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Interlaboratory analytical comparison of fatty acid concentrations in serum or plasma☆

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ABSTRACT

Background: There are a large number of clinical studies focusing on the measurement of individual fatty acids in serum or plasma; however, few studies have focused on the interlaboratory comparisons of these measurements. The National Institutes of Standards and Technology (NIST), in collaboration with the National Institutes of Health Office of Dietary Supplements (NIH-ODS) and the Centers for Disease Control and Prevention (CDC), has initiated a quality assurance program for assessing and improving the comparability of individual fatty acid measurements in serum and plasma.
Methods: This is a performance-based study so participants are encouraged to use their laboratory's methods for the quantification of the individual fatty acids that they typically measure in the unknown serum or plasma samples along with a control material. The control materials used to date are SRM 1950 Metabolites in Human Plasma and SRM 2378 Fatty Acids in Frozen Human Serum.
Results: To date, two studies of the Fatty Acid Quality Assurance Program (FAQAP) have been completed with 11 and 14 participants, respectively. The agreement among the laboratories for individual fatty acids was within 20% for 70% of the data submitted. Laboratories were also requested to run triplicate analyses for each unknown sample. The precision of the individual laboratory data was generally good, with relative standard deviations <20%.
Conclusions: The results from the first two exercises indicate the need for additional assessment of the comparability among laboratories doing these measurements. Future studies will be conducted with the goals of increasing the number of participating laboratories, increasing awareness of the need to use control materials, and improving the comparability among laboratories.

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1. Introduction

The measurement of individual fatty acids, hydrolyzed from lipids, as opposed to total triglycerides found in serum or plasma, is becoming more important in clinical studies. Recent studies have investigated the links between increased concentrations of omega-3 fatty acids and anti-inflammatory responses such as in the severity of osteoarthritis following joint injury [1]. Correlations between the concentrations of omega-3 fatty acids in blood and breast tissue as related to breast cancer incidence [2], the associations between omega-3 fatty acids and arterial stiffness [3], and the levels of a specific omega-3 fatty acid, DHA, during resistance training in elderly individuals [4] have also been studied. As potential indicators of specific diseases, studies have looked at the link between serum concentrations of linoleic acid and the incidence of liver cirrhosis [5], selected fatty acids and type 2 diabetes [6], and saturated fatty acids and cardiovascular risk [7]. Mental health experts are comparing the concentrations of long chain polyunsaturated fatty acids (PUFA) in attention-deficit/hyperactivity disorder patients and their relatives [8] and investigating a potential role for long-chain PUFA in schizophrenia [9]. A recent review article [10] discusses the role of DHA in Alzheimer's disease and other brain functions. What was not addressed, however, is the accuracy and intercomparability among the data from the numerous studies of individual fatty acids in serum and plasma.

To address the accuracy of fatty acid measurements, the National Institute of Standards and Technology (NIST) in collaboration with the National Institutes of Health (NIH) has developed 2 Standard Reference Materials (SRMs), 1 plasma-based and 1 serum-based, characterized for the content of individual fatty acids. SRM 1950 Metabolites in Human Plasma (http://srmd.nist.gov) was a collaboration between NIST and NIH National Institute of Diabetes and Digestive and Kidney Disease (NIDDK); it was intended to represent "normal" human plasma [11]. SRM 2378 Fatty Acids in Frozen Human Serum was developed as a collaboration between NIST and NIH Office of Dietary Supplements (ODS) and was intended to represent 3 concentrations of fatty acids in serum, namely, a "normal" level, a level indicative of individuals taking flaxseed

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supplements, and a level indicative of individuals taking fish oil supplements. The value assignments of individual fatty acids in both of these SRMs (Supplemental Table 1) were based on measurements performed by NIST and the Centers for Disease Control and Prevention (CDC). Additional information on the SRMs, including descriptions of the methods used for the certification analyses, is available in the respective Certificates of Analysis, which can be found at http://www.nist.gov/srm/.

To begin to address the interlaboratory comparison of data, NIST, CDC, and NIH-ODS initiated an interlaboratory analytical comparison exercise for the determination of fatty acid concentrations in human serum and plasma in 2012 followed by a second exercise in 2015. This is one of 3 clinical quality assurance programs (QAPs) currently conducted by NIST [12] for the determination of micronutrients, vitamin D metabolites, and fatty acids in serum and plasma matrices, the Micronutrients Measurement QAP (MMQAP) [13–16], the Vitamin D QAP (VitDQAP) [17], and the Fatty Acid QAP (FAQAP), respectively. Given the similarity in the operations of these programs, NIST has consolidated the 3 programs into one larger program, the NIST Clinical QAP (ClinQAP). The primary goals of the ClinQAP are to support the comparability of clinical measurements through the MMQAP, VitDQAP, and the FAQAP and to monitor and support the emerging measurement needs of the clinical community. FAQAP is a performance-based program so participating laboratories are requested to use the analytical procedures that they typically use in their laboratories for these analyses and report data for those fatty acids that they typically quantify. There is no cost for participating in the FAQAP, and there is no pass/fail assessment. The results from the first 2 exercises of the FAQAP are presented and discussed in this paper.

2. Materials and methods

2.1. Description of materials

The first exercise of the FAQAP was conducted in 2012 with 11 laboratories returning data (Table 1) for the content of individual fatty acids in SRM 2378 (prior to its release as an SRM and therefore as an unknown sample) along with SRM 1950, which was distributed as the control sample with values assigned for fatty acid content. SRM 2378 consists of 3 serum materials collected from: (1) donors who did not take fish or flaxseed oil supplements for one month prior to collection, (2) donors who took flaxseed oil supplements for a minimum of one month prior to collection, and (3) donors who took fish oil supplements for a minimum of one month prior to collection. SRM 1950 is designed to represent “normal” human plasma. Plasma was obtained from 100 individuals (equal number of men and women) in a narrow age range (40 to 50 y) who had undergone an overnight fast prior to blood draw. The second exercise of the FAQAP was conducted in 2015 with 14 laboratories returning data (Table 1). Three unknown serum samples previously used in MMQAP studies were distributed along with 1 vial of each level of SRM 2378 as the control samples. For each exercise, participating laboratories were provided with four vials of each of the unknown samples and one vial of each of the control samples. Each vial contained approximately 1 mL of serum or plasma.

Table 1
Participants in the 2 FAQAP exercises (in alphabetical order).

Laboratory	Participated in	
	Exercise 1 (2012)	Exercise 2 (2015)
Bumrungrad Hospital Public Company Limited Bangkok Thailand		x
Centers for Disease Control and Prevention (CDC) National Biomarkers Branch Atlanta, GA USA	x	x
Cornell University Division of Nutritional Sciences Ithaca, NY USA	x	
Craft Technologies Wilson, NC USA		x
Hanyang University Department of Food and Nutrition, College of Human Ecology Seoul Korea	x	
Health Canada Nutrition Research Division Ottawa, ON Canada		x
Lipid Analytical Labs Guelph, ON Canada	x	
Matar Pathology Clinical Chemistry South Brisbane, Queensland Australia		x
Mayo Clinic Biochemical Genetics Laboratory Rochester, MN USA	x	x
Minnesota Department of Health Public Health Laboratory Saint Paul, MN USA	x	x
National Institutes of Health LMBB, DICBR, NIAAA Rockville, MD USA	x	
National Institute of Standards and Technology (NIST) Chemical Sciences Division Gaithersburg, MD USA	x	x
OmegaQuant, LLC Sioux Falls, SD USA	x	
Polytechnic Institute of Bragança Escola Superior de Tecnologia e Gestão Bragança Portugal		x
The University of Auckland Auckland Science Analytical Services, School of Biological Sciences Auckland New Zealand	x	x
University of California Los Angeles (UCLA) Center for Human Nutrition Los Angeles, CA USA		x
University of Michigan Cancer Center Ann Arbor, MI USA		x
University of Waterloo Department of Kinesiology Waterloo, ON Canada	x	x
USDA-ARS Western Human Nutrition Center Davis, CA USA		x

2.2. Instructions for exercises

Participants were requested to perform triplicate measurements of each unknown sample using their laboratory's analytical protocols for the measurement of the concentrations of individual fatty acids currently being determined in their laboratory. In addition, they were requested to analyze three subsamples of SRM 1950 (exercise 1) or 1 subsample of each level of SRM 2378 (exercise 2) as the control samples. A target list of fatty acids was provided (Table 2); however, participants did not need to quantify all of these compounds and could add additional compounds when reporting data. The participants were requested to report results, using three significant figures, in units of either μg/g or μmol/L and to provide brief descriptions of their analytical procedures. The analytical procedures used by the laboratories are briefly summarized in Supplemental Table 2.

2.3. Data compilation

For both exercises, laboratories were assigned numerical identification codes in order of receipt of data with the exception of the NIST laboratory. In the first exercise, four laboratories reported the data in μg/g with the remaining laboratories reporting as μM. In the second exercise, seven laboratories reported the data in μg/g, six laboratories reported the data in μM, and one laboratory reported data in mg/mL. The conversions between the units reported and the alternate units were