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DEVELOPMENT OF A CERTIFIED REFERENCE MATERIAL FOR THE ANALYSIS OF NICOTINAMIDE IN MULTIVITAMIN

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Abstract: A multivitamin certified reference material (CRM) was developed for the analysis of nicotinamide. The certification value was assigned by ID-LC/MS as primary method for nicotinamide. The stability monitoring was conducted periodically, and the stability monitoring results agree with the certified value within their uncertainties.

Keywords: ID-LC/MS, nicotinamide, multivitamin, CRM

1. INTRODUCTION

Multivitamin formulations are the most widely consumed dietary supplements in the marketplace. The composition of multivitamin formulations must be labeled on the products to manage the appropriate intake. Controlling the quality of the products depends on reliable analytical measurements. Development of well-characterized CRM will support to validate or periodically control the quality of analytical measurement for testing laboratories. Our laboratory, the National Metrology Institute of Korea, developed a multivitamin CRM (KRISS CRM #108-10-010) and nicotinamide was certified by isotope dilution mass spectrometry (IDMS) method [1] up to this time. Other representative vitamins (folic acid, riboflavin, thiamin, etc) in this CRM will be certified according to plan. This article describes the certification results and the stability monitoring results of nicotinamide in this CRM.

2. EXPERIMENTS

CRM Production: KRISS CRM #108-10-010 (batch number 100628) "Multivitamin Powder for the Analysis of Nicotinamide" was prepared based on the procedures maintained in our laboratory. Raw material contains mainly nicotinamide as a niacin source according to the label on the product. Multivitamin (25 Bottles, 90 tablets/bottle) was obtained from a local market. The raw material was pulverized, and sieved to select particle size under 100 μm. The material was then homogenized for 10 hours of V-mixing. The material was bottled into 20 mL amber bottles in 10 g per unit. The bottles were purged with argon gas and tightly sealed with Teflon lined caps. A total of 200 units were prepared and stored at a -20 ^{o}C deep-freezer.

Value Assignment and Homogeneity Test: The certification of nicotinamide in multivitamin CRM was carried by ID-LC/MS method [1]. Following the in-house protocol for value assignment and homogeneity test, 10 bottles with even intervals of bottling sequence were selected. One subsample (0.1 g) from each bottle was analyzed, and the mean of 10 measurement results was assigned as the certified value. Between-bottle homogeneity of the analyte was assessed by the standard deviation among bottles (SD_{bb}).

Uncertainty Evaluation: Details for evaluating uncertainty of the certified value with this type of certification scheme were described in our other paper [2, 3] and brief description is given here.

$$u(C_{cert}) = \sqrt{u_{\text{char,sys}}^2 + SD_{\text{bb}}^2}$$

Where $u_{\text{char,sys}}$ is the combined uncertainty of all uncertainty sources that give same systematic effects to the measurement value of all bottles. SD_{bb} is standard deviation between bottles, and it includes all uncertainty sources ($u_{\text{char,random}}$) that cause random variation of multiple measurement results.

Stability Monitoring: The assigned value of CRM was periodically monitored for the material stored at -20 ^{o}C. The same analytical methods used for the initial certification have been used for the stability monitoring.

3. RESULTS AND CONCLUSION

Certification of nicotinamide in multivitamin was accomplished along with 1 year stability monitoring. Figure 1 shows the measurement results of 10 bottles on nicotinamide in the CRM. Between-bottle homogeneity for nicotinamide is 2.3 % expressed as among-bottle relative standard deviation. Table 1 listed the final certified value with expanded uncertainty at 95 % level of confidence.

Table 1. Certified value of multivitamin CRM (KRISS CRM #108-10-010)

Compound	Assigned Value (g/kg)	Exp. Uncertainty (g/kg)
Nicotinamide	19.9	1.05

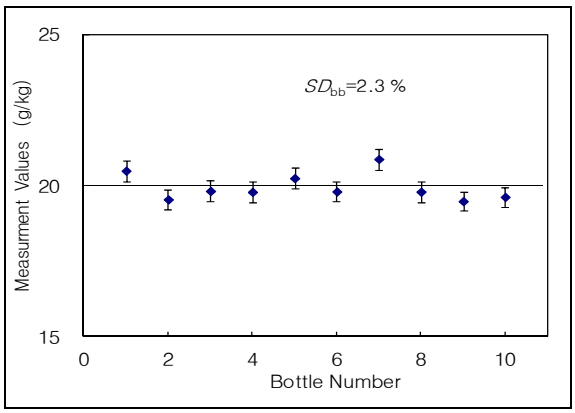

Figure 1. Homogeneity test result of nicotinamide in multivitamin CRM (KRISS CRM #108-10-010). RSD_{bb} is the relative standard deviation of measurement values among bottles. Error bars are expanded measurement uncertainties with 95 % confidence levels

After the certification of the CRM, stability monitoring has been conducted by the analytical method used for the certification of the CRM. This CRM has been stored at -20 ^{o}C, the stability monitoring was carried out after 1, 2, 12 months of the certification. The stability monitoring results were shown in Figure 3, and agree with the certified value within their uncertainties.

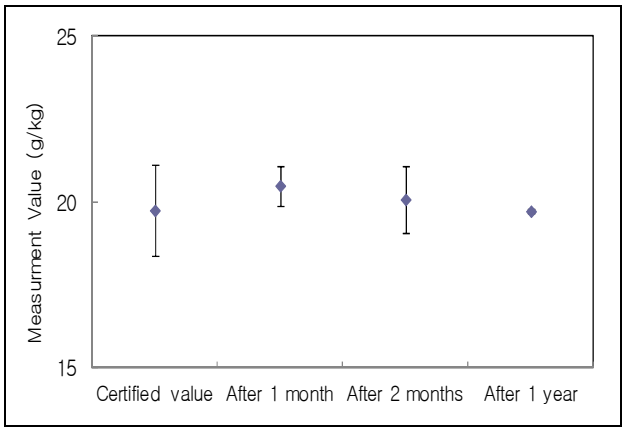

Figure 3. Stability monitoring results of nicotinamide in the multivitamin CRM (KRISS CRM #108-02-001) stored at -20 ^{o}C

4. CONCLUSION AND FURTHER WORK

A multivitamin CRM for the analysis of nicotinamide was developed. The certification and stability monitoring were done by an ID-LC/MS method. We plan to certify other vitamins as related analytical methods are developed and established in our laboratories.

5. REFERENCES

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