩素やオゾン等による酸化反応を受けて、より有害影響の強いオキソ型 (P=O) 反応物に変化し、これらの健康影響リスクが予想以上に高いことを報告した[3]。これら以外にも潜在的に健康影響リスクが高い残留農薬が存在する可能性が高いと予想されるので、食品の安全性の更なる確保のためには、分析対象となるすべての残留農薬の標準品の品質管理を通じた分析値の信頼性の向上が今後重要になってくると考えられる。

本研究では、qNMR の品質管理法への応用を目的に、我々が開発中の SI トレーサビリティを確保した qNMR を有機リン系農薬イソキサチオンオキソン (isoxathion oxon: IXO) の市販標準品の純度決定および品質評価に適用した。さらに、従来法と qNMR による結果を比較し、分析値の妥当性を検証するとともに、qNMR が従来法に代わる迅速且つ簡便な品質管理法として有効であり、計量学的にも従来法に比べ信頼性の高い結果を得たので報告する。

## II　研究方法

### 1. 試薬および試液

高純度ヘキサメチルジシラン (hexadimethyldisilane: HMD) は、和光純薬工業（株）製特注品、重アセトン (acetone-$d_6$) は、Isotec 製 (99.9 atom% D) を用いた。フタル酸ジエチル (diethyl phthalate: DEP) は、（独）産業技術総合研究所製の認証標準物質 (Certified Reference Material: CRM) (品番 NMIJ CRM 4022-b: 純度 99.74 ± 0.09 (mol/mol%)) を用いた。アセトン (acetone) は、和光純薬工業（株）製の残留農薬・PCB 試験用を用いた。イソキサチオンオキソン (isoxathion oxon: IXO) 標準品 2 ロット (Lot 1, 2) は、A 社製を用いた。なお、IXO 標準品 2 製品 (Lot 1, 2) の成績書に記載の情報を Table 1 に示した。

Teble 1.　Information of isoxathion oxon standards.[a)]

| Sample | Lot | Quality | Purity (%)[b)] | Melting point (℃) |
|---|---|---|---|---|
| Isoxathion oxon standard | 1 | Yellow-brown, crystalline powder | 96.9 | 49.5 |
| | 2 | White, crystalline powder | 98.9 | 51.7 |

a) The sample infomation is written in the certificates.
b) The purity means the area percentage of the main peak on GC/FID.

### 2. 装置

核磁気共鳴装置 (NMR)：オートサンプラー付き JNM-ECA600 (600 MHz)（日本電子（株）製）。qNMR のケミカルシフト値は、HMD (hexamethyldisilane) を基準シグナル (0 ppm) とし、δ 値を ppm 単位で表した。

ガスクロマトグラフ / 質量分析計 (GC/MS)：HP 6890 GC / 5973 MS (Hewlett Packard 製)。

### 3. qNMR 用標準液の調製および HMD の濃度校正

HMD 約 100 mg を精密に量り取り、acetone-$d_6$ 25 mL に定容した。この溶液を acetone-$d_6$ で 5 倍希釈したものを qNMR 用標準液とした。qNMR 用標準液中の HMD の濃度 817.7 ± 5.6 μg/mL (= 5.5865 ± 0.0388 mmol/L, n = 3, AV ± SD) を下記に従い、DEP により校正して求めた。すなわち、CRM の一つである DEP 約 10 mg を精密に量り取り、qNMR 用標準液 1.0 mL に溶解した。この溶液 0.6 mL を NMR 試験管 (5 mm φ × 200 mm, S-type (和光純薬工業 (株) 製)) に封入したものを HMD 濃度校正用試料溶液とした。この溶液を qNMR に付し、DEP の $CH_2 \times 2$ および HMD の $CH_3 \times 6$ に由来するシグナル面積、分子量、濃度等を式 (1) に代入し、qNMR 用標準液中の HMD の濃度を校正した。

$$W_{HMD} = \left( \frac{M_{HMD} \times I_{HMD}}{H_{HMD}} / \frac{M_{DEP} \times I_{DEP}}{H_{DEP} \times W_{DEP}} \right) \times \frac{P_{DEP}}{100} \quad \text{--- (1)}$$

ただし、$W_{HMD}$, $W_{DEP}$ = HMD および DEP の濃度 (mg/mL)、$M_{HMD}$, $M_{DEP}$ = HMD および DEP の分子量 (MW 146.38 および 222.24), $H_{HMD}$, $H_{DEP}$ = HMD の $CH_3$ × 6 および DEP の $CH_2$ × 2 のプロトン数、$I_{HMD}$, $I_{DEP}$ = HMD の $CH_3$ × 6 および DEP の $CH_2$ × 2 のシグナル面積, $P_{DEP}$ = DEP の純度 (99.74%)。

## 4. qNMR による IXO の純度測定

IXO 標準品 (Lot 1 および 2) を約 10 mg 精密に量り取り、予め調製した qNMR 用標準液 1.0 mL に溶解した。この溶液 0.6 mL を NMR 試験管に封入したものを試料溶液とした。この溶液を qNMR に付し、HMD のシグナル強度面積、IXO に由来するそれぞれの特定シグナルの相対面積、分子量、濃度等を式 (2) に代入し、IXO の純度を算出した。

$$P_{IXO} = \frac{I_{IXO} / H_{IXO}}{I_{HMD} / H_{HMD}} \times \frac{M_{IXO} \times W_{IXO}}{M_{HMD} / W_{HMD}} \times 100 \quad \text{--- (2)}$$

ただし、$W_{HMD}$, $W_{IXO}$ = HMD および IXO の濃度 (mg/mL)、$M_{HMD}$, $M_{IXO}$ = HMD および IXO の分子量 (MW 146.38 および 297.24), $I_{HMD}$, $I_{IXO}$ = HMD および IXO の特定基のシグナル強度面積, $H_{HMD}$, $H_{IXO}$ = HMD および IXO の特定基のプロトン数, $P_{IXO}$ = IXO の純度 (%)。

## 5. qNMR 測定条件および解析処理

qNMR 測定条件の基本情報は Table 2 に示した。qNMR データ解析には、得られた Free Induction Decay (FID) 信号データを定量解析ソフトウェア (日本電子 (株)、開発中) に導入して自動処理した。すなわち、このソフトウェア上で、qNMR データをフーリエ変換 (Window 関数 : function = exponential, BF = 0.10 Hz, zero filling = 1, T1 = T2 = 0%, T3 = 90%, T4 = 100%) および自動位相調整を行い、HMD および特定シグナルの積分範囲等を設定後、予め入力した HMD および IXO の濃度、分子量、特定基のプロトン数等の化合物情報から自動解析処理を行い、定量値 (純度 %) を式 (2) に従い算出した。

Table 2. Instruments and acquisition parameters.

| | |
|---|---|
| Spectrometer | ECA600 (JEOL) |
| Probe | 5 mm broadband autotune probe |
| Spectral width | - 5 - 15 ppm |
| Data points | 32000 |
| Auto filter | on (8 times) |
| Flip angle | 90° |
| Pulse delay | 60 s (>5*$T_1$) |
| Scan times | 8 |
| Sample spin | no spin |
| Probe temperature | 25℃ |
| Solvent | acetone-$d_6$ |
| qNMR reference material | hexamethyldisilane (HMD) |
| Primary standard material | diethyl phthalate (DEP) (NMIJ CRM4022-b) |

## 6. GC/MS 測定

IXO (Lot 1 および 2) を精密に量り取り、acetone に溶解し 10 ppm に正確に調製し、下記の条件の GC/MS に付し、保持時間 21.1 分に観察された IXO のピーク面積を求めた。

GC/MS 条件 : カラム, DB-5 MS fused-silica capillary column (0.25 mm i.d. × 30 m, 0.25 μm (Agilent 製)); カラム温度, 70℃ (2 min) → 15℃ /min → 190℃ → 1.5℃ /min → 220℃ → 10℃ /min → 290℃ (3 min); キャリアガス, He; ガス流量, 1.2 mL/min; 注入量, 1.0 μL; 注入法, Pulsed splitless; 注入口温度, 250℃ ; イオン源温度, 280℃ ; イオン化法, EI; イオン化電圧, 70 eV; スキャン範囲, *m/z* 45 ～ 550; SIM モニターイオン, *m/z* 161 (base ion of IXO)

# Ⅲ 結果および考察

## 1. qNMR の原理と測定条件

核磁気共鳴 (NMR) 法は有機化合物の分子構造を決定するための代表的な定性分析法の一つであり、様々な分野で利用されている。qNMR による定量分析は、$^1$H-NMR で得られる化学シフトの異なる各プロトンシグナル面積比が各置換基に由来する水素原子の数の比を表す特性を利用した方法である。$^1$H-NMR において、シグナル面積比は分子中の個々の置換基上の水素原子数の比に対応する。さらに 2 つのシグナルが異なる化合物 (A, B) に由来する場合には個々のシグナル面積と化合物の濃度は関係式 (3) で表すことができる。

$$\frac{I_A}{I_B} = \frac{H_A m_A}{H_B m_B} = \frac{H_A W_A / M_A}{H_B W_B / M_B} \quad \text{--- (3)}$$

$$P_{sample} = \frac{I_{sample} / H_{sample}}{I_{std} / H_{std}} \times \frac{M_{sample} \times W_{sample}}{M_{std} / W_{std}} \times P_{std} \quad \text{--- (4)}$$

ただし、I = シグナル面積、H = 特定基のプロトン数、m = モル濃度、W = 重量、M = 分子量、P = 純度 %、sample = 試料、std = 基準物質。

よって、2 つの化合物の内、一方の化合物として純度が明らかな基準物質 (std) を用いれば、モル比と溶液の調製値の関係から測定対象の化合物の含量 (純度) を決定できる関係式 (4) が成り立つ。qNMR による定量分析は、関係式 (4) を利用し、純度あるいは濃度が既知の基準物質を予め加えた溶液中で測定対象の化合物の $^1$H-NMR 測定を行い、得られたスペクトル上に観察される基準物質と測定対象の化合物に由来するシグナル面積、水素数および濃度比から定量値を算出する方法である。関係式 (4) からわかるように、測定対象化合物の標準品を必要としないことが qNMR の特徴である。

現在、一般的に利用されている $^1$H-NMR 測定初期条件では、プロトンシグナル面積は整数値として得られれば化合物中の置換基の水素数が推測できるため、得られるシグナル面積の定量性を犠牲にして感度や S/N を優先した条件に設定されている。一方、qNMR による定量分析では、各シグナル

面積の定量性を厳密に確保することが不可欠であるため、Pauli および Saito らの報告[4,5]を参考に Table 2 に示すように測定条件を設定した。すなわち、シグナル面積の定量性の確保には、パルスにより励起された磁化が次にパルスを照射されるまでに十分緩和していなければならないため、パルス遅延時間をシグナルのスピン - 格子緩和時間 ($T_1$) の 5 倍以上に設定した。更に、ラジオ波 (RF) パルスが観測中心から離れるほど強度が低下し、観測幅の両端では定量誤差を与えるため、測定対象のスペクトル範囲が観測幅の 80% 以内になるように −5 ppm ～ 15 ppm を測定範囲とした。また、本研究では、シム調整を厳密に行い、良好なシグナル形状および S/N を得た上で測定し、得られた FID 信号データを定量解析ソフトウェア（日本電子（株）開発中）に導入して、同一処理条件下で自動処理し、一元的に定量値を算出した。qNMR による 1 測定当たりの所要時間は約 20 分であり、且つ得られた測定値は高い再現性を示し、不確かさは概ね 1.0% 以内であった。

## 2. qNMR 基準物質の設定と SI トレーサビリティの確保

qNMR 基準物質としては、*p*- トルエンスルホン酸[6]、フタル酸水素カリウム[7]、ジメチルスルホン[8]、安息香酸[9] などが既に報告されているが、これらのシグナルが測定対象の化合物のシグナルと重なってしまった場合には基準物質として使えない。よって、qNMR 基準物質を選択する場合には、測定対象化合物のシグナルを予測し、シグナルが重ならない物質を事前に選択して使用する必要があるばかりか、得られたスペクトルは基準物質のシグナルと混ざった状態で得られるため、測定対象の化合物の構造解析と定量分析を同時に行おうとした場合、利便性が悪いという欠点がある。そこで、qNMR 基準物質としてヘキサメチルジシラン (HMD) を用いることとした。HMD は、沸点 112-113℃であり、高温測定用の NMR 基準物質として用いられるものである。HMD は、通常の $^1$H-NMR で基準物質として用いられるテトラメチルシラン (teramethylsilane: TMS) と同様に 0 ppm にシグナルを示すため、得られた qNMR スペクトルは、通常の $^1$H-NMR と同等であり、一般的な測定対象化合物のシグナルと重ならない。そのうえ、$^{13}$C-NMR や 2D-NMR による構造解析用データの測定時にも障害となるシグナルを示さない。低沸点の TMS と異なり秤量が可能であり、揮発性がやや低い点でも qNMR の基準物質として適している。

しかしながら、現在、SI にトレーサブルな HMD が流通していないため、厳密な純度値あるいは濃度値が要求される qNMR 基準物質としてそのまま用いることができない。そこで、qNMR による分析値の SI トレーサビリティの確保のため、Fig. 1 に示すように計量学的に妥当な手順によって値付けされ、計量学的トレーサビリティーが証明された CRM の一つであるフタル酸ジエチル (diethyl phtalate: DEP) を一次標準として用い、qNMR 標準液中の HMD の濃度を校正した後に、HMD を二次標準として測定対象化合物の qNMR 測定を行う 2 段階の方式を用いることとした。すなわち、qNMR 標準液に DEP を溶解し、DEP の (-$OCH_2$-) × 2 に由来するシグナル (4.27 ppm) に対する qNMR 標準液中の HMD の ($CH_3$-) × 6 に由来するシグナル面積比を測定し、関係式 (1) より HMD の濃度 (817.7 ± 5.6 μg/mL, n = 3) を校正した。このようにして、HMD を qNMR 基準物質として用いた際の測定対象化合物の定量値の SI トレーサビリティは、CRM の DEP を介して実現した。

## 3. qNMR による IXO の品質評価

分析対象試料として残留農薬試験用 IXO 標準品 2 ロット (Lot 1, 2) を用い、添付の成績書に記載の情報を Table 1 に示した。Lot 1 は、黄褐色結晶性粉末で、融点 49.5℃、GC/FID 分析のピーク面積百分率より求めた純度値は 96.9% であ

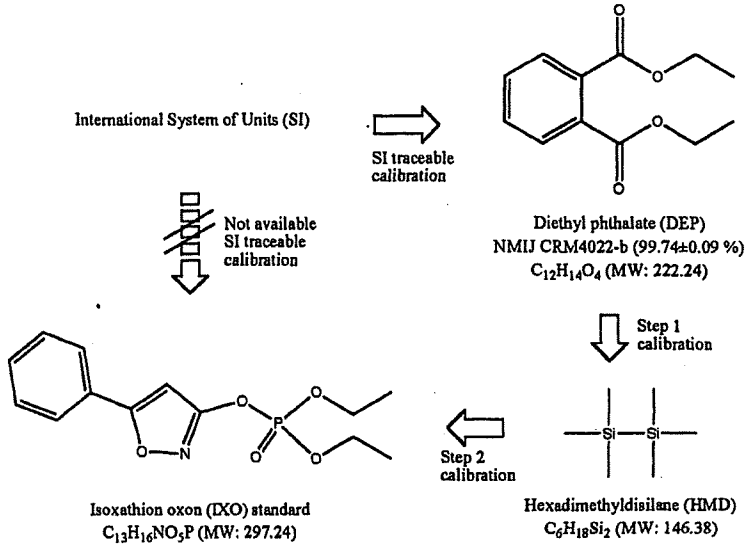


Fig. 1.　Strategy of SI-traceable quality control based on qNMR.

り、一方、Lot 2 は白色結晶性粉末で、融点 51.7℃、純度値 98.9% と値付けられており、Lot 2 の方がその性状からも純度が高いと予想されるものであった。両者を qNMR 標準液にそれぞれ溶解し、qNMR 測定を行い、得られたスペクトルを Fig. 2 に示した。重溶媒には IXO の溶解性と溶媒シグナルが測定対象のシグナルと重ならないことを考慮して acetone-$d_6$ を用い、各プロトンシグナルの帰属を a ～ e で示した。その結果、Lot 2 では、IXO に由来する a ～ e のシグナルと基準物質の HMD に由来するシグナル以外に、微量の不純物に由来すると思われる小さいシグナル (2.72 ppm) のみ観察されたのに対し、Lot 1 では IXO のシグナル以外に分解物または製造原料に由来すると思われるシグナル (1.20, 3.94, 6.40, 7.44, 7.75 ppm) が観察され、明らかに Lot 1 の純度が Lot 2 に対して低いことが予想された。次に、qNMR スペクトル上に観察された基準物質 HMD および IXO に由来する各シグナル面積、水素数、濃度等を関係式 (2) に代入し、それぞれの純度値を算出した (Table 3)。その結果、Lot 2 は、c を定量用シグナルとして用いた場合、96.3 ± 0.2% とやや低い純度値を算出したが、その他 a, b, d, e を用いた場合、98.6 ± 1.1 ～ 99.4 ± 0.6% の純度値を与え、a ～ e の平均値は 98.5 ± 1.3% であった。この値は、Lot 2 に添付の成績書に記載の GC/FID 面積百分率による純度値 98.9% とほぼ等しい。一方、Lot 1 は、a ～ e を定量用シグナルとして用いた場合、75.1 ± 0.9 ～ 75.8 ± 0.9% の純度値を与え、その平均値は 75.4 ± 0.2% であった。この値は、Lot 1 に添付の成績書に記載の GC/FID 面積百分率による純度値 96.9% と大きな開きがあった。GC/FID 分析のピーク面積百分率による純度測定は、不揮発性成分等の不純物が含有されていないことを前提としている。さらに、あらゆる不純物のレスポンスファクターが主成分と同じであると仮定して、クロマトグラム上に観察されるすべての成分のピーク面積の総和に対する測定対象化合物のピーク面積百分率を求め、純度値とするとしており、元素組成比の異なる不純物を含む混合物の純度値は原理的に正確に求められるものではない。Lot 1 の qNMR スペクトル上には不純物のシグナルがはっきりと観察されていることを考慮すると、Lot 1 に添付の成績書に記載されていた純度値を質量 % 純度値として扱うことは不適切であると考えられた。

なお、別に他の有機リン系農薬として、ダイアジノン、ダイアジノンオキソン、フェンチオン (MPP)、フェンチオンスルホキシド、クロロピリホス、クロロピリホスオキソンおよびイソキサチオン標準品についても qNMR による純度検定を同様な方法で行ったが、不純物に由来するシグナルは観察されず、それぞれの成績書記載の純度値と総じてほぼ等しい値を与え (データ未収載)、これらの記載の純度値が正しいことが確認できた。

Table 3. Summary of the determined purity by qNMR and the relationship between he value and the peak area ratio measured by GC/MS.

| | | Isoxathion oxon | | | |
|---|---|---|---|---|---|
| | | Lot 1 | | Lot 2 | |
| qNMR | | | | | |
| Target signal (ppm) | | Purity (%) | SD (%) | Purity (%) | SD (%) |
| a | 7.85 | 75.3 | 0.8 | 99.0 | 0.3 |
| b | 7.49 | 75.1 | 0.9 | 99.3 | 0.5 |
| c | 6.81 | 75.5 | 0.7 | 96.3 | 0.2 |
| d | 4.25 | 75.8 | 0.9 | 99.4 | 0.6 |
| e | 1.32 | 75.4 | 0.9 | 98.6 | 1.1 |
| AV | | 75.4 | 0.2 | 98.5 | 1.3 |
| GC/MS | | | | | |
| Area ratio[a)] | | 76.4 (75.3) | | 100 (98.5) | |

a) The area ratio was calculated from the absolute peak area values of lot 1 and 2, which were 459744 and 602045, respectively.
AV = average, SD = standard deviation.

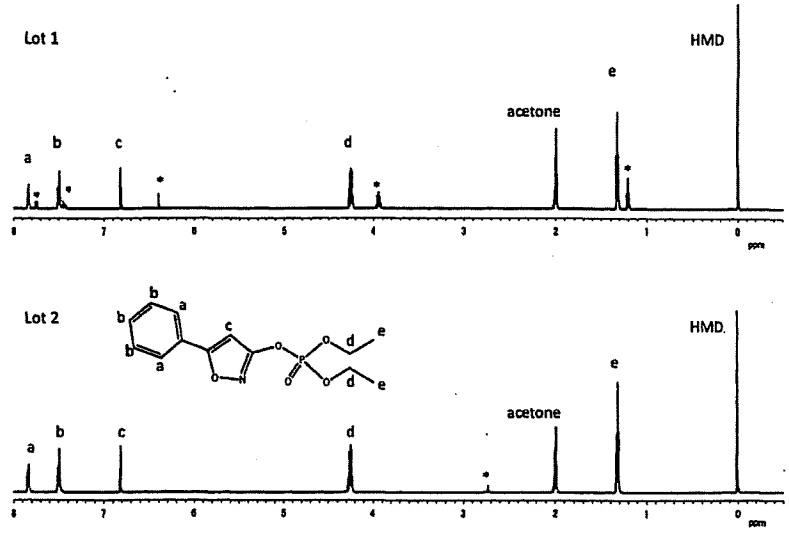


Fig. 2. qNMR spectra of isoxathion oxon standards (Lot 1 and 2).
* : signals of minor compound in the standards.

### 4. GC/MS による IXO の測定

qNMR による IXO の純度測定の結果、Lot 1 および Lot 2 の純度がそれぞれ平均 75.4% および 98.5% と算出された。この結果の妥当性を検証するために、GC/MS により両者のピーク面積値を測定し、結果を比較した。Fig. 3 には、IXO のベースイオン *m/z* 161 における SIM 測定による GC/MS クロマトグラムを示した。Lot 1 および Lot 2 は共に保持時間 21.1 分に IXO のピークを示し、Lot 2 の IXO のピーク面積が 602045 であるのに対して Lot 1 は 459744 であった。同一化合物の同条件における GC/MS のピーク面積の比は絶対量の比に等しいことから、Lot 1 と Lot 2 の相対面積比を求めたところ、Lot 2 を 100% としたとき Lot 1 が 76.4% となった。さらに qNMR で求めた Lot 2 の純度値 98.5% で補正したところ、Lot 1 の純度値は 75.3% となり、qNMR で求めた値とほぼ等しい結果となった。以上のことから、qNMR で求めた Lot 1 および Lot 2 の IXO の純度値が正しいことが証明された。

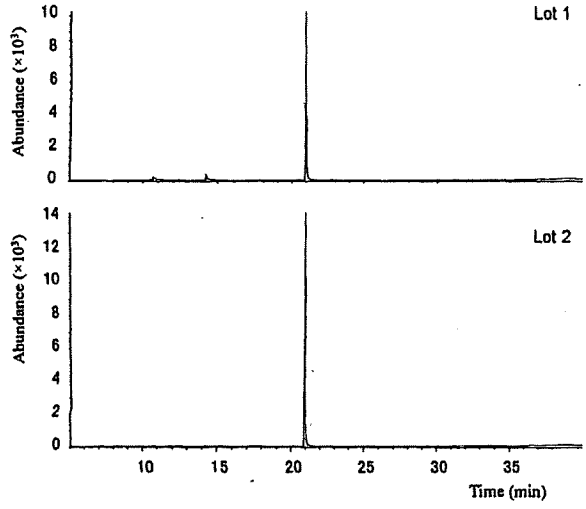


Fig. 3. GC/MS profiles of isoxathion oxon stadards Lot 1 and 2. The profiles were recorded by SIM mode at base ion *m/z* 161 of isoxathion oxon.

## Ⅳ 結論

残留農薬標準品の内、有機リン系農薬イソキサチオンオキソン標準品の品質管理法としての qNMR の有効性を検証した。qNMR 基準物質としてヘキサメチルジシラン (HMD) を採用し、認証標準物質フタル酸ジエチル (DEP) を一次標準として用いて濃度校正することによって分析値の SI トレーサビリティを確保しつつ、qNMR の利便性を拡張した。qNMR は、計量学的に正確な値を求めることが可能な方法であるだけでなく、測定対象と同一の標準品を必要としない点で従来法とは全く異なった方法である。このことを利用して従来法では困難である残留農薬イソキサチオンオキソン標準品の純度検定が簡便且つ迅速に行えることを示した。qNMR スペクトルデータはすべてのシグナルが正確な定量性を持つため、品質管理に有用な参照スペクトルとなり得る。現在、qNMR は、残留農薬、食品添加物、医薬品、健康食品および天然物等あらゆる有機化合物の定量法として、あるいは品質評価法として、次世代の信頼性の高い分析法として発展すると思われ、我々は、分析精度の更なる向上、応用範囲の拡充を目指して開発を行っているところである[1]。

## Ⅴ 謝辞

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「報　文」

# ニュージーランドにおける水道の水質管理制度

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**要旨**：ニュージーランドにおける水道の水質管理制度について主に政府及び関係機関のホームページ上で公開されている情報を基に整理した。ニュージーランド国政府は1993年に健康局を保健省に改組して水道事業の監督強化に取り組むとともに、水道事業の登録、水道事業者の格付け制度、ニュージーランド国版水安全計画（Public Health Risk Management Plans: PHRMP）などの様々な水質管理に関連する制度を創設した。さらに、2008年に保健（飲料水）改正法2007を施行し、以前に創設した制度の導入、水質基準の遵守などを義務化した。また、ニュージーランド国環境省は水道水源の水質保全を図るために水道水源のための環境基準制度を創設するなど、国の関係機関が連携しながら、現在及び将来の水道水質の安全性確保に向けた取り組みを強化している。

**キーワード**：ニュージーランド、水安全計画、水質管理制度
**分類項目**：水道行政（010201）、環境行政（010204）、水質管理一般（120101）、海外事情一般（140801）

## 1. はじめに

「飲料水の水質リスク管理に関する統合的研究」では水道水質基準の逐次改正等に資する情報の収集と水道システム全体のリスク管理のあり方に関する提言を目的として、7分科会を設置して研究を行っている。このうち、水質管理分科会では水道水の安全性を確保するための集水域管理及び水質管理について、ニュージーランドを含む約10カ国を対象とした調査を実施し、いくつかの注目すべき制度に関する情報を収集、整理した。

ニュージーランドでは、政府保健省（Ministry of Health）が、水道水質の改善による国民の健康の保護を目的とした保健（飲料水）法の改正を2007年に提案した。保健省は、1980年代からのニュージーランド国中央政府の機構改革及び機構の簡素化に伴って水道事業を監督する仕組みが混乱したため管理が十分にはできていない状況であり、当時の健康局（Department of Health）は供給される水道水質についてほとんど情報を持ち合わせていなかったことが法改正の背景[1)]にあると説明している。当時の実情として、45～50％の水道において塩素注入に関する監視が適切でなかったこと、28％の水道では配水区域における細菌検査を実施していなかったこと、細菌検査を配水区域内で実施している水道においても40％はその頻度が4回／年でしか行われていなかったことなどを挙げている。このような状況を改善するため、ニュージーランド国政府は1993年に水道事業を監督していた健康局を保健省に改組し、水道事業の監督業務の強化に取り組みだした。法の改正はその一環であり、保健（飲料水）法2007（Health（Drinking Water）Amendment Act 2007）は2008年から施行されることになった。また、保健省は水道事業者の格付け制度、ニュージーランド国版水安全計画（Public Health Risk Management Plans: PHRMP）などの様々な水質管理に関連する制度を創設している。ここでは、近年、強化されつつある同国の水質管理の仕組みについて報告する。

## 2. 調査項目と調査方法

ニュージーランド国の概要、水道の法律・制度、水質基準、消毒・残留塩素の保持、水道事業体の格付け制度、情報提供の制度と内容、水安全計画などを調査した。主要な情報はニュージーランド国政府保健省、環境省（Ministry for the Environment）及び環境科学研究所（Environmental Science Research Institute Ltd.）のホームページから入手

した。

## 3. ニュージーランド及び水道の概要

### (1) ニュージーランドの概要と水道の創設

ニュージーランドの人口は423万人、国土面積は27万534平方キロメートル、降水量は年間640mm～1,500mm 程度である[2]。首都のウェリントン市では最初の公共用水道が1874年に完成しており、オークランド市においてもほぼ同じごろに公共用水道が建設されている。水道が建設された1800年代後半は欧州からの移民が増加した時期であり、ニュージーランド独立の30年以上前になる。

### (2) 水道事業の監督[3]

1) 地区健康局（District Health Board: DHB）

保健省は水道に関する法律や水質基準等の制定とその確実な施行を担っており、水道事業者を直接監督する役割は地域ごとに設置された21のDHB が担当している。DHB は地域の衛生状態の改善と促進、プライマリ・ケア、セカンダリーケア、障害者へのサービス提供の業務に加え、水道分野では適切な水道水質が維持されていることを確認する役割が与えられている。水道水質の異常など緊急の場合に給水停止を命じる権限を有している。

2) 水道水評価官[4,7]

（Drinking-Water Assessor: DWA）

従来、DHB に配属された健康保護官（Health Protection Officer）により行われてきた水道の監督は、保健（飲料水）改正法2007の成立により、DWA が担うことになった。DWA は同法の規定に基づいて任命された機関、または機関に雇用された個人もしくは契約者で、国家資格に位置付けられている過程を終了した後、ISO17020の認定を取得している機関により DWA として認定される。DWA は水道事業者に対する立ち入りの権限、記録の閲覧と複写、情報提供の要求、査察・調査・検査の実施などの権限が付与される。

### (3) 水道事業の登録[5]

保健省では2005年 6 月現在1,953の水道が登録されているものの、保健（飲料水）改正法2007の成立以前は登録の義務がなかったため、未登録の水道はさらに1,000近くあると推計している。今後、すべての水道が登録することになるため、数年後には正確な水道の数が明らかになる。

### (4) 水道の定義と水道事業の種類[6]

保健（飲料水）改正法2007は水道（Drinking-water Supply）を「飲料水を給水点（給水点は含まない）まで供給する公有または私有の常設及び臨時のシステムで、配水管網、井戸、貯水池、給水タンク車を条件に関係なく含む。」と定義している。また、保健（飲料水）改正法2007が適用される水道の規模を、給水人口が25人以上で年間の給水日数が60日以上または、年間の給水人口と給水日数の積が6,000人・日以上の水道としており、水道管または給水タンク車による供給方法を問わず、この条件をみたす給水システムが水道として取り扱われる。比較的規模の大きい水道はDistrict、City Council などの地方自治体により運営されており、小規模な水道として公共機関以外が設置した水道及び学校内の水道などが含まれる。同法に基づく水道の分類を表-1に示した。

表-1　水道事業者の分類（保健（飲料水）改正法2007）

| 水道の種類 | 主な要件 |
|---|---|
| 大規模水道事業者（Large drinking-water suppliers） | 給水人口が10,001人以上で年間給水日数が60日以上 |
| 中規模水道事業者（Medium drinking-water suppliers） | 給水人口が5,001人～10,000人で年間給水日数が60日以上 |
| 小規模水道事業体（Minor drinking-water suppliers） | 給水人口が501人～5,000人で年間給水日数が60日以上 |
| 極小規模水道事業体（Small drinking-water suppliers） | 給水人口が101人～500人で年間給水日数が60日以上 |
| 近隣水道事業体（Neighborhood drinking-water suppliers） | 給水人口が25人～100人で年間給水日数が60日以上<br>または年間の給水人口と給水日数の積が6000・人・日以上 |
| 農村水道事業体（Rural Agricultural drinking-water suppliers） | 上記５つの水道事業者のうちで、給水量の75%以上が農業に使用されているもの |

(5) 地方自治体と水道事業の運営

地方自治体には広域的な組織（Regional Council）と地域的な組織（Territorial Authority）がある。地域的な組織は73あり、そのうちの16は人口５万人以上の City で、残りは District である。地域自治体は上下水道、雨水管理、地域災害対策、地域交通計画、建築規制、土地開発規制などの事務を行っている。一方、広域自治体は環境保全、海岸・河川管理、大規模災害対策、広域的な交通計画など国土管理に関する広域的事務を行っている

地域自治体が運営する水道の数は全体の20％程度であるが、全人口の約70％に給水している。水道の課題として、公衆衛生施策の確立が各自治体に求められているが、複数の水道では経済的、財政的な問題を抱えているとされている。

4. 水道に関する法律及び制度の概要[7)]

(1) 水道に関する法律

ニュージーランドでは、水源水質は環境省が所管する水道水源のための環境基準（National Environmental Standard for Sources of Human Drinking Water: NES)、浄水場及び配水システムは前述の保健（飲料水）改正法、貯水槽等の給水システムはビル・住宅局（Department of Building and Housing）が所管するビル法（Building Act）により管理している。

(2) 保健（飲料水）改正法2007[6)]

保健（飲料水）改正法2007は、適用は任意とされてきた様々な水質管理制度を義務化するために改正された。保健省によれば、それぞれの制度を有機的に連携させた総合的な管理システムとして運用することが可能になり、水道の関係者、住民や報道機関、水道事業者及び政府、自治体の担当者が水道事業に対して相互に最大の支援が行えるようになったとしている。義務化された主な内容は次のとおりである。

①水質基準の遵守と基準に適合するために、実用的かつ必要な対策の導入
②水道事業者に対する水安全計画（PHRMP）の導入
③水源から給水栓までの汚染防止に有効かつ合理的な対策の実施
④水道水評価官（DWA）制度の実施
⑤法律の遵守に関する記録の保管と公表
⑥緊急時における適切な対応
⑦罰則の導入による法律遵守の改善

法律の施行以前においてこれらの制度は義務化されておらず、水道事業者の自主的な努力、申請などに委ねられていた。

(3) 小規模事業体への技術、財政支援制度[8)]

保健（飲料水）改正法2007の成立に伴い水質基準の遵守が義務化された。保健省は保健（飲料水）改正法の成立を見越し、水質基準の遵守を担保するための措置として2005年に小規模事業体に対する技術支援プログラム（Technical Assistance Programme: TAP）及び財政支援プログラム（Capital Assistance Programme: CAP）を設けた。TAP は給水人口が5,000人以下の水道事業体が費用を必要とせず利用することが可能で、後述する水安全計画の策定支援に焦点を置いており、水道施設の効率的、効果的な運転支援が行えるとしている。CAP は安全な水道水の供給に必要な設備の設置に必要な資金の提供を行うもので、まず TAP を適用して技術的な改善点を特定することが求められている。

(4) 水質管理に関する重要な制度

ニュージーランドにおける水質管理の重要な制度の概要を以下に示した。

①水道水の水質基準[9)]（Drinking Water Standards for New Zealand 2005（Revised 2008））

1984年に制定され、水質基準の項目と最大許容値（Maximum Acceptable Value）及び水質基準の適合基準などが定められている。（６章参照）

②水道事業体の格付け制度[10)]（Public Health Grading of Drinking Water Supplies）

格付け制度の目的は水道事業体の安全で良質な水道水の安定供給能力を公表することとされており、格付けの評価に当たっては公平で正確に行われていることが第三者機関により確認されるシステムが確立されている。（８章参照）

③水道情報提供サービス[11)]（National Drinking-Water Information System: WINZ）

WINZ は様々な水道水質に関する情報を収集するネットワークシステムであり、水道事業の

特徴、各水道の格付け結果、水質基準の達成状況など水質管理に必要な情報が収集されている。（10章参照）

④水安全計画[12]（Public Health Risk Management Plans：PHRMP）

WHO 飲料水質ガイドラインの第4章に示されている水安全計画と同じもので、リスク評価に基づく管理計画を策定し実施することが求められている。（9章参照）

⑤水質統計[13]（Annual Report on the Microbiological and Chemical Quality of Drinking-Water Supplies in New Zealand）（10章参照）

化学物質及び微生物の水質検査結果の統計で、毎年とりまとめられている。

⑥水質管理指針[14]（Guidelines for Drinking-Water Quality Management in New Zealand）

水質基準を満足させるための技術的な指針。我が国では日本水道協会が発行している水道施設設計指針、水道施設維持管理指針に相当する。

## 5. 水道の水源水質保全制度[15]

### (1) 導入の経緯

ニュージーランド国環境省は水道水源域の水質保全を目的とした環境基準を2007年に公布し、広域的な自治体に対して地域的な計画を策定する際に、水道水源を保全する考えを盛りこむよう求めている。環境基準の根拠法は水資源管理法（Resource Management Act 1991）32条であり、下流部の水道水質を守るために上流部の活動を規制する妥当性について、保健（飲料水）改正法2007が水道事業体に対して水質基準を満足するために実際的かつ必要な対策を導入することを求めていることも根拠としている。保健省は同法が導入された背景として、国内16の広域的な自治体のうち、水道水源に対して包括的な保護の規定を持っているのは3つにすぎず、NES を水道水の安全性を確保するためのマルチバリアのひとつとして位置づけたとしている。対象は、水道水源になっている表流水、湖水、地下水で、同法は水源水質を保護するための手順を定めている。

### (2) 制度の概要

NES は水道水源を保全するために実効的な対応を可能にしている。水道水源の上流部で認可されている排水、利水、ダム、水の流れの変更などが原因で水道の安全性に悪影響を与えている可能性がある場合、水源の水質に影響する排水の禁止など、水道水質に影響する行為の許可を取り消すことができる。また、地域計画において許可された活動が、既存の浄水処理で造りだされる水道水の安全性に悪影響を及ぼさないこと確実にするよう求めている。さらに、化学物質の漏出事故など、下流部の水質に悪影響を及ぼす可能性があるような水質事故が発生した場合、下流の水道事業者に対する通報など、原因者が行うべき行為を予め設定しておくよう定めている。

### (3) 広域的な自治体の役割

広域的な自治体が水源水質に影響するような行為の認可のための規則を導入する場合に考慮すべき事項が定められている。まず、水道水源の性質及び流域の特性を考慮した上で認可する行為のアセスメントを行うことが定められている。また、認可の条件を設定すること及び認可した行為が既存の方法で処理された水道水の安全性や水道水としての性状を損ねないことを確認するよう定めている。この内容は地方計画が新たに策定される場合や修正される場合に適用される。NES は水道水源の保護に不十分であると地域的な自治体が考える場合は、水資源管理法を根拠としてさらに厳しい規則を導入することを可能としている。

## 6. ニュージーランドにおける水道水の水質基準[9]

### (1) 水質基準の全体構成及びその概要

#### 1) 全体の構成と概要

水質基準には、最大許容値（Maximum Acceptable Value：MAV）と水質基準の適合基準（Compliance Criteria）が示されている。毒性は、ほぼ WHO 飲料水質ガイドラインに沿った評価を行って MAV を設定している。適合基準は複雑で、水道の様々な条件によって基準が異なっており、水質項目のカテゴリーごとに詳細に定められている。

水質基準項目として微生物が3項目、化学物質が116項目、放射性物質が3項目挙げられている。一覧を表-2に示した。そのほか、遵守義務のない34の外観的（Aesthetic）項目とその指針値が示さ