PROPOSALS FOR THE USE OF REFERENCE MATERIALS AND FOR THE DEVELOPMENT OF IN-HOUSE QUALITY CONTROL MATERIALS FOR FOOD ANALYSIS

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Abstract

A summary is presented of factors to be considered in the development of food-based in-house quality control materials to augment available Reference Materials and for frequent, concerted data quality control. Some guidelines are offered regarding approaches to the many considerations required for such an endeavour. Preliminary draft recommendations containing a sequence of steps has been compiled as a starting proposal for a food quality control material development scheme, for a range of natural matrices and measurands. In addition, information on the selection and utilization of Certified Reference Materials and procedures for performance interpretation and corrective action is provided.

1.INTRODUCTION

Accurate data on the chemical composition of raw agricultural products and foods derived therefrom are needed to (i) assess effects of farm management practices and food processing on nutrient and toxic chemical content of retail food products, (ii) establish the essentially of nutrients or toxicology of toxicants, (iii) identify adequate, sub-adequate, or marginal intakes by the population, (iv) establish nutrient dietary requirements, (v) accumulate baseline concentration data and (vi) comply with legal labelling requirements. It is evident from scientific and technical publications that there is much inconsistent information, not only in the case of trace or ultratrace inorganic and organic analyses with high operational and competence demands, but also in the determination of major elements and constituents [1-5]. Reasons for the general lack of agreement among laboratories arise from a multitude of factors influencing the reliability of the final results, including presampling, sampling, sample handling and manipulation, measurement, data handling and interpretation, contamination control, data quality control and analyst competence.

Within the laboratory's quality control program, incorporation of appropriate, compositionally-similar reference materials (RMs) (defined as any material, device or physical system for which definitive numerical values can be associated with specific properties and that is used to calibrate a measurement process) is a valuable, cost-effective aspect of a good quality control program, and a way of transferring accuracy from well defined methods of analysis to the laboratory [6-10]. Results obtained with the RM taken concurrently through the analysis with actual samples are compared with the certified values. Closeness of agreement indicate performance of the analytical method and may suggest the need for modifications to reduce errors.

Although there is a steadily increasing number of natural matrix materials for an ever increasing number of measurands, making selection of appropriate materials for a given analytical task more and more feasible, the high cost of many materials may be an impediment to their acquisition in developing countries. The question arises whether development of in-house quality control materials (QCMs), complimentary to certified RMs, specific to the food laboratories' needs, may be a feasible alternative. These in-house QCMs could be used on a frequent basis, complimented by less frequent incorporation of more expensive RMs. This chapter presents a summary discussion of (i) practical aspects for the proper use of RMs and QCMs in analytical laboratories and (ii) approaches to the development of QCMs or in-house RMs. It deals with practical aspects of the selection, preparation and analytical

characterization of in-house materials and provides some practical examples. Information here is a summary and much more detailed information and instructions can and should be formulated to provide specific guidance to laboratories proposing to develop food QCMs.

2. UTILIZATION OF AVAILABLE REFERENCE MATERIALS

2.1. Available food and related biological reference materials

Food and agricultural sciences encompass a wide variety of existing natural biological and environmental (non-biological) materials of primary and secondary relevance. Materials of agricultural and food relevance (agronomy, nutrition, environment, research, regulation etc.) can be grouped as follows: biological - animal body fluids and products, animal tissues, flours and cereal products, terrestrial plants, other foodstuffs, marine animals and aquatic plants; environmental - soils, fertilizers, sediments, sewage sludges, minerals, rocks and fresh waters. The primary interest of the typical food analyst would likely be the biological materials and would principally encompass foodstuffs, plant materials, and other related biological products.

Proliferation of RM's has reached the point where, in addition to information available in catalogues of RM developing and issuing agencies, and a multitude of scientific publications, several very useful reviews and compilations of available products and suppliers exist [6, 11-19]. Table 1 lists names of major suppliers of a variety of biological and non biological RM's which include food and related biological materials of interest to this chapter. Table 2 presents a fairly complete listing of currently available food and related biological RMs of relevance to the laboratory engaged in analysis of food, agricultural and related biological products, certified for a variety of inorganic and organic constituents.

2.2. Utilization of reference materials

The incorporation of appropriate RMs into the analytical scheme, utilizing good methods and other aspects of a quality control program, is the most convenient, cost-effective mechanism by which to assess, monitor and maintain analytical data quality and ensure accuracy of results. Discussion of the roles and uses of RMs is provided in several publications [7, 8, 10, 30, 31]. The analyst should attempt to make full use of existing RMs but whether bona fide RMs or other quality control materials are used, guidelines in this section are similarly applicable. These contents are summarized versions based on published proposed protocols for plants [32] and soils [31] discussing the concept and role of RMs, and procedures for their selection and utilization in the determination of inorganic measurands.

2.2.1. Prerequisites for use of RMs

Compliance with several prerequisites must be established in order to properly use RMs. 1. An appropriate analytical method must be applied, by appropriately qualified and trained personnel in a suitable physical (equipment, materials, reagents and laboratory conditions necessary for the proper execution of the method) and administrative (understanding of and support for appropriate data quality by managers) environment. The role of the analyst is of direct paramount importance; analyst training, experience, familiarity with the problem on hand, skill, attitude, motivation and judgement are necessary prerequisites with which satisfactory solution of analytical problems is possible. 2. Suitable quality control / quality assurance procedures should be routinely in use and the need for appropriately reliable analytical information must be recognized. The analytical system must be in a state of statistical control. The method under test should usually give a precision with the RM and other homogeneous materials equal to or better than the uncertainty reported for the RM in the certificate. 3. When dealing with the

determination of total concentrations of measurands, that is, the sum of all the measurand concentrations in all material (sample) phases and molecular species, it must be ascertained that the method is in fact measuring all of the measurand. For elemental determinations, the sample decomposition or extraction procedure must bring into solution all of the material; no grains or insoluble fraction must be left behind [eg 33]. In addition, the element must be in the correct oxidation state required by the procedure.

2.2.2. Procedures for RM selection

For correct and effective use of an RM, the material selected must be appropriate to the task. The material must resemble, as closely as possible in all respects, the actual materials being analyzed. It must be very similar with respect to matrix and must contain the measurand at a concentration level and form (eg. native form, speciation) similar to the commodity undergoing analysis. Furthermore, the RM must be sufficiently homogeneous so that test portions of size commensurate with the analytical method can be used. Ideally two or three materials should be chosen to bracket the measurand composition of the sample. 1. Select an RM, by consulting sequential concentration value tables for materials which have listed concentration values, for the measurand of interest, equal to or similar to those expected in the test material. In conjunction with descriptive name tables, select the material approximating the laboratory sample to be controlled with respect to general type (ie. matrix, based on name) as well as the measurand level expected. 2. Follow the same approach to choose, if possible, a second or third RM, of similar matrix, approximating the analytical samples, to match (or bracket) the sample with respect to concentration of the given measurand. 3. For multimeasurand (multielement) analyses, that is the determination of more than one measurand (element) on the same laboratory sample, go through the identical material selection steps for the second, third... measurand (element) to choose appropriate materials for each of these respective measurands. The rate of incorporation of RM is at the discretion of the analyst and could range from less than 1 RM test portion / 100 samples (more typical) to more than 1 RM test portion /10 samples, depending on the nature of the work and data quality requirements. Stocks of RMs can be conserved by including laboratory control materials for more frequent monitoring, reserving RMs for critical control.

2.2.3. Procedures for RM utilization

Major uses of RMs within the measurement process are generally: (a) analytical calibration, (b) quality control, (c) analytical method development and evaluation and (d) production and evaluation of other RMs and control materials [8, 10, 30]. Utilization of natural matrix RMs for establishing calibration functions [34] is not generally recommended due to uncertainties in certified concentrations. Such uncertainties, resulting from material inhomogeneity and certification measurement errors, are generally several fold greater than the compositional uncertainties for pure elements or pure compounds usually used for calibration solutions; the use of calibration solutions prepared from high purity, pure elements and compounds is preferred for calibration.

The recommended mode of RM usage is for analytical data quality control to establish method performance (bias) and to monitor and maintain data quality [30]. Errors in measurement can arise in the three component steps of an analytical method: sampling, sample manipulation and measurement. Thus, the aggregate of all steps subsequent to the point at which the material is introduced into the scheme of analysis will be monitored for performance. Follow the steps below for RM utilization: 1. Ensure that the analytical system is in a state of statistical control (as stipulated under Prerequisites). 2. Following certificate instructions for material usage and handling, incorporate the RM(s) into the scheme of analysis, at the earliest stage possible ie. prior to the beginning of sample decomposition. Take it through the entire analytical procedure at the same time and under the identical conditions as the actual

analytical samples in order to correctly monitor all the sample manipulation and measurement steps. 3. For multimeasurand (multielement) determinations, should different sample preparation and measurement procedures (ie. different analytical methods) be indicated for the different measurands, take separate test portions of the RM through the entire relevant analytical scheme for proper quality control.

The latest appropriate certificates or reports of analysis or other relevant publications issued with the RM must be consulted and used and other published tables should only be used as guides. These documents are integral components of the RM technology as they provide analytical (certified) information, estimates of uncertainties, instructions for the correct use of the material and other relevant information. RMs can monitor the performance of laboratory procedures subsequent to the point of introduction of the RM. Activities occurring prior to this such as sampling, preservation, storage and presampling considerations are generally impossible to monitor by use of RMs. Both the reference and actual samples must undergo identical, simultaneous handling. It is also important that the reference and actual sample measurand concentrations be reasonably close since method performance can vary dramatically with concentration, and conclusions at one level may not be applicable to other levels.

Reference Materials are best used on a regular basis. Their sporadic use when trouble is suspected is legitimate but systematic measurement within a quality control framework will generally be more informative and is highly recommended. RMs may be used as the sole quality control material or they may be used in conjunction with in-house or locally produced control materials in a systematic manner in order to conserve the former.

2.2.4. Performance interpretation and corrective action

When possible, the analysis of several RM, spanning the concentration range of interest, is the most useful way to investigate measurement bias. The "Handbook for SRM Users" by Taylor [30] is recommended for detailed discussion of Reference Material use. The method under test should usually give a precision (standard deviation) with the RM equal to or better than the overall uncertainty reported for the RM by the issuer. Results from the analysis of the RM are then compared with the certified value. The two will generally not agree exactly due to measurement errors in each. Whether the two differ significantly is ascertained by comparing the two values, and their uncertainties using simple statistical tests. If the confidence intervals intersect, the measured concentration value agrees with the certified value, and the analyst can deduce, with some confidence, that the method is applicable to the analysis of materials of similar composition. Otherwise there is disagreement and the method as applied exhibits a bias. One of the following calculation steps can be followed to estimate agreement of the measured and certified concentration values:

1. Case with all parameters available: Compare the 95% confidence levels calculated from the standard deviation, number of analyses and the student t statistic with the confidence or tolerance interval of the Reference Material using the following equations:

$$X_1 - X_2 = ts(1/n_1 + 1/n_2)^{1/2} \qquad (1)$$

$$s^2 = [(n_1-1)s_1^2 + (n_2-1)s_2^2]/(n_1 + n_2 - 2) \qquad (2)$$

where:
X_1 is the mean concentration found by the user for the Reference Material,
X_2 is the certified, recommended or reference value for the Reference Material,
s_1 is the standard deviation estimated from n_1 determinations by the user,
s_2 is the standard deviation reported for the Reference Material in the

certificate or report of analysis based on n_2 determinations, t is the student t statistic

The difference $X_1 - X_2$ is compared to the right hand side of equation (1) using the t value for 95% confidence ($p = 0.05$). Should the difference be greater (positive or negative) a discrepancy exists between the measured and certified concentration values which indicates that the analytical procedure is not operating well. Should it be ascertained that an unacceptable bias exists, a correction for it should not be applied; instead, diagnostic steps should be taken to identify sources of unacceptable bias or imprecision and corrective action should be taken to eliminate or reduce errors.

2. Case with missing n_2 and negligible uncertainty in the Reference Material certified value: Compare the absolute value of the estimated bias $X_1 - X_2$ with a critical value based on

$$X_1 - X_2 = ts_1 / (n_1)^{1/2} \qquad (3)$$

using uncertainty parameters only for the measurements carried out by the analyst. Proceed further as in case 1.

3. Case with missing n_2 and specified uncertainty in the Reference Material: Compare the absolute value of the estimated bias $X_1 - X_2$ with a critical value based on

$$X_1 - X_2 = ts_1 / (n_1)^{1/2} + u \qquad (4)$$

where u is the uncertainty of the certified concentration reported in the certificate of analysis. Proceed further as in case 1.

There are not too many instances where the uncertainty for the Reference Material is characterized by a standard deviation, s_2, and corresponding number of determinations, n_2. Thus cases 2 and particularly 3 will most often be the ones of necessity. The uncertainty, u, in case 3 is not necessarily a standard deviation or standard error but can reflect symmetric or asymmetric estimates of imprecision and possible systematic errors among methods used in certification.

3.DEVELOPMENT OF IN-HOUSE QUALITY CONTROL MATERIALS

In respect of the development (defined as the composite of all activities involving selection, preparation, characterization and certification) of RMs as well as in-house QCMs, a number of important requirements must be taken into consideration [35]. The major considerations are in general: (a) RM development philosophy, (b) end use requirements, (c) selection of materials, (d) preparation, (e) physical and chemical characterization, (f) certification, (g) documentation and (h) distribution. This section deals with an expanded listing of these factors to be applied to the development of in-house natural matrix food and biological quality control materials for inorganic and organic constituent chemical composition control.

3.1. Selection of matrices representing food and related products and measurands

Selection of materials is made in consideration of primarily: (1) the availability of similar RMs; (2) the laboratory's specific requirements. The choice is then on the basis of specific matrix and specific measurand. The term matrix component refers to the sum total of all constituents in the material aside

from those constituents being determined, which are denoted measurands. Clearly, what is a matrix component to one analyst, may be a measurand to another. Thus, in the case of analyses for elemental content, components such as dietary fibre, ash, protein, fat and carbohydrate are classified as matrix components and are used to define the nature of the material. In the more restricted case of analyses for strictly trace elements, the major elements such as Ca, N, P, K and Na may additionally be classified as matrix components. Regarding selection of food matrix, in addition to considering the laboratory's requirement, it may strengthen the validity and broader usefulness and applicability of the QCM to consider: (1) representativeness of the material to the population of products in production and commerce as evidenced by indications of worldwide consumption of food products (Table 3) [35, 36]; (2) matrix as exemplified by food and agricultural commodity classes (Table 4) [37]; and (3) matrix as represented by the food triangle depicting proportions of the major food matrix components influencing analytical performance, namely fat, protein and carbohydrate [38]. Naturally-occurring matrices to be considered in future developments of food-based RMs and QCMs include in general: animal tissues, plant tissues, marine tissues and oils, fresh full-fat food and marine products and drinking waters; pure elemental and compound standards required for method calibration may also be of related interest. Materials collected and archived under environmental specimen banking activities are good guides to the choice of required control materials; in fact surpluses of actual materials carefully collected and processed for environmental banking can serve as candidate materials.

Measurands can be placed into four major groups: total elements, speciated-elements, organics and matrix constituents. Although great strides have been made in the two decades since the first biological RMs appeared on the scene with elemental composition values for a range of elements, there still is a dearth of elemental concentration data for a wide range of nutritionally, toxicologically, clinically and environmentally pertinent elements. Some of the elements for which total concentration information is still required, usually at the low end of concentration range but occasionally at the high end are: Al, Ba, B, Be, Br, Cs, F, I, Li, Mo, N, Pt, S, Sb, Si, Sn, Th, Ti, Tl, U, V, W, rare earth elements and radionuclides. Little information is available with respect to the chemical forms or species in which elements occur. In the first approximation, bioavailable, extractable or leachable levels of elements are of interest. Secondly, at a higher degree of sophistication, data on the levels of the actual species, inorganic moieties such as nitrate, ammonium, phosphate, bromide, bromate, iodide, iodate and molecular species of which the elements are constituents would be of relevance to those conducting mechanistic and speciation research. Organic measurands of interest include those of nutritional significance, an increasing number of which are required for nutritional labelling such as vitamins, fat, lipids, dietary fibre, ash, protein and carbohydrates. Concomitantly, these values must be accompanied by scientifically sound definitions (eg. total, soluble dietary fibre; total, sulfated ash; total, unsaturated, unsaturated, polyunsaturated fat and individual lipids; simple sugars and complex carbohydrates). Other organics in foods and feedstuffs of toxicological concern include chlorinated pesticides, PCBs, PAHs, drug residues, sterols, aflatoxins and toxics in shellfish. The development of control materials for microbiological and DNA measurements, in its infancy, are challenging endeavours.

The result, after selection and acquisition from commercial sources, pilot or large scale preparation, is a product denoted a "candidate quality control material" which, depending on the outcome of final physical and chemical characterization, can become an in-house QCM.

3.2. Preliminary draft recommendations for development of in-house quality control materials

Information concerning the development, preparation and analytical certification of reference and control materials was initially only scattered in scientific and technical publications by individual and agency developers. In recent years, a number of reports have appeared compiling preparatory and measurement details on biological materials of direct or indirect interest to those embarking on such a

venture [25, 39, 40, 41]. Details by this author on his long term preparatory and measurement activities [42, 43], in the many internal reports from IRMM/BCR on preparation and European Commission Reports on interlaboratory analyses of BCR materials and guidelines from BCR [44] and ISO [45, 46] are most worthwhile to be consulted. Based on a perusal of these and many original publications and reports, the following sequence of 26 steps has been compiled as a starting proposal for a food quality QCM development scheme. This list is followed by a definition of the item, and a summarized description/discussion.

1. Nomenclature and definitions of reference and control materials
2. Nomenclature and definitions of 'Certified Values' and related concentration terms
3. Overall measurement system
4. Material preparation
5. Physical characterization
6. Material stability
7. Material homogeneity
8. Analytical characterization (certification) philosophy - approaches to the establishment of concentration values
9. Definition of analytical methods
10. Selection of measurands for characterization
11. Performance of analytical methods
12. Selection of analytical methodologies
13. Selection of analysts / laboratories
14. Selection of statistical protocols, uncertainty statements
15. In-house (initiating/coordinating laboratory) characterization
16. Cooperative interlaboratory analytical characterization campaign
17. Data quality control of in-house and interlaboratory analyses
18. Critical evaluation of the methods used by cooperators
19. Evaluation of data on technical merits
20. Evaluation and selection of multilaboratory/multimethod analytical data
21. Statistical treatment of data
22. Calculation of concentration values and associated uncertainties
23. Reporting of results and information
24. Publication of protocol followed
25. Testing and applying this protocol
26. Future status of reference and informational values

1. Nomenclature and definitions of reference and control materials

Analytical QCMs are of various kinds and a plethora of names has been used to describe the variety of pure compound, synthetic and natural matrix products produced [7]. The literature reveals names such as: standard reference material, certified reference material, reference material, biological reference material, international biological standard, international reference sample, certified natural standard, certified standard sample, uncertified standard, standard sample, analyzed sample, reference sample, reference standard, synthetic standard, matrix reference material, surrogate reference material, simulated reference material, intermediate reference material, comparative standard, primary reference material, secondary reference material, working reference material, routine working reference material, second generation biological reference material, quality control sample, check sample, primary standard, primary reference substance, secondary standard, manufacturer's standard, production standard, technical

material, technical standard, primary reference material, analytical standard, analytical reference standard, analytical reference material, analytical master standard,, reference standard, pure standard compound, reference compound of certified purity an working standard. ISO and NIST have firm definitions of RMs and SRMs; official guidelines for in-house quality control materials would be welcomed.

2. Nomenclature and definitions of 'Certified Values' and related concentration terms

Concomitantly a similarly bewildering array of terms referring to associated numerical values has appeared in the literature: certified (value or concentration), uncertified, non-certified, attested, consensus, probable, possible, most likely, recommended, informational, mean, overall mean, preferred mean, average, median, indicative, usable, guaranteed, proposed, provisional, tentative, best, select mean, calculated mean, magnitude, estimate, true, preferred accepted, assigned, target, published and manufacturer's. According to the International Organization for Standardization (ISO) only the following terms have been officially recognized (for RMs) and official guidelines for in-house quality control materials would be welcomed.

Certified value (of a given quantity): for a certified reference material, the value that appears in the certificate or other documentation accompanying the material, this value having been certified by a technically valid procedure.

Uncertified value (of a given quantity): for a reference material, the value of a quantity obtained by interlaboratory the material, but which is not certified by the producer or by any other Agency. (Note: an uncertified value may be given for information only).

Consensus value (of a given quantity): for a reference material, the values of a quantity obtained by interlaboratory testing, or by agreement between appropriate bodies or experts. (Note: a consensus value could, through appropriate action by a certifying body, become a certified value).

Best estimate or reference value (of the value of a given quantity): an estimate of the value that is optimized by taking into account both metrological and technical judgement and statistical factors.

3. Overall measurement system

For analytical values from the characterization exercise to be meaningful, the measurement process must produce precise numerical values of the property under analysis that are free of, or corrected for, all known systematic errors within agreed upon or practical limits required for the end use of the material; such values are also related to the "true value". Existing RMs can be used within an accuracy-based measurement system to serve as vehicles for transfer of accuracy of a definitive method to the measurement process and the numerical data generated therefrom [8-10].

4. Material preparation

Collection/preparation refers to all of the physical (and chemical) steps necessary to bring the starting material to RM status. It constitutes a major and important phase of RM development and entails many considerations in the many required steps for proper execution of RM development. Major considerations include (a) planning, (b) material selection, (c) collection, (d) preparation, (e) characterization, (f) storage and (g) documentation; each of these can be further subdivided. Attention to detail in all collection / preparation steps is mandatory. The flowchart in Table 5 [47] presents a

general summary of steps applied to the collection and preparation of biological, environmental, clinical and geological RMs based on collective descriptions in several reports offering good preparatory descriptions [7, 40, 42, 48-62]; a wealth of preparative and physical characterization information may be found in internal reports of the Institute of Reference Materials and Measurements, Geel. This comprehensive listing attempts to cover all possibly required steps in the preparative scheme and it should be recognized that not all steps are required in every instance and that the sequence and details will vary. A summary of additional details is in [47]; as well the certificates/reports of investigation accompanying RMs issued by the many organizations such as IRMM, IAEA, NIES, NIST, NRCC may be consulted.

5. Physical characterization

Physical characterization involves visual and microscopic examination, observation of appearance, colour and powder flow characteristics, determination of particle size, shape and distribution by sieving and microscopy, effects of particle size on chemical composition, moisture loss/pickup and demixing/settling during storage and transport.

6. Material stability

Long term integrity of an RM/QCM is a necessary condition for confidence in assigned values. Changes over time may be due to: evaporation or chemical reactions under the influence of temperature or light, precipitation, bacteriological activity, interaction of the material with the container in which it is stored, etc. These changes may impact on the matrix physical and chemical composition and measurand values and are especially a matter of concern for organic or volatile components and with solutions. Material stability should be tested under conditions which accelerate the changes which might occur under usual conditions during storage and in the laboratory.

7. Material homogeneity

Homogeneity refers to the variation of measurand concentration among test portions taken from the same and different containers. An indication of homogeneity is established by measurements with precise techniques and is the first chemical characterization to be conducted prior to the certification exercise. Estimates of homogeneity can be had from CVs from determinations by the initiating laboratory, from interlaboratory cooperative analytical determinations and by ANOVA of results within and between containers.

8. Analytical characterization (certification) philosophy

Probably the most difficult and challenging task of the QCM development process is analytical characterization (certification), that is, the process of obtaining concentration data which approach as closely as possible the "true value", together with uncertainty limits. Chemical characterization for quantification or certification purposes, encompasses measurand selection based on nutritional, toxicological and environmental significance as well as availability of suitable analytical methodologies and analysts. It includes selection of certification protocols based on definitive, reference and validated methodologies, selection of expert analysts applying conceptually different approaches, selection, development, assessment and validation of methodologies and adaptation of statistical protocols for data analysis [20, 63, 64].

The literature on RM certification indicates that there are two broad types of approaches for the characterization of RMs: (1) statistical and (2) measurement. The statistical approach relies on the in-

depth application of statistical calculations to a body of, often widely scattered and discordant, analytical results obtained from diverse exercises. The approach based on measurement emphasizes laboratory measurement aspects and deals more in detail with various diverse analytical measurement possibilities to generate a coherent dataset, followed by necessary minimal calculations. Major approaches to characterization/certification may be classified as:

(1) Definitive method - one organization
(2) Independent reference methods - one organization
(3) Independent reference and validated methods by selected expert analysts - multiple organizations and laboratories
(4) Volunteer analysts, various methods - multiple organizations and laboratories
(5) Method-specific - characterization by a specific, validated method by selected expert or experienced analysts - multiple organizations and laboratories.

The QCM developer will have to determine which approaches are within his reach and appropriate for the venture.

9. Definition of analytical methods

Three methodology terms should be kept in mind as they are intimately integrated into the measurement system and the first two are utilized in the characterization of QCMs. A definitive method of chemical analysis is one which has a valid and well-described theoretical foundation, has been experimentally evaluated to lead to negligible systematic errors and a high level of precision. Definitive methods provide the fundamental basis for accuracy in chemical analysis. Such methods usually require highly skilled personnel, are time-consuming as well as expensive to perform. A reference method is a method of proven and demonstrated accuracy established by direct comparison with a definitive method or with a primary RM. Since reference methods may also be moderately sophisticated, their use may not always be possible. Reference methods can be used to produce secondary reference materials, and control the accuracy of quality assurance procedures. The term field method denotes any method of chemical analysis used in applications requiring large numbers of measurements on a routine basis usually with automated instrument systems capable of producing highly precise (but not necessarily accurate) data.

10. Selection of measurands for characterization

Refer to above for a list measurands of possible interest in food analysis.

11. Performance of analytical methods

Analytical procedures are subject to many sources of error starting with sampling and sample preparation and ending with the calculation and recording of the results. Their accuracy, systematic error and precision, cannot readily be evaluated by means of any single test. However, a substantial part of the whole procedure can generally be tested by the use of appropriate analytical quality control materials, especially certified RMs. There is a need to ensure good performance for the purpose of QCM characterization.

12. Selection of analytical methodologies

The large number of measurand/material combinations for which concentration values are targeted necessitates a large number of analytical methods. In work on the elemental certification of 12 RMs for 303 assigned values [42] 13 major classes of methods were used including the usual currently used single- and multi-element instrumental techniques ranging from atomic absorption and emission spectrometry, mass spectrometry, neutron activation analysis and electrochemically-based techniques to the classical Kjeldahl method for nitrogen, light absorption spectrometry, fluorometry and gravimetry. Purposely, an attempt was made to get wide-ranging techniques and procedures with different sample preparation steps, including no decomposition as in instrumental neutron activation analysis and particle induced X-ray emission spectrometry, as well as different detection/measurement techniques.

Analytical methods should include nuclear methods [65, 66]. In the above work [42, 65] six different variants of neutron activation analysis (NAA) methods were employed including: instrumental neutron activation analysis, instrumental neutron activation analysis with acid digestion, neutron activation analysis with radiochemical separation, neutron capture prompt gamma activation analysis, epithermal instrumental neutron activation analysis, and neutron activation analysis with preconcentration. Methods based on NAA were found to rank typically in the middle of the range with the three other major analytical methods (atomic absorption spectrometry, atomic emission spectrometry, mass spectrometry) with respect to precision. NAA methods, however, distinguished themselves by often exhibiting superior accuracy. These facts, together with the need for no sample treatment in the case of INAA, the version used in the vast majority of NAA applications, make contributions by NAA methodologies, extremely valuable to RM/QCM characterization.

13. Selection of analysts / laboratories

Following selection of appropriate and desired methods of analysis, analysts in participating laboratories are selected on the basis of their established capabilities (competence, experience, motivation, healthy scepticism concerning results obtained). The reliability of the analysis seems to depend much more on the analyst than on technique.

14. Selection of statistical protocols, uncertainty statements

Statistical protocols for homogeneity testing, in-house and outside laboratory analyses, dealing with aberrant data and calculation of assigned values and depiction of associated uncertainties must be selected. Analysis of variance (ANOVA) and variance component calculations would be typical; various plots (eg. concentration versus unit, concentration versus laboratory number, concentration versus observation number) could be made for inspecting, assessing and selecting results for use in calculating reference and informational concentration values and uncertainties. It is recommended to have input from a statistician.

15. In-house (initiating/coordinating laboratory) characterization

Depending on the extent and complexity of the QCM project, the initiating laboratory will make a major or minor contribution to the analytical characterization effort. This will principally depend on locally available methodological, instrumental and technical competencies. The laboratory should be involved in preliminary analyses, homogeneity studies, contributions to final reference values as well as coordinating the overall preparation and characterization effort.

16. Cooperative interlaboratory analytical characterization campaign

Should a large number of materials and a wide range of measurands be involved and there be lack of requisite techniques in the initiating laboratory, involvement of outside analysts will be necessary. Following selection of targeted and desired methods of analysis, analysts should be selected on the basis of their established capabilities. A conscious attempt should be made to get wide-ranging techniques and procedures including different sample preparation steps. Clear, sufficiently detailed instructions and forms for reporting methodological details and analytical results are to be provided.

17. Data quality control of in-house and interlaboratory analyses

Usual data quality control procedures should be in place in the initiating laboratory and a request for the same should be made to outside participants. Emphasis is placed on the importance to the undertaking of the simultaneous incorporation of appropriate RMs into the scheme of analysis and specific instructions for their selection and use may be forwarded. Reliability of the data generated in the characterization exercise is related to the concept of 'traceability', that is the relating of acquired data to a national or international reference through an unbroken chain of comparisons all having stated uncertainties [67].

18. Critical evaluation of the methods used by cooperators

Critical evaluation of analytical methods and procedures used is complementary to, but independent, from evaluation of submitted results. Complete descriptions of methods followed may be submitted as scientific journal articles or laboratory notes. Evaluation relies on the initiating analyst's experience and his interpretation of the validity and appropriateness of the applied methods and procedural details as they relate to the specific matrices and measurands under investigation. Many combinations of sample treatment, and detection and measurement schemes will lead to multiple variants of each method; each must be considered.

19. Evaluation of data on technical merits

This item is closely related to 18. A good and interesting approach is ingrained in the RM development activities of the European Commission (BCR) whereby meetings between organizers of the RM program and participating analysts from member countries are held for dialogue to critically assess results

20. Evaluation and selection of multilaboratory/multimethod analytical data

Information to be requested from participating analysts to aid in data evaluation can include: brief details on sample preparation, instrumentation used and detection limit (and definition) for each measurand; analysts involved in analyses; the number of instrumental readings taken to give each mean concentration; calibration; instrumental precision; unusual occurrences observed during the work; nominal subsample masses taken; concentration results. Similar information is separately provided for materials utilized for quality control. Analytical results are perused and requests for clarification, remeasurement or additional information are made as required. Prior to final calculations of reference and information values, the analytical concentration results are carefully inspected using technical, statistical (variation and bias) and judgement criteria to remove aberrant, outlying or non - representative data.

21. Statistical treatment of data

Dealing with outliers is an early order of business, carried out in perhaps three stages: (1) deletion of obviously erroneous, aberrant or outlying data, (2) inspection of concentration versus laboratory number plots and deletion of all data for a measurand/matrix with excessive within-laboratory variation or systematic errors (bias) relative to data from the other laboratories; confirmation of rejection by noting performance with certified RMs (3) repetition of (2) and rejection of additional individual outliers or entire sets from a laboratory when their retention has a serious impact on final uncertainty (spread of accepted results). Outlier rejection criteria can include the following considerations: (1) poor within-laboratory precision compared to that of other laboratories, (2) poor within-subsample precision (within-laboratory instrumental precision) compared with similar parameters of other laboratories, (3) laboratory systematic error judged by deviation of laboratory mean from overall mean, (4) accuracy, based on performance with certified RMs, (5) within-laboratory precision with certified RMs, (6) assessment of the technical merit of the analytical procedure, (7) number of subsamples analyzed compared to that in other laboratories. The usual analysis of variance (ANOVA) and variance component calculations can be carried out.

It is this author's view that, in certification, painstaking care is needed in the selection of the cooperating laboratories and analytical methods and the main effort is in the generation of an excellent, tight dataset with small systematic errors and uncertainties, which is then subjected to minor mathematical manipulations to arrive at final property measures [63]. Abbey [68-71] has carried out many interesting statistical manipulations and calculations of literature-reported data for standard rocks, recalculating published recommended elemental concentration values using a variety of estimates (... "gamma transformation", "dominant cluster mode", geometric means, Gastwirth median) of means, medians and modes. He clearly and forcefully observes that "Given a highly incoherent set of results for the determination of each constituent of a proposed reference sample, the originator is faced with the difficult problem of estimating the 'true' concentration. No known test can prove the validity of a concentration value derived from a mass of incoherent data" [71].

22. Calculation of concentration values and associated uncertainties

This is final step in certification. To avoid what has been denoted 'confusion as to the meaning of the uncertainties that are attached to the concentration values for trace elements in biological materials' and to avoid 'statements that cannot be interpreted in a meaningful quantitative or statistical way', guidelines for evaluating and expressing uncertainty should be consulted [72]. The reference value can be computed as the mean of equally-weighted individual laboratory means. The associated SD can be calculated from the three variance components representing within-unit (σ_w^2), among-unit (σ_u^2) and among-laboratory/ method (σ_L^2) variation according to the equation

$$SD = (\sigma_w^2 + \sigma_u^2 + \sigma_L^2)^{1/2} \qquad (5)$$

where each σ indicates the estimates of the associated variance component obtained from a type I (hierarchal) variance component analysis. The SD is the basis for calculation of a 95% confidence interval or uncertainty interval for a future single observation. The following statement has been used by the author in reports of analysis for cooperatively produced AAFC/NIST RMs [73]:

Reference values, weight percent or mg/kg (ppm), presented in Reports of Investigation provided with these Reference Materials are based on the dry material and are equally-weighted means of results from generally at least two, but typically several, different analytical methods applied by analysts in different

laboratories. Uncertainties are estimates expressed either as 95% confidence intervals or occasionally as intervals based on ranges of accepted results for a single future determination based on a sample weight of at least 0.5 g. These uncertainties, based on among-method and laboratory, among-unit and within-unit estimates of variances, include measures of analytical method and laboratory imprecisions and biases and material inhomogeneity.

23. Reporting of results and information

A document should be prepared for each QCM developed. The documentation is typically a certificate issued by the certifying agency or a report of investigation whose sole authority is the author. Critically important information should be included to define and describe the material, describe its preparation and characterization, list numerical values for properties together with the associated uncertainties (as well as their definitions), stipulate minimum weight to be taken for analysis, indicate conditions of storage and include other details necessary for the analyst to correctly and fully utilize the material. BCR, ISO and other guidelines for contents of certificates should be consulted [49, 74].

24. Publication of protocol followed

In-depth treatment of all aspects of the development procedures should be available in accessible technical or scientific publications for information of the analyst/user. These documents or supplementary published material may also contain a listing of all individual data, final values, methods and analysts.

25. Testing and applying this protocol

It would be beneficial if at least parts of the particular proposed protocol adopted for the development of QCMs was subjected to preliminary testing and modification if required prior to full application.

26. Future status of reference and informational values

The credibility associated with the QCM is directly related to the degree of confidence placed in the developing organization. The work should be thoroughly and competently conducted so that no periodic updating of recommended values need be done.

4. COMMENTS AND CONCLUSIONS

The ideas formulated here, for food materials, are a summary and interpretation of information found in many sources. The proposed steps are a starting point for the development of a much more comprehensive document with more detailed information and instructions, formulated to provide specific guidance to laboratories proposing to develop food QCMs. These instructions can be adapted to other materials of interest to this committee with additional specific details, and a proposal is made for the preparation of one comprehensive report on the topic of development of in-house QCMs. A secondary aim of such a report will be to increase the awareness of the analyst and scientist in the concept, role and utility of existing RMs in data quality and to stimulate increased RM use as a cornerstone of the quality control program to establish, monitor and maintain analytical data quality.

Reliability and confidence in the stated characteristics of the developed QCMs is a basic critical criterion for their use for quality control. Applications of methods of chemical analysis are fraught with many sources of error and countless opportunities exist for the introduction of error into the final results.

Measurement systems must therefore be operated under a complete, regularly-applied quality assurance program if results are to be meaningful. Characterization philosophy rests on the concept of independent methodology, the application of theoretically and experimentally different measurement techniques and procedures to generate method-independent concordant results. The developer should be aware of the need for, and possible shortage of, highly competent analysts required for characterization work, the difficulties of good work at trace and ultratrace levels and methodological deficiencies for specific measurands. Throughout the overall task of development there is a requirement for a critical approach by critical analytical and measurement scientists in order to produce top quality control materials.

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TABLE 1. SUPPLIERS OF FOOD AND RELATED BIOLOGICAL REFERENCE MATERIALS FOR CHEMICAL COMPOSITION QUALITY CONTROL

Code	Name [a]
AAFC	Agriculture and Agri-Food Canada (see NIST)
AMM	Academy of Mining and Metallurgy, Poland
ARC	Agricultural Research Centre, Finland
BCR	Institute for Reference Materials and Measurements (IRMM), Belgium (Community Bureau of Reference (BCR)
BOWEN	Dr. H.J.M. Bowen, United Kingdom
CANMET	Canada Centre for Mineral and Energy Technology, Canada
CII	Comité Inter-Instituts d'Etudes des Techniques Analytiques de Diagnostic Foliaire (France)
CSRM	Pb-anal, Kosice, Slovakia
CZIM	Slovak Institute of Metrology, Slovakia
EPA	U.S. Environmental Protection Agency, USA
FISHER	Fisher Scientific Company, USA
GBW	National Research Centre for Certified Reference Materials, China
GHENT	Department of Internal Medicine, University Hospital, Belgium
IAEA	International Atomic Energy Agency, Austria
ICHTJ[b]	Commission of Trace Analysis of the Committee for Analytical Chemistry of the Polish Academy of Sciences, Poland
INCT[b]	Institute of Nuclear Chemistry and Technology
IGGE	Inst. of Geophysical and Geochemical Exploration, China
IRANT	Institute of Radioecology and Applied Nuclear Techniques, Czechoslovakia
KL	Kaulson Laboratories Inc., USA
LGC	Laboratory of the Government Chemist, United Kingdom
LIVSVER	Swedish National Food Administration, Sweden
NIES	National Institute for Environmental Studies, Japan
NIST	National Institute of Standards and Technology, USA
NRCC	National Research Council Canada, Canada
NYCO	Nycomed Pharma, Diagnostica, Norway
SHINR	Shanghai Institute of Nuclear Research, China

[a] Major, mainly government agency suppliers, adapted from [11, 16 17] which includes complete names and addresses.

[b] Terminology recently changed from ICHTJ to INCT.

TABLE 2. CURRENTLY AVAILABLE FOOD AND RELATED BIOLOGICAL REFERENCE MATERIALS FOR CHEMICAL COMPOSITION FROM, MAINLY, GOVERNMENT AGENCY SUPPLIERS[a]

Material	Code[b]
Foodstuffs	
Cabbage Leaves	AMM-CL-1
Animal Muscle (pork)	ARC/CL-AM
Carrot Powder	ARC/CL-CP
Milk Powder	ARC/CL-MP
Potato Powder	ARC/CL-PP
Total Diet	ARC/CL-TD
Wheat Flour	ARC/CL-WF
Skim Milk Powder	BCR-CRM 063R
Wholemeal Flour (vitamins)	BCR-CRM-121
Margarine (vitamins)	BCR-CRM-122
Spiked Skim Milk Powder	BCR-CRM-150
Spiked Skim Milk Powder	BCR-CRM-151
Soya-Maize Oil Blend (fatty acids)	BCR-CRM-162
Beef-Pork Fat Blend (fatty acids)	BCR-CRM-163
Anhydrous Milk Fat (fatty acids, etc.)	BCR-CRM-164
Bovine Muscle	BCR-CRM-184
Bovine Liver	BCR-CRM-185R
Pig Kidney	BCR-CRM-186
Natural Milk Powder	BCR-CRM-187
Spiked Milk Powder	BCR-CRM-188
Wholemeal Flour	BCR-CRM-189
Whole Rapeseed	BCR-CRM-190R
Brown bread	BCR-CRM-191
Defatted Peanut Meal (aflatoxin)	BCR-CRM-262
Defatted Peanut Meal (aflatoxin)	BCR-CRM-263
Defatted Peanut Meal (aflatoxin)	BCR-CRM-264
Mussel Tissue	BCR-CRM-278R
Whole Milk Powder (aflatoxin)	BCR-CRM-282
Whole Milk Powder (aflatoxin)	BCR-CRM-283
Whole Milk Powder (aflatoxin)	BCR-CRM-284R
Whole Milk Powder (aflatoxin)	BCR-CRM-285
PCBs in Cod Liver Oil	BCR-CRM-349
PCBs in Mackerel Oil	BCR-CRM-350
Whole Rapeseed	BCR-CRM-366
Whole Rapeseed	BCR-CRM-367
Maize Flour (deoxynivalenol)	BCR-CRM-377
Maize Flour (deoxynivalenol)	BCR-CRM-378
Wheat Flour (deoxynivalenol)	BCR-CRM-379
Whole Milk Powder	BCR-CRM-380R
Rye Flour	BCR-CRM-381
Wheat Flour	BCR-CRM-382
Haricot Beans	BCR-CRM-383
Lyophilized Pork Muscle	BCR-CRM-384
Peanut Butter (aflatoxin)	BCR-CRM-385R

Wheat Flour (deoxynivalenol)	BCR-CRM-396
Peanut Butter (aflatoxin)	BCR-CRM-410R
Milk Powder (vitamins)	BCR-CRM-421
Cod Muscle	BCR-CRM-422
Pesticides in Pork Fat	BCR-CRM-430
Porcine Muscle (chloramphenicol)	BCR-CRM-444
Porcine Muscle (chloramphenicol)	BCR-CRM-445
Rapeseed Oil (oil, moisture, volatiles)	BCR-CRM-446
Rapeseed Oil (oil, moisture, volatiles)	BCR-CRM-447
Rapeseed Oil (oil, moisture, volatiles)	BCR-CRM-448
PCBs in Natural Milk Powder	BCR-CRM-450
Total & Methylmercury in Tuna Fish	BCR-CRM-463
Total & Methylmercury in Tuna Fish	BCR-CRM-464
Rice Flour (amylose)	BCR-CRM-465
Rice Flour (amylose)	BCR-CRM-466
Rice Flour (amylose)	BCR-CRM-467
Wheat (ochratoxin)	BCR-CRM-471
Wheat (ochratoxin)	BCR-CRM-472
Mussel Tissue (butyltins)	BCR-CRM-477
Mixed Vegetables (vitamins)	BCR-CRM-485
Pig Liver (vitamins)	BCR-CRM-485
Haricots Beans (dietary fibre)	BCR-CRM-514
Carrot (dietary fibre)	BCR-CRM-515
Apple (dietary fibre)	BCR-CRM-516
Full Fat Soya (dietary fibre)	BCR-CRM-517
Bran Breakfast Cereal (dietary fibre)	BCR-CRM-518
Anhydrous Butter Fat (triglycerides...)	BCR-CRM-519
PCDDs & PCDFs in Unspiked Milk Powder	BCR-CRM-532 (RM)
PCDDs & PCDFs in Unspiked Milk Powder	BCR-CRM-533 (RM)
PCDDs & PCDFs in Unspiked Milk Powder	BCR-CRM-534 (RM)
Mussel (dc-saxitoxin)	BCR-CRM-542
Mussel (dc-saxitoxin)	BCR-CRM-543
Cod Liver Oil (OCPs)	BCR-CRM-598
Milk Powder (PCDDs, PCDFs)	BCR-CRM-607
Kale	BOWEN's Kale
Apple	CII
Cabbage	CII
Lettuce	CII
Fish Tissue	EPA-SRS903
Tea	GBW-07605
Tea	GBW-08505
Rice Flour	GBW-08502
Wheat Flour	GBW-08503
Cabbage	GBW-08504
Fluoride Composition in Corn	GBW-08506
Fluoride Composition in Corn	GBW-08507
Mercury in Rice	GBW-08508
Non Fat Milk Powder	GBW-08509
Pork Liver	GBW-08551
Mussel	GBW-08571
Prawn	GBW-08572

Rye Flour	IAEA-V-8
Milk Powder	IAEA-A-14
Milk Powder	IAEA-152
Milk Powder	IAEA-153
Milk Powder	IAEA-321
Mussel Homogenate	IAEA-142/OC
Mussel Homogenate	IAEA-142/TM
Sucrose	IAEA-C-6
Sucrose	IAEA-CH-6
Radionuclides in Whey Powder	IAEA-154
Whey Powder	IAEA-155
Mediterranean Tuna Fish	IAEA-352
Brandy (alcohol)	LGC-5000
Wine (alcohol)	LGC-5001
Wine (alcohol)	LGC-5002
Wine (alcohol)	LGC-5003
Lager Shandy (alcohol)	LGC-5004
Lager (alcohol)	LGC-5005
Cider (alcohol)	LGC-5006
Ethanol/Water (alcohol)	LCG-5404
Ethanol/Water (alcohol)	LCG-5405
Ethanol/Water (alcohol)	LCG-5406
Ethanol/Water (alcohol)	LCG-5407
Ethanol/Water (alcohol)	LCG-5408
Chocolate Confectionery	LGC-7016
Sugar Confectionery	LGC-7017
Yellow Fat Spread (fat)	LGC-7004
Malted Milk Biscuit (fat)	LGC-7005
Milk Powder (fat)	LGC-7006
Milk Drink Powder (fat)	LGC-7007
Corn Oil (pesticides)	LGC-7008
White Bread Flour	LGC-7003
Beef/Pork Meat	LGC-7000
Pork Meat	LGC-7001
Pork/Chicken Meat	LGC-7002
Pork Meat	LIVSVER-SMRI-94-1
Tea Leaves	NIES-CRM-7
Rice Flour	NIES-CRM-10A
Rice Flour	NIES-CRM-10B
Rice Flour	NIES-CRM-10C
Fish Tissue	NIES-CRM-11
Fatty Acids & Cholesterol in a Frozen Diet Composite	NIST-SRM-1544
Total Diet	NIST-SRM-1548a
Non Fat Milk Powder	NIST-SRM-1549
Cholesterol & Fat Soluble Vitamins in Coconut Oil	NIST-SRM-1563
Oyster Tissue	NIST-SRM-1566b
Wheat Flour	NIST-SRM-1567a
Rice Flour	NIST-SRM-1568
Brewers Yeast	NIST-SRM-1569
Bovine Liver	NIST-SRM-1577b
Organics in Cod Liver Oil	NIST-SRM-1588

Infant Formula	NIST-SRM-1846
Baby Food Composite	NIST-SRM-2383
Corn Kernel	NIST-RM-8413
Bovine Muscle Powder	NIST-RM-8414
Whole Egg Powder	NIST-RM-8415
Microcrystalline Cellulose	NIST-RM-8416
Wheat Gluten	NIST-RM-8418
Mixed Diet	NIST-RM-8431a
Corn Starch	NIST-RM-8432
Corn Bran	NIST-RM-8433
Whole Milk Powder	NIST-RM-8435
Durum Wheat Flour	NIST-RM-8436
Hard Red Spring Wheat Flour	NIST-RM-8437
Soft Winter Wheat Flour	NIST-RM-8438
Furans & Dioxins in Fish	NRCC-CARP-1

Plants

Aquatic Plant (Lagarosiphon major)	BCR-CRM-060
Aquatic Plant	BCR-CRM-061
Olive Leaves	BCR-CRM-062
Beech Leaves	BCR-CRM-100
Spruce Needles	BCR-CRM-101
Hay Powder	BCR-CRM-129
Single Cell Protein	BCR-CRM-273
Single Cell Protein	BCR-CRM-274
Sea Lettuce (Ulva lactuca)	BCR-CRM-279
Rye Grass	BCR-CRM-281
Compound Feed (aflatoxin)	BCR-CRM-375
Compound Feed (aflatoxin)	BCR-CRM-376
White Clover	BCR-CRM-402
Plankton	BCR-CRM-414
Lichen (trace elements)	BCR-CRM-482
Aquatic Plant (Cr)	BCR-CRM-596
Spruce Twigs and Needles	CANMET-CLV-1
Spruce Twigs and Needles	CANMET-CLV-2
Artichoke Leaves	CII
Codia Discolor Leaves	CII
Cotton Leaves	CII
Eucalyptus Leaves	CII
Hevea Leaves	CII
Maize Leaves	CII
Olive Leaves	CII
Orange Leaves	CII
Palm Leaves	CII
Peach Leaves	CII
Golden Apple Leaves	CII
Cox's Orange Apple Leaves	CII
Vine Leaves	CII
Tobacco Leaves	CII
Sugarbeet Leaves	CII

Oak Leaves	CII
Alfalfa	CII
Hay	CII
Rye-Grass	CII
Barley Straw	CII
Blond Peat	CII
Pine Bark	CII
Carnation	CII
Pine Needles	CII
Rice Straw	CII
Bush Branches and Leaves	GBW-07602
Bush Branches and Leaves	GBW-07603
Poplar Leaves	GBW-07604
Peach Leaves	GBW-08501
Codonopsis p.	GBW-09501
Cotton Cellulose	IAEA-V-9
Hay Powder	IAEA-V-10
Cellulose	IAEA-C-3
Wood	IAEA-C-4
Wood	IAEA-C-5
Clover	IAEA-156
Sea Plant	IAEA-307
Lichen	IAEA-336
Grass	IAEA-373
Oriental Tobacco Leaves	ICHTJ-CTA-OTL-1
Virginia Tobacco Leaves	ICHTJ-CTA-VTL-2
Cantharellus t. (fungus)	LIVSVER-FUNGUS
Pepperbush	NIES-CRM-1
Chlorella	NIES-CRM-3
Sargasso seaweed	NIES-CRM-9
Apple Leaves	NIST-SRM-1515
Peach Leaves	NIST-SRM-1547
Spinach Leaves	NIST-SRM-1570a
Citrus Leaves	NIST-SRM-1572
Tomato Leaves	NIST-SRM-1573a
Pine Needles	NIST-SRM-1575
Fluoride in Vegetation	NIST-SRM-2695
Corn Stalk	NIST-RM-8412

Animal tissues and fluids

OCPs in Animal Feed	BCR-CRM-115
Human Serum (Cortisol)	BCR-CRM-192
Human Serum (Cortisol)	BCR-CRM-193
Bovine Blood (Pb/Cd)	BCR-CRM-194
Bovine Blood (Pb/Cd)	BCR-CRM-195
Bovine Blood (Pb/Cd)	BCR-CRM-196
Human Serum	BCR-CRM-303
Human Serum	BCR-CRM-304
Human Serum (progesterone)	BCR-CRM-347
Bovine Urine (diethylstilboestrol)	BCR-CRM-386

Bovine Urine (dienoestrol)	BCR-CRM-387
Bovine Urine (hexooestrol)	BCR-CRM-388
Bovine Urine (diethylstilboestrol)	BCR-CRM-389
Bovine Urine (dienoestrol)	BCR-CRM-390
Bovine Urine (hexooestrol)	BCR-CRM-391
Human Hair	BCR-CRM-397
Human Serum (creatinine)	BCR-CRM-573
Human Serum (creatinine)	BCR-CRM-574
Human Serum (creatinine)	BCR-CRM-575
Human Serum (estradiol)	BCR-CRM-576
Human Serum (estradiol)	BCR-CRM-577
Human Serum (estradiol)	BCR-CRM-578
Bovine Liver	CZIM-LIVER
Fish	EPA-FISH
Human Hair	GBW-07601
Human Hair	GBW-09101
Lyophilized Human Urine	GBW-09102
Lyophilized Human Urine	GBW-09103
Pb in Freeze-dried Human Urine	GBW-09104
Pb in Freeze-dried Human Urine	GBW-09105
F in Lyophilized Human Urine	GBW-09106
F in Lyophilized Human Urine	GBW-09107
Bovine Serum	GBW-09131
Bovine Blood	GBW-09132/3/4
Human Serum	GBW-09135
Human serum	GHENT-SERUM
Animal Bone	IAEA-H-5
Animal Bone	IAEA-A-12
Animal Blood	IAEA-A-13
Copepoda	IAEA-MA-A-1/TM
Copepoda Homogenate	IAEA-MA-A-1/OC
Fish Flesh	IAEA-MA-A-2/TM
Fish Flesh	IAEA-MA-B-3/RN
Shrimp Homogenate	IAEA-MA-A-3/OC
Human Hair	IAEA-085
Human Hair	IAEA-086
Cockle Flesh	IAEA-134
Fucus (Sea Plant Homogenate)	IAEA-140/OC
Fucus (Sea Plant Homogenate)	IAEA-140/TM
Blood	KL-100-H
Blood	KL-100-L
Blood	KL-100-M
Serum	KL-146-I
Serum	KL-146-II
Serum	KL-147-I
Serum	KL-147-II
Serum	KL-148-I
Serum	KL-148-II
Urine	KL-110-H
Urine	KL-110-L
Urine	KL-140-M

Urine	KL-140-I
Urine	KL-140-II
Urine	KL-142-I
Urine	KL-142-II
Albacore tuna	NIST-RM-50
Human Serum	NIST-SRM-909
Lead in blood	NIST-SRM-955a, b, c, d
Oyster tissue	NIST-SRM-1566
Bovine Liver	NIST-SRM-1577a
PCBs in Human Serum	NIST-SRM-1589
Inorganics in Human Serum	NIST-SRM-1598
Organics in Whale Blubber	NIST-SRM-1945
Toxic Metals in Urine	NIST-SRM-2670
Fluoride in Urine	NIST-SRM-2671
Mercury in Urine	NIST-SRM-2672
Fluoride in Vegetation	NIST-SRM-2695
Human Lung	NIST-SRM-4351
Human Liver	NIST-SRM-4352
Serum	NYCO-105
Serum	NYCO-212
Whole blood	NYCO-904
Whole blood	NYCO-905
Whole blood	NYCO-906
Urine	NYCO-108
Dogfish Liver	NRCC-DOLT-2
Dogfish Muscle	NRCC-DORM-2
Lobster Hepatopancreas	NRCC-TORT-2
Non Defatted Lobster Hepatopancreas	NRCC-LUTS-1
Human Liver	SHINR-NH

[a] Compilation of materials adapted from [6, 11-17, 20-29], prepared for determination of: stable isotopes, major, minor and trace elements, radionuclides, speciation, organic nutrients, proximate constituents, organic contaminants and radionuclides.

[b] Codes are defined in Table 1 and are a combination of producer codes and product identities assigned by the producer; no codes have been assigned by CII. These Reference Materials are generally available from the listed issuing organizations as well as from other distributors. Several older materials may not be available, however, from primary sources but are included for completeness and for their usefulness and because they may still be available on the secondary market.

TABLE 3. ANNUAL WORLDWIDE PRODUCTION OF CROPS AND LIVESTOCK PRODUCTS, 1980 (1000 metric tons)[a]

Commodity	Production	Commodity	Production
Cereals	1,570,673	Oranges	39,798
Sugar cane	730,723	Apples	35,660
Roots and tubers	487,113	Coconuts	35,422
Wheat	444,534	Cabbages	35,139
Cow milk whole, fresh	427,887	Wine	33,921
Paddy rice	399,779	Millet	28,918
Maize	392,249	Hen eggs	27,456
Vegetables and melons	347,859	Rye	27,368
Sugar beets	268,722	Buffalo milk	27,209
Potatoes	225,718	Cottonseed	27,155
Barley	162,402	Watermelons	25,071
Horsemeat	142,166	Plantain	21,265
Cassava	122,134	Dry Onions	19,410
Sweet potatoes	107,254	Groundnuts in shell	18,901
Sugar, centrifugal, raw	85,431	Dry beans	14,664
Soybeans	83,481	Cotton lint	14,391
Grapes	65,255	Mangoes	14,342
Sorghum	58,435	Sunflower seed	13,174
Pigmeat	54,999	Sugar, noncentrifugal	12,362
Tomatoes	50,153	Cheese (all kinds)	11,376
Pulses	47,408	Dry peas	11,085
Beef and veal	45,350	Rapeseed	10,574
Oats	42,647	Olives	10,544
Seed cotton	42,111	Cucumbers and Gherkins	10,524
Bananas	39,254	Carrots	10,087

[a] Adapted from [35, 36]. Only commodities with annual production in excess of 10,000 (x 1000 metric tons) are listed here.

TABLE 4. FOOD AND AGRICULTURAL COMMODITY CLASSES[a]

Cereal products	Nuts and nut products
Dairy Products	Sugar and sugar products
Eggs and egg products	Beverages
Meat and meat products	Species and condiments
Fish and marine products	Plants and products
Vegetables and products	Cacao bean and products
Fruit and fruit products	Total diets
Fats and oils	Animal feeds

[a] From [37].

TABLE 5. Flowchart of General reference material collection and preparation steps[a]

PLANNING
Overall planning and development of framework

MATERIAL SELECTION

COLLECTION
Selection of collection location
Selection of collection equipment and materials
Collection and acquisition
Interim Transport and storage

PREPARATION
Selection of processing equipment and materials
Production procedure investigation
Development and organization of processing facilities
Preliminary processing
Preliminary drying
Preliminary crushing/coarse grinding
Milling/grinding
Particle size fractionation (sieving)
Homogenization
Interim collection of processed material
Interim physical characterization
Stabilization
Interim chemical characterization
Stability testing
Packaging

CHARACTERIZATION
Final physical characterization
Chemical characterization (homogeneity)

STORAGE

DOCUMENTATION

[a] From [47]