Chemistry Specifications for Chemistry Services Contractors

National Toxicology Program

Logistics and Handling

Final

August 11, 2016

1. Chemical Procurement (CP)

1. The contractor shall identify sources and availability for required chemicals or test articles.
    1. The Contractor shall check the NTP chemical inventory for each chemistry support contract to determine if the chemical(s) is/are available from the other contract laboratories prior to identifying other sources.
2. The contractor shall post the sourcing and quotation information, including the supplier certificate of analysis (COA), to the NTP IMS as it is received.
3. As directed by the COR, the Contractor shall procure the necessary quantities (for costing purposes, assume ≤ 200 kg).
4. The contractor shall post the expected delivery date to the NTP IMS as soon as it is known.
5. The contractor shall examine the material on receipt and record the condition of the material, including the shipping container(s) and contents, the shipped material (chemical, test article, etc.) and the lot number. The record shall include a photograph of the shipping container and contents, and the shipped material. A photo of the test article is not necessary unless required by the COR. All photographs of the test article shall include color and size scales.
6. For each test article received, the Contractor shall enter the chemical name, CAS registry number, source, amount received, lot number, and receipt date, along with other appropriate identifying information, into an electronic inventory system.
7. The Contractor shall store the received chemical under the manufacturer's recommended conditions until handling is complete.
8. The contractor shall report the work done in this functional activity following the reporting requirements given in Section 4. Reporting Requirements.

2.2.1.2. Logistics: Functional Activity: Chemical Handling (CH)

1. As directed by the COR the contractor shall perform some or all of the following manipulations on chemicals, test articles, or samples. Chemical Handling may be applied to any chemical or test article, including high throughput screen (HTS) chemicals, and biological or environmental samples.
    1. Homogenize the material.

2. Reduce the particle size to an appropriate size, as necessary (typically ≤ 100 µm).
3. As necessary, repackage the test material into smaller containers for easier handling at the testing laboratories.
    1. Liquids for non-inhalation studies shall be repackaged into 30-gallon stainless steel drums.
4. As necessary, prepare (≤ 100 mL) and dispense small quantities (≤ 200 uL) of test article solutions, in a solvent designated by the COR, into well-plates. Plates to be used typically have 96- or 384-wells.

2. At the request of the COR, the Contractor shall prepare and submit for COR approval, a chemical handling plan describing the proposed manipulations to be performed on the material.
3. The contractor shall visually examine the received chemical, test article, or sample and record the condition of the material, including the shipping container(s) and contents, and the shipped material (chemical, test article, dose formulation, vehicle, or biological sample).
4. All chemicals, test articles, or samples (specified material) shall be photographed upon receipt.
    1. Photographs shall include the shipping container(s) and the specified material itself.
    2. Photographs of the specified material shall be taken against a color spectrum reference card that also includes a scale to estimate particle size.
    3. Photographs shall be posted to the NTP IMS as soon as they are available.
    4. The COR may grant exceptions to the photography requirement for chemicals, test articles or samples procured in small amounts.
5. Upon receipt of a bulk test article, the Contractor shall remove a single, 100-g archive samples and sufficient (minimum 10) 5-g analytical samples to cover the time period over which the test article is anticipated to be active in the program.
    1. The archive sample shall be stored at ≤ –20ºC
    2. Analytical samples shall be stored frozen (~ –20ºC)
6. The Contractor shall complete the handling of newly procured chemicals within 2 weeks of receipt.

7. The contractor shall report the work done in this functional activity following the reporting requirements given in Section 4. Reporting Requirements.

2.2.1.3. Logistics: Functional Activity: Chemical Storage (CS)

1. As directed by the COR, the contractor shall store at its facility chemicals, test articles, dose formulations, vehicles, and/or biological samples received from NTP-designated laboratories or Investigators.
2. The contractor shall examine the material on receipt and record the condition of the material, including the shipping container(s) and contents, and the shipped material (chemical, test article, dose formulation, vehicles, or biological samples). The record shall include a photograph of the shipping container and contents, and the shipped material, including a color scale. The COR may grant exceptions to the photography requirement for chemicals, test articles or samples received in small amounts.
3. For each chemical, test article, or sample received, the Contractor shall enter the chemical name, CAS registry number, source, amount received, lot number, and receipt date, along with other appropriate identifying information, into an electronic inventory system.
4. Once receiving has been completed, the Contractor shall update the appropriate inventory with the applicable identification codes (lot number, study number, etc.) and amount received.
5. The contractor shall report the work done in this functional activity following the reporting requirements given in Section 4. Reporting Requirements.

2.2.1.4. Logistics: Functional Activity: Shipment (SHIP)

1. As directed by the COR, the contractor shall aliquot, package, and/or ship test articles, chemicals, dose formulations, vehicles, high throughput screen (HTS) chemicals and solutions, and/or biological samples to NTP-designated toxicology laboratories or Investigators. The Contractor shall notify the recipient of its intent to ship.
2. As directed by the COR, the contractor shall arrange for transport of test articles, chemicals, dose formulations, vehicles, HTS chemicals and solutions, and/or

biological samples from NTP-designated toxicology laboratories or Investigators to its facility.

3. When the purpose of the shipment is to transfer bulk test article to a toxicology laboratory in support of an in vivo toxicology test, the contractor shall include a 5-g frozen reference sample of the bulk test article with the shipment. Smaller amounts of frozen reference material can be sent with the approval of the COR.
4. The Contractor shall ensure that materials are shipped under conditions that will ensure their stability.
5. All shipments shall conform to the requirements given in Section 3. Health and Safety Minimum Requirements and all applicable local, state, and federal regulations.
6. At least 24 hours prior to shipment, the Contractor shall notify the recipient of the ship date and expected delivery date of the shipment.
7. The Material Safety Data Sheet and/or other sample information (e.g., Certificate of Analysis) as directed by the COR, shall be provided with all chemicals shipped by the Contractor to an NTP-designated laboratory.
8. The contractor shall report the work done in this functional activity following the reporting requirements given in Section 4. Reporting Requirements.

5. Protocols Development (PD)

1. General Requirements

1. The Contractor shall develop protocols for use by NTP-designated laboratories and/or investigators.
2. Protocols shall be developed for the following analysis types:
    1. Formulation Preparation (Part 5.2.1)
    2. Formulation Method Validation (Part 5.2.2)
    3. Formulation Analysis (Part 5.2.3)
    4. Chemical or Test Article Handling and Analysis (Part 5.2.4)

2. Protocol Requirements

1. Formulation Preparation

1. The Contractor shall develop a formulation mixing protocol for a designated chemical or test article in a specified vehicle.
2. The mixing protocol shall be based on the Formulation Development (FD) or Formulation Development and Validation (FDV) assignment.
3. The mixing protocol shall describe the step-by-step procedure required to prepare a uniform formulation at the volume or weight prepared for the FDV.
4. The mixing protocol shall include long-term storage requirements determined in the FDV stability evaluation.

2. Formulation Method Validation

1. The Contractor shall develop a protocol describing the validation procedure for a designated chemical or test article in a specified vehicle.
2. The validation protocol shall be based on the validation performed as part of an FDV, and shall describe the step-by-step procedure required to perform a full method validation, excluding method verification (Section 2.3, Part 3.2.1.2.2.1 – 3).

3. Formulation Analysis

1. The Contractor shall develop a protocol describing the analysis procedure for a designated chemical or test article, formulated in a specified vehicle.
2. The analysis protocol shall be based on the validated method described in Part 5.2.2, above and the formulation analysis requirements found in ether, the Specifications for the Conduct of Studies to Evaluate the Toxic and Carcinogenic Potential of Chemical, Biological, and Physical Agents in Laboratory Animals for the National Toxicology Program (NTP), January 2011, Part IV.D. Formulation Analysis. URL: http://ntp.niehs.nih.gov/ntp/Test_Info/FinalNTP_ToxCarSpecsJan2011.pdf, or the Specifications for the Conduct of Studies to Evaluate the Reproductive and Developmental Toxicity of Chemical, Biological, and Physical Agents in Laboratory Animals for the National Toxicology Program (NTP), May 2011. URL:

http://ntp.niehs.nih.gov/ntp/Test_Info/FinalNTP_ReproSpecsMay2011_508.pdf.

3. The COR shall indicate the appropriate specification to use, dependent on the study supported.

4. Chemical or Test Article Handling and Analysis

1. At the direction of the COR the contractor shall develop protocols for the receipt, storage, initial and subsequent analyses of the chemical, test article or sample, including any special chemical handling requirements.
2. Receipt and storage requirements described in the protocol shall be derived from the Comprehensive Chemical Analysis (CCA, Section 2.2, Part 1).
3. Analysis methods described in the protocol shall include procedures to establish identity upon receipt.
    1. The protocol identity method shall employ spectrophotometric, or other appropriate techniques, derived from the CCA.
4. Analysis methods used to determine purity, described in the protocol(s) shall be based on the validated dose analysis method for the chemical, test article or sample and shall include an internal standard.
    1. The protocol purity method shall employ calculation of a relative response factor (RRF) for replicate analyses of the chemical or test article and a frozen reference sample of the same lot.
    2. A mean and 95% confidence interval (CI) shall be calculated for the frozen reference sample RRF.
    3. The RRF for the chemical or test article is compared to the RRF for the frozen reference.
    4. When the RRF for the chemical or test article, lies outside the 95% CI of the frozen reference standard, the testing lab shall be instructed to contact the study director.

5. The Contractor shall perform the method as described by the draft Characterization Protocol using an aliquot of the bulk chemical, test article, or sample.

5. Additional Requirements

1. The Contractor shall report the work done in this Functional Activity following the reporting requirements given in Section 4. Reporting Requirements.