National Institute of Standards and Technology
U.S. Department of Commerce

ISOTOPE METALLOMICS QUALITY ASSURANCE PROGRAM (IMQAP) CONSORTIUM
COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT

Article 1. Introduction

This Cooperative Research and Development Agreement ("**Agreement**" or "**CRADA**") is entered into by and between ("**Collaborator**") and the National Institute of Standards and Technology ("**NIST**") (Collaborator and NIST referred to individually or collectively herein as "**Party**" or "**Parties**," as appropriate). This Agreement is effective on the date of the last authorized signature hereto ("**Effective Date**").

Article 2. Purpose and Authority

2.1 The purpose of the NIST Isotope Metallomics Quality Assurance Program ("**IMQAP**") Consortium ("**Consortium**") is to develop and evaluate measurement methods and standards, including reference materials, to support quality and comparability of metal isotope measurements for the isotope metallomics community ("**Purpose**"). The Consortium's efforts are intended to advance measurement capabilities, provide measurement assurance strategies, support the development of a variety of matrix-based RMs value-assigned for a range of stable metal isotopic compositions, and collect data to support the development of best practices and standard methods for the isotope metallomics community. NIST does not endorse any of Collaborator's products or services that are used in the course of the Consortium. Notice of the Consortium was published in the Federal Register as 90 FR 42746 on September 4, 2025.

2.2 NIST enters into this Agreement pursuant to its authority granted under 15 U.S.C. 272(b) and (c), 272a, 273, and 3710a. Collaborator enters into this Agreement with the understanding that each participant in this Consortium (each individually, "**Consortium Member**," and two or more, "**Consortium Members**") that is legally permitted to enter into a CRADA will be bound by the terms and conditions enumerated herein. If Collaborator is an agency or department of the Federal Government (such Consortium Members referred to individually and collectively herein as the "**Federal Government**"), to the extent that the terms of the attached Appendix B conflict with the terms of this Agreement, the terms of Appendix B shall control and by this reference are made a part hereof and incorporated herein. Entities that are legally prohibited or not legally authorized to enter into a CRADA may, at NIST's discretion, be permitted to participate in the Consortium under an agreement other than a CRADA with terms that will differ, as necessary, from the terms of this Agreement. Foreign governmental entities may, at NIST's discretion, be permitted to participate in the Consortium under an appropriate international agreement.

Article 3. Membership and Collaborative Research

3.1 **Membership**. Collaborator shall be a Consortium Member as of the Effective Date. Collaborator acknowledges that NIST may publicly display Collaborator's name as a Consortium Member, including on NIST's website.

3.2 **Research Plan**. The research and development activities of the Consortium are detailed in the research plan at Part III of the attached Appendix A ("**Research Plan**"), which by this reference is made a part hereof and incorporated herein. The Research Plan shall be performed on a reasonable efforts basis.

3.3 **Contributions and Personnel**. NIST shall provide administrative and scientific supervision for the Consortium and the Research Plan, and the NIST individual responsible for managing the Consortium and the Research Plan ("**NIST Consortium Manager**") is identified at Appendix A. NIST's and Collaborator's respective contributions of material and equipment and/or any other property to the Consortium and the Research Plan (respectively, "**NIST Contributions**" and "**Collaborator Contributions**") are listed in Appendix A, as well as the respective personnel

of each Party who will contribute to the Research Plan (for each Party, its "**Project Team**"). NIST cannot contribute funds to Collaborator under this Agreement; however, Collaborator may contribute funds under this Agreement. Additional terms relating to the use of NIST Contributions and Collaborator Contributions are detailed at Article 3.4(i) and Article 5, below.

3.4 **NIST Contractors**.

i. Collaborator acknowledges and agrees that some or all of the research activities described in the Research Plan may be performed by the employees, subcontractors, or consultants of non-federal organizations funded by NIST to perform such activities ("NIST Contractors"). NIST Contractors are not employees of NIST. Collaborator hereby permits NIST to share with NIST Contractors any material Collaborator Contributions and information that Collaborator provides to NIST pursuant to this Agreement. In accordance with Article 4.1, below, no Proprietary Information is expected to be exchanged by the Parties under this Agreement. Collaborator agrees that NIST shall not be responsible to Collaborator for any loss, claim, damage, or liability resulting from NIST Contractors' use of any Collaborator Contributions or information of Collaborator.

ii. Any NIST Contractors are identified in Appendix A. NIST Contractors' individual personnel may vary throughout the performance of the Research Plan. The NIST Consortium Manager may periodically request an updated list of NIST Contractors' personnel throughout the performance of the Research Plan, and such information shall be available to Collaborator at Collaborator's request. NIST is not responsible for the conduct of any NIST Contractors.

3.5 **Steering Committee**. For the purpose of discussing and planning the Research Plan and to guide and track the Consortium's technical progress, a steering committee made up of at least one representative of NIST and at least one representative of each Consortium Member ("**Steering Committee**") shall be formed. It is anticipated that each member of the Steering Committee will serve a minimum term of one year, and members may be reappointed. The Steering Committee will meet and confer with the NIST Consortium Manager in order to aid in the planning and coordination of the performance of the Research Plan, and the NIST Consortium Manager shall have final authority in all decisions.

3.6 **Conduct.** Collaborator agrees that each member of its Project Team will abide by all applicable regulations, policies, and procedures relating to safety, security, and conduct and adhere to all applicable building and restricted area access controls while on NIST premises.

Article 4. Proprietary Information and Publication of Results

4.1 **Proprietary Information**. The Parties agree that no Proprietary Information will be exchanged between the Parties under this Agreement. "**Proprietary Information**" means scientific, business, or financial information, which may embody trade secrets, when such information is developed exclusively at private expense, except if such information:

i. was in the possession of NIST and/or the Federal Government before receipt from Collaborator; or
ii. is or becomes a matter of public knowledge through no fault of NIST and/or the Federal Government; or
iii. is received by NIST and/or the Federal Government from a third party without a duty of confidentiality; or
iv. is disclosed by Collaborator to a third party without a duty of confidentiality on the third party; or
v. is independently disclosed by NIST and/or the Federal Government with Collaborator's prior written approval; or
vi. is independently developed by NIST and/or the Federal Government without reference to information disclosed hereunder.

4.2 **Research Results**. The Parties agree that all recorded data first produced by Collaborator and/or NIST in the performance of the Research Plan and during the term of this Agreement ("**Research Results**") shall be exchanged between Collaborator and NIST. NIST and Collaborator shall each have the right to use and disclose the Research Results in accordance with the terms of this Agreement and agree only to those delays in the public disclosure of the Research Results that are provided for herein. The Collaborator agrees to being identified in publications or presentations and the Research Results being linked to the Collaborator and measurement procedure(s) (i.e., method, platform, model number).

4.3 **Publication of Research Results and Collective Results.** It is the intention of the Parties to this Agreement to jointly and collaboratively draft and submit for publication the collective Research Results of the Consortium Members ("**Collective Results**"). Until the date of the first publication of the Collective Results, Collaborator agrees to maintain the confidentiality of the Collective Results and not to disclose the Collective Results to any third party who is not also a Consortium Member. NIST will provide Collaborator with at least thirty (30) days to review the proposed publication of the Collective Results to ensure that no Proprietary Information is contained therein. Collaborator may publish Collaborator's own Research Results after the first publication of the Collective Results, provided that Collaborator's publication references the Consortium.

Article 5. Material and Equipment

5.1 **Ownership & Use of Collaborator Contributions.**

i. **Collaborator Contributions**. Collaborator Contributions, as detailed in Appendix A, may include, *inter alia*, material and equipment contributed by Collaborator to the Consortium for use in the Research Plan. Collaborator grants to NIST and the Federal Government, and to other Consortium Members as NIST determines necessary, the right to use Collaborator Contributions for the purpose of the Consortium in the performance of the Research Plan. The U.S. Government shall not be responsible for damage to Collaborator Contributions or other property acquired by NIST for the purpose of the Consortium in the performance of the Research Plan. Any equipment or material purchased by NIST with funds paid by Collaborator under this Agreement shall be the property of NIST.

ii. **Equipment.** Collaborator Contributions in the form of equipment are and will at all times remain the property of Collaborator, unless the Parties agree in writing on an alternative disposition of the same. At the earlier of the conclusion of the Consortium, the expiration or termination of this Agreement, or the relevant amendment or updating of Appendix A, NIST and/or the Federal Government will return to Collaborator or request Collaborator's retrieval of all equipment at Collaborator's sole risk and expense.

iii. **Material**. Collaborator Contributions in the form of material are provided under this Agreement with no expectation of being restored to Collaborator. NIST agrees to retain control over such material, and NIST shall use, store, and dispose of the same in accordance with all applicable laws and regulations. Notwithstanding the foregoing and as detailed in the Research Plan, NIST may transfer Collaborator's material to third parties for non-profit research purposes, including the development of NIST standards and reference materials, NIST may use such material in the development of NIST standards and reference materials, and NIST may distribute such standards and reference materials that incorporate Collaborator's material. Should Collaborator wish to provide material for use in the Research Plan but prevent it from being used and distributed by NIST in the development of standards and reference materials, Collaborator must specifically identify that material to which Collaborator wishes this exception to apply in the list of Collaborator Contributions in Appendix A. NIST shall be under no obligation to accept any such excepted material from Collaborator. Should NIST accept such excepted material, Collaborator should provide it separately from any other of Collaborator Contributions and label it accordingly. At the earlier of the conclusion of the Consortium, the expiration or termination of this Agreement, or the relevant amendment or updating of Appendix A, NIST and/or the Federal Government will return to Collaborator or destroy any excepted material of Collaborator not already expended in the performance of the Research Plan.

5.2 **Ownership & Use of NIST Contributions - Material.** At its discretion, NIST Contributions may include providing to Collaborator certain material, including blinded samples of NIST Standard Reference Materials® ("**SRMs**"), NIST Reference Materials ("**RMs**"), or Research Grade Test Materials ("**RGTMs**"), in accordance with the Research Plan. Except as necessary in the case of blinded samples, NIST will identify any such material NIST Contributions in writing at the time they are provided to Collaborator. Collaborator shall use such material only in the performance of the Research Plan and not for any commercial purposes, such as screening, production, or sale, for which a commercialization license may be required. Collaborator agrees to retain control over such material and not to transfer it to others, including other Consortium Members. Collaborator shall not use the material NIST Contributions for any clinical purposes. Collaborator shall not use the material NIST Contributions in human or animal subjects other than to the extent necessary for the performance of the Research Plan, and agrees to comply with all federal rules and regulations applicable to the Research Plan and the handling of such material. NIST reserves the right to distribute any material NIST Contributions to third parties and to use them for its own purposes. At the earlier of the conclusion of the Consortium or the expiration or termination of this Agreement, Collaborator shall return, destroy, or otherwise dispose of NIST's material as mutually agreed by the Parties.

5.3 **Contributions of Consortium Members.** Collaborator and NIST agree not to sell, distribute, sublicense, modify, disassemble, reverse engineer, or otherwise alter the equipment and/or material contributed to the Consortium by one another and/or other Consortium Members, except as explicitly provided for herein.

Article 6. Intellectual Property

6.1 **Copyright in Research Results**. Any compilations or publications of Research Results or Collective Results that are prepared by federal employees are not subject to copyright in the United States, in accordance with 17 U.S.C. 105. Should Collaborator independently prepare any compilation of Research Results or other written work relating to the Consortium and/or the Research Plan, Collaborator hereby grants to the U.S. Government a paid-up, non-exclusive, irrevocable, world-wide license to reproduce or have reproduced, prepare or have prepared in derivative form, and distribute or have distributed copies of such compilation or written work for Government purposes.

6.2 **CRADA Inventions**. The Parties do not intend to conceive of any inventions in the performance of the Research Plan. The Parties agree that any invention conceived by the Parties and/or the Federal Government in the performance of the Research Plan ("**CRADA Invention**") shall be dedicated to the public domain to be freely used by all. Collaborator hereby acknowledges that NIST and/or the Federal Government, pursuant to any applicable requirements of 15 U.S.C. 3710a(b), has offered Collaborator the option to obtain a license to NIST's and/or the Federal Government's ownership in any CRADA Invention conceived by employees of NIST and/or the Federal Government, and that Collaborator affirmatively declines the option to license or acquire any interest in any such CRADA Invention. Although neither Party shall seek patent protection for any CRADA Invention, Collaborator grants to NIST and the Federal Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced any CRADA Invention that is conceived solely by Collaborator throughout the world by or on behalf of the U.S. Government.

6.3 **Intellectual Property Protection.** The Parties agree to neither seek intellectual property protection for nor attempt to enforce any intellectual property rights, including copyright, in either any CRADA Invention or any work authored in the performance of the Research Plan, including any publication of the Research Results or Collective Results, or in any other intellectual property resulting from the performance of the Research Plan. Both Parties agree not to seek patent protection for any CRADA Invention, any of which shall instead be dedicated to the public domain to be freely used by all.

6.4 **Inventions of NIST Contractors.** NIST Contractors have the right under 35 U.S.C. 200 *et seq.* to elect to retain title to their interest in any invention created by NIST Contractors' employees in accordance with 35 U.S.C. 202(c). Ownership rights stemming from any of NIST Contractors' elections are not subject to the provisions of this Agreement.

6.5 **No Other Rights.** Except as explicitly provided herein, no rights in the intellectual property of either Party that preexists this Agreement or is created outside and independent of this Agreement are transferred or conveyed hereunder.

Article 7. Expiration, Termination and Amendments

7.1 **Expiration.** This Agreement is effective as of the Effective Date and shall expire on the date listed in Appendix A.

7.2 **Termination.** Collaborator and NIST shall each have the right to terminate this Agreement, with or without cause. Termination by one Party will be effective upon thirty (30) days' written notice to the other Party. NIST may terminate this Agreement immediately in the event of either: (i) direct or indirect control of Collaborator is transferred to a foreign company or government; or (ii) if Collaborator is already controlled by a foreign company or government, that control is transferred to another foreign company or government.

7.3 **Amendments.** Should a need arise for NIST to modify the terms and conditions of this Agreement, the details of the Research Plan, or any other NIST information contained in Appendix A, NIST may propose to each Consortium Member that has signed a CRADA identical modifications in the form of a CRADA amendment. NIST will require all Consortium Members that have signed a CRADA to accept the same modified terms and conditions. NIST may terminate this Agreement immediately if such an amendment is not signed by Collaborator within the time prescribed by NIST. Except for changes to Collaborator's Project Team, should Collaborator need to modify any of the Collaborator Information at Part II of Appendix A, including a need to modify Collaborator's named Principal

Investigator, Collaborator should notify the NIST Consortium Manager of the need for such modification, and NIST will prepare an amendment to effectuate the modification. No amendment to this Agreement will be effective until fully signed by both Parties.

7.4 **Project Team Modifications.** If either Party wishes to remove and/or add personnel from/to its Project Team, such Party may request such an update using the instructions and form set forth at Appendix C, which is attached hereto. The process set forth at Appendix C is solely for changes to a Party's Project Team and does **not** include changes to either Party's Principal Investigator, the latter of which must be accomplished via the amendment process set forth above. Updates to a Party's Project Team are **not** amendments to this Agreement, and as such, the individual signing a proposed Project Team update on behalf of either Party need not be an individual who is authorized to legally bind the relevant Party. The proposed changes to the Project Team may only be implemented **after** the Party requesting the change has received a countersigned acknowledgement of the proposed change from the other Party in the form set forth at Appendix C.

Article 8. Miscellaneous

8.1 **Entire Agreement**. This Agreement constitutes the entire agreement of the Parties with respect to the matters set forth herein and supersedes and replaces in the entirety any prior understanding, written or oral, between the Parties concerning such matters.

8.2 **Counterparts.** This Agreement may be signed in one or more counterparts, each of which shall be deemed to be an original and all of which when taken together shall constitute the same Agreement. Any signed copy of this Agreement made by photocopy, facsimile, or PDF Adobe format shall be considered an original.

8.3 **NO WARRANTY. ANY MATERIAL, EQUIPMENT, SOFTWARE, SERVICE, AND/OR OTHER PROPERTY PROVIDED BY EITHER PARTY UNDER THIS AGREEMENT IS PROVIDED "AS IS" WITHOUT ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, AS TO ANY MATTER WHATSOEVER. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT, OR AS TO THE CONDITION OR OWNERSHIP OF ANY RESEARCH OR PRODUCT, WHETHER TANGIBLE OR INTANGIBLE, MADE OR DEVELOPED UNDER THIS AGREEMENT**.

8.4 **Advertising and Use of Name.** Each Party agrees not to use the name of the other Party on any commercial advertisement or promotional material for any product or service that is directly or indirectly related to this Agreement or to the Consortium without prior written approval by the other Party, except that NIST may use, disclose, and publicly display Collaborator's name to identify the Consortium Members to third parties. For the avoidance of doubt, Collaborator shall be free to display or reference any Research Results made publicly available by NIST as long as such display or reference by Collaborator does not imply endorsement by NIST, the Department of Commerce, the U.S. Government, or any subunit of the foregoing entities.

8.5 **Public Statements by Collaborator.** Collaborator may use the following text on its websites, publications, and promotional material without further approval by NIST.

"[Collaborator] is collaborating with the National Institute of Standards and Technology (NIST) in the Isotope Metallomics Quality Assurance Program (IMQAP) Consortium to develop and evaluate methods and reference materials in support of quality and comparability of metal isotope measurements in the isotope metallomics community. NIST does not evaluate commercial products under this Consortium and does not endorse any product or service used. Additional information on this Consortium can be found via Federal Register Notice 90 FR 42746."

8.6 **Export Control**. NIST and the Federal Government comply with, and Collaborator agrees to comply with, all applicable export laws and regulations, including but not limited to the International Traffic in Arms Regulations (22 C.F.R. Part 121 *et seq.*) and the Export Administration Regulations (15 C.F.R. Part 730 *et seq.*), for all equipment, materials, and information shared under this Agreement. Without limitation, Collaborator agrees that it will not in any form export, re-export, resell, ship, or divert, or cause to be exported, re-exported, resold, shipped, or diverted, directly or indirectly, and product or technical data or software furnished under this Agreement or the direct product of such technical data or software to any foreign national, firm, or country, including foreign nationals

employed by Collaborator, for which the U.S. Government or any agency thereof at the time of the conduct requires an export license or other governmental approval without first obtaining such license or approval.

8.7 **Assignment**. Except as explicitly provided for herein, neither this Agreement nor any rights or obligations of either Party hereunder shall be assigned or otherwise transferred by either Party without the prior written consent of the other Party.

8.8 **Liability & Indemnification.**

i. The U.S. Government shall not be responsible for any damage to any equipment, material, or other property, tangible or otherwise, contributed by Collaborator under this Agreement.

ii. Collaborator shall indemnify and hold harmless the U.S. Government for any loss, claim, damage, or liability of any kind caused to or by Collaborator's Project Team arising in connection with this Agreement, except to the extent that such loss, claim, damage, or liability arises from the gross negligence or wrongful acts of NIST and/or the Federal Government and/or their employees. NIST and the Federal Government's responsibility for payment of tort claims in connection with the performance of the Research Plan is governed by, *inter alia*, the Federal Tort Claims Act, the Federal Employees Compensation Act, and the Antideficiency Act.

iii. Collaborator shall indemnify and hold harmless the U.S. Government for any loss, claim, damage, or liability of any kind arising out of the use by Collaborator, or others acting on its behalf or under its authorization, of the research results of NIST and/or the Consortium Members, the Collective Results, or any other research and/or technical development or product arising from the Research Plan and/or received by Collaborator under this Agreement or out of any use, sale, or other disposition of the same by Collaborator or others acting on its behalf or with its authorization.

iv. IN NO EVENT WILL EITHER PARTY BE HELD LIABLE FOR ANY LOST REVENUES, LOST PROFITS, OR ANY INCIDENTAL, INDIRECT, CONSEQUENTIAL, SPECIAL, OR PUNITIVE DAMAGES OF ANY KIND ARISING OUT OF THIS AGREEMENT, PARTICIPATION IN THE CONSORTIUM, OR THE PERFORMANCE OF THE RESEARCH PLAN. Collaborator enters into this Agreement with the understanding that each Consortium Member has agreed or will agree to the preceding statement.

8.9 **Governing Law.** The construction validity, performance, and effect of this Agreement for all purposes shall be governed by and construed in accordance with the laws of the United States. Any legal action concerning this Agreement shall be brought in the federal district courts of the United States.

[Signatures Follow on Next Page]

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives as follows:

Signatory for Collaborator:

_____ _____
Date

Contact Information for Notices:

Signatory for NIST:

_____ _____
Jeffrey DiVietro, PhD Date
Deputy Director, NIST Technology Parternships Office

Contact Information for Notices:

NIST Technology Partnerships Office
Consortia Agreements Specialist
100 Bureau Drive, Gaithersburg, MD 20899-2200

Email: Agreements@nist.gov

Appendix A
RESEARCH PLAN AND RELATED INFORMATION

PART I. Project & NIST Information

1. **Consortium Title:** Isotope Metallomics Quality Assurance Program (IMQAP) Consortium.
(*Parties may use this title for public disclosure and management reporting.*)

2. **NIST's Principal Investigator (PI) and Consortium Manager**: (*NIST PI may change at NIST management's sole discretion.*)

   Dr. Jacqueline Mann
   NIST Chemical Sciences Division
   100 Bureau Drive, Gaithersburg, Maryland 20899
   Telephone: (301) 975-4472
   Email: jacqueline.mann@nist.gov

3. **Duration of Agreement:** From the Effective Date through November 30, 2030.

4. **NIST Project Team and Services, Facilities, Intellectual Property, Material, and/or Equipment Contributions**:

   NIST Project Team (NIST Federal Employees):
   - Jacqueline Mann (646.01)
     NIST PI and Consortium Manager
   - Melissa Phillips (646.00)
   - Steve Christopher (646.01)
   - Rebecca Kraft (646.01)
   - Korina Menking-Hoggatt (646.01)
   - John Molloy (646.01)
   - Johanna Camara (646.02)
   - Ashley Beasley Green (645.08)
   - Niksa Blonder (646.04)
   - Antonio Possolo (776.04)
   - David Newton (776.03)

   NIST Contributions: NIST will contribute measurement expertise, experimental design expertise, statistical analysis expertise, personnel, facilities, and instrumentation.

5. **Other Participants**:

   NIST Contractors:
   - To be determined and added via Amendment to the Consortium, as needed

Part II. Collaborator Information

PLEASE CHECK ALL THE APPROPRIATE BOX(ES) BELOW.

1. The Research Plan potentially involves human subjects within the meaning of 15 C.F.R. Part 27, and Collaborator agrees to take all steps required by NIST to ensure compliance with 15 C.F.R. Part 27, or involves live vertebrate animals within the meaning of 7 U.S.C. 2131 et seq. and 9 C.F.R. Parts 1, 2, and 3, and Collaborator agrees to take all steps required by NIST to ensure compliance with 9 C.F.R. Parts 1, 2, and 3, the U.S. Government Principles (USGP or Principles) for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, and, when applicable, the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals, 2015, as mandated by § 2 of the Health Research Extension Act of 1985, as codified in 42 U.S.C. 289d.

   ☐ Collaborator certifies that research potentially involving human or animal subjects shall not begin until documentation of the appropriate reviews and certifications have been provided to and approved by NIST.

2. **Collaborator Eligibility.** Collaborator certifies the following to NIST, and the Collaborator agrees to notify NIST within thirty (30) days of any change in the following:

☐ Collaborator certifies that it is incorporated or organized under the laws of one of the states or territories of the United States.

☐ Collaborator certifies that it is **not** subject to the control of any foreign government or foreign company.

☐ Collaborator certifies that it is partially or wholly owned by the following foreign government:

☐ Collaborator certifies that it is not owned by any foreign government, but it is organized under the laws of the following foreign country: .

☐ Collaborator certifies that it **is** subject to the control of the following foreign parent company in the following foreign country:

☐ Collaborator certifies that it has a manufacturing presence in the United States.

3. **Participation in other Federally Funded Projects.** Collaborator certifies that:

☐ Collaborator's participation in this Consortium is **not** related to any research supported by other Federal or NIST Funds.

☐ Collaborator's participation in this Consortium **is** related to research supported by Federal (including NIST) funding, which is identified as follows:

(*attach additional pages as necessary*)

4. **Collaborator's DUNs/UEI/TIN/VAT**:

5. **Collaborator's Principal Investigator(s)**:

6. **Collaborator Project Team and Services, Facilities, Intellectual Property, Material, and/or Equipment Contributions**:

Collaborator Project Team (include each individual's name):

All of the above-named individuals are full-time employees of Collaborator. ☐ Yes ☐ No
If no, identify non-employees and their affiliations:

If no, NIST TPO & NIST OCC consult.

Collaborator Contributions:

Part III. Research Plan

Background: Naturally-occurring stable metal isotope analytics in the health and medical sciences (Isotope Metallomics) has demonstrated high potential for clinical biomarker development, diagnostics and prognostics. Isotopic biomarkers demonstrate higher sensitivity and specificity for some pathologies compared to standard biochemical markers as they are less susceptible to complex biochemical processes than traditional molecular-based biomarkers. For instance, Copper (Cu) isotope ratios can detect breast and colorectal cancers several months earlier than traditional biomarkers and Calcium (Ca) isotopes in blood and urine are able to detect musculoskeletal diseases such as osteoporosis years before the standard method of Dual X-ray absorptiometry (DXA). Chronic diseases like diabetes, cardio-vascular diseases, and cancers are the leading cause of death worldwide. It is estimated that by 2030 the cost of these diseases will reach $47 trillion worldwide. The yearly cost of these diseases to the American medical system is more than $1 trillion and only growing larger. In response to the ever-rising costs, there is a clear movement away from the current reactive intervention-based healthcare model toward predictive, preventive, and personalized medicine (PPPM) for optimal and cost-effective healthcare. This new model will demand a new generation of biomarkers that are capable of early detection and provide for effective monitoring of targeted therapies. Isotope analytics are emerging as powerful tools for addressing this need.

Objective/Goal: The objective of the Isotope Metallomics Quality Assurance Program IMQAP is to develop and evaluate measurement methods and standards to support quality and comparability of metal isotope measurements for the isotope metallomics community with the aim of facilitating the adoption of isotope analytics by clinical laboratories and practitioners. The NIST IMQAP Consortium will focus on improving the metal isotope measurement methodologies and capabilities employed by the isotope metallomics community. The isotope metallomics stakeholders are interested in evaluating in-house methods on an array of challenging, real-world matrices (e.g., clinical) to demonstrate that their performance is comparable to that of the broader community and that their methods provide accurate results. The isotope metallomics community originate from diverse fields and few consensus or official methods have been fully recognized or evaluated in this area. The IMQAP will be a unique tool for assessing the quality of measurements and provide educational feedback about performance that can assist participants in improving laboratory operations, such as proposing method adjustments to improve accuracy or precision. Additionally, community-wide measurement challenges can be addressed through further collaborative efforts, and NIST will benefit from stakeholder participation and knowledge to guide the production and maintenance of reference materials.

Approach:

The focus of this Consortium is to evaluate, develop, and standardize methods of characterization for metal isotopes in clinical/biological materials improving overall comparability within the community and enabling Consortium Members to improve the accuracy and precision of their measurements and build the quality and confidence needed for adoption of metal isotopes as a tool in the clinical setting. The IMQAP Consortium will work together to address the following goals:

- Evaluate the applicability of current reference materials to meet the needs of the isotope metallomics community. If needed, develop new reference materials to support advancement of the isotope metallomics measurement community.
- Evaluate the suitability of current measurement approaches (e.g., repeatability and comparability) to measure the suite of relevant metal isotopes using interlaboratory exercises based on candidate reference materials (i.e., NIST Standard Reference Materials® ("**SRMs**"), NIST Reference Materials ("**RMs**") or Research Grade Test Materials ("**RGTMs**"))and/or commercial products.

- Utilize common clinical/biological materials to collect reproducibility data in support of measurement assurance and standards development.
- Propose tests(s) that can be standardized through the clinical lab standards organization or similar consensus process, using outcomes from Consortium efforts as a foundation.

NIST will organize and lead the Consortium, coordinate interlaboratory studies, test, analyze, and maintain internally and externally generated data from the Consortium. NIST will also provide expertise in production, characterization and delivery of SRMs, RMs, and RGTMs.

Collaborators will actively participate in meetings and standards related activities; participate in interlaboratory studies; generate data; supply personnel, expertise, material, equipment and/or other like contributions; contribute expertise related to the measurements and validations of metal isotopes in clinical/biological samples and their application as early detection biomarkers and treatment monitors in human health.

Joint Tasks:

- Identify the gaps in reference materials needed by the isotope metallomics stakeholders for method development and validation as well as instrument calibration.
- Perform characterization measurements for value-assignment of metal isotope composition for SRMs, RMs, and RGTMs.
- Contribute potential clinical/biological materials for development into SRMs, RMs, and RGTMs.
- Assess the results of interlaboratory studies for determination of best practices/measurement methods for metal isotope measurements.

Expected Outcomes

- A suite of clinical/biological reference materials value-assigned for various metal isotopes (e.g., Ca, Cu, Fe, Mo, Sr, Zn) will be developed.
- A series of publications and presentations related to optimal measurement methods for high accuracy and low uncertainty of metal isotopes in clinical/biological samples. All publications and presentations shall be vetted through the steering committee and NIST.
- Adoption of metal isotopes as an early detection/biomarker and treatment monitoring tool by clinical labs and practitioners.

Benefits to the Parties:

NIST:

- The Consortium will provide insight into what is actively taking place within the isotope metallomics community and where the gaps are that need to be filled to facilitate adoption by clinical labs and practitioners. Via this Consortium, NIST will have access to the current measurement approaches being used which will assist in enabling NIST to focus on areas with the most need while protecting the input of

Consortium Members. The Consortium directly supports the NIST mission to advance measurement science and develop standards that are greatly needed by this community.

- In addition, or in the alternative, certain Consortium Members may share with NIST, at their discretion, their own materials for purposes of the Research Plan, including for composition or property characterization.
- In furtherance of its standards development pursuits and the goals of this Consortium, NIST may transfer such material of Consortium Members to third parties for non-profit research purposes, NIST may use such material of Consortium Members in the development of, NIST SRMs, NIST RMs, and NIST RGTMs, and NIST may distribute to third parties the SRMs, RMs, and RGTMs that incorporate the material of Consortium Members.
- This Consortium directly advances NIST's mission to support U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life. The IMQAP Consortium will enable NIST to work directly with academic/industry partners on the emerging field of isotope metallomics to ensure delivery of the highest quality measurements and standards to facilitate the adoption of this innovative tool by clinical laboratories and practitioners.

Collaborators:

- Unique, direct relationship between standards development entity, industry, and academia.
- In part, NIST promotes the generation and use of accurate and comparable measurement methods by certifying and providing over 1100 NIST Standard Reference Materials® ("**SRMs**") and reference materials ("**RMs**") with well-characterized compositions or properties or both. SRMs and RMs are used to perform instrument calibrations, to verify the accuracy of specific measurements, and to support the development and validation of new and existing measurement methods as part of overall quality assurance programs. Collaborators will benefit from standardized methods and fit-for-purpose (e.g., matrix-matched) reference materials that help ensure the accuracy and comparability of their measurements.
- In support of the Consortium's goals, NIST may, at its discretion, share with certain Consortium Members blinded samples of NIST SRMs, RMs, and/or RGTMs, at no cost to the member. With such materials, the Consortium Members may undertake analyses using their own facilities and equipment. The results of such analyses will in turn be shared with NIST, and the aggregation of analyses will form part of the Collective Results.

Collaborator Capabilities:

Consortium members will contribute expertise in the measurement of stable metal isotopes in biological materials such as from experience as a researcher, skill with statistical analysis of stable isotope data, specifically with isotope-delta ratio data, and knowledge in the application of stable metal isotope analytics in the health and medical science as related to clinical biomarker development, diagnostics and prognostics.

Appendix B
FEDERAL AGENCY & DEPARTMENT COLLABORATOR ADDENDUM

If Collaborator is an agency or department of the Federal Government, Collaborator is entering into this Consortium through this Agreement with NIST and one or more non-Federal Consortium Members who have signed a CRADA with NIST. Collaborator enters into this Agreement subject to the following additional terms:

1. The NIST Consortium Manager is responsible for the scientific and technical conduct of the Research Plan on behalf of NIST. Collaborator's designated Principal Investigator(s) is responsible for the scientific and technical conduct of the Research Plan on behalf of Collaborator.

2. Neither NIST nor Collaborator may contribute funds to Consortium Members that are not part of the U.S. Government under this Agreement. If applicable, Collaborator may either provide funds or in-kind contributions to NIST, and Collaborator will be invoiced according to the schedule in Appendix A. Where applicable, at NIST's discretion, an in-kind contribution of equivalent value may be substituted for all or part of the membership fee. An in-kind contribution is a non-monetary contribution that may take the form of personal property (e.g., equipment and supplies), capital equipment, real property, work to be performed at either Party's facilities, and/or services that are directly beneficial, specifically identifiable, and necessary for the successful performance of the Research Plan.

3. Collaborator may terminate this Agreement immediately upon written notice to NIST.

4. The obligations to indemnify and hold harmless NIST identified at Article 8.8 do not apply to Collaborator.

5. The Research Plan potentially involves human and/or live vertebrate animal subjects and Federal Agency Collaborator agrees to take all steps required by NIST to ensure compliance with 15 C.F.R. Part 27, and 7 U.S.C. 2131 et seq. and 9 C.F.R. Parts 1, 2, and 3, respectively, and certify section 1 of Part II of Appendix A accordingly.

6. **Collaborator need not provide responses at sections 2, 3, and 4 of Part II of Appendix A.**

Appendix C
UPDATES TO NIST OR COLLABORATOR PROJECT TEAM

*To request a change to its Project Team, either Party may complete the template on the following page using the step-by-step instructions below. This template **may not** be used to update any portion of Appendix A or Appendix B or the terms and conditions of the Agreement **other than** the Project Team; specifically, it may **not** be used to update either Party's Principal Investigator or to update the list of NIST Contractors.*

Background Information

Step A. Identify Collaborator using the same name found in the original Agreement.

Step B. Identify the NIST Agreement number associated with the original Agreement (typically a sequence of numbers and letters beginning with "CN").

Step C. Identify the date on which the request is being sent to the non-requesting Party.

Requesting Party & Changes

Step D. Identify the Party requesting the update ("Requesting Party") by checking the relevant box.

Step E. Identify the change to Requesting Party's Project Team, i.e., an addition of personnel, a removal of personnel, or both, by checking the relevant box.

Step F. List the personnel that are being added to and/or removed from Requesting Party's Project Team.

Step G. List all personnel on Requesting Party's proposed updated Project Team, including each individual's name, email address, and affiliation if not a full-time employee of the requesting Party.
NOTE: NIST's Project Team will **not** include any individuals other than NIST federal employees.

Implementing Changes

Step H. Authorized Representative for Requesting Party signs and dates form to memorialize request.
NOTE: This is **not** an Amendment to the Agreement; instead, it is an update to one Party's Project Team.

Step I. Requesting Party sends completed and signed form to the non-requesting Party ("Non-Requesting Party") via email using the information provided on the signatory page of the Agreement.

Step J. Non-Requesting Party receives partially-executed form from Requesting Party. If Non-Requesting Party has no objections, Non-Requesting Party countersigns form and returns it to Requesting Party via email.
NOTE: If Non-Requesting Party objects to changes to Requesting Party's Project Team, has questions about the changes, or fails to respond Requesting Party's email with a countersigned copy of the form, the requested changes to the Project Team may **NOT** be implemented. Requesting Party may **ONLY** implement the proposed changes to its Project Team **AFTER** it is in possession of a fully-executed copy of the form.

Step K. Requesting Party receives countersigned form from Non-Requesting Party and implements acknowledged changes to Requesting Party's Project Team.

CRADA Identification Number:

Collaborator:

Notice of Project Team Update

NIST Isotope Metallomics Quality Assurance Program (IMQAP) Consortium

Agreement Details	
Collaborator	
NIST Agreement #	
Date of Request	

Party Requesting Change: ☐ NIST ☐ Collaborator

Change to Personnel: ☐ Addition ☐ Removal ☐ Both

Added Individuals	Removed Individuals
Updated Project Team	
All of the above-named individuals are full-time employees of Requesting Party. ☐ Yes . ☐ No If no, identify non-employees and their affiliations: ***If no, NIST TPO & NIST OCC consult.***	

☐ Requesting Change on Behalf of
☐ Acknowledging Change on Behalf of

NIST

Signature

Date

Name

Title

☐ Requesting Change on Behalf of
☐ Acknowledging Change on Behalf of

COLLABORATOR

Signature

Date

Name

Title