Chemistry Specifications for Chemistry Support Contractors

Division of Translational Toxicology (DTT)

Reporting Requirements

1. Introduction

A deliverable is the product of work done on this contract; the finished result of a step of work; or any unique and verifiable product, result or capability to perform a service that must be produced to complete a process, phase or project under this contract.

1. Required Reports (see below) for all contract activities shall comply with the requirements found in the DTT Chemistry Specifications with respect to submission milestones, report formats and content, and reporting timeframes.
2. All submitted electronic copies of Required Final Reports must be Section 508-compliant. A description of requirements for 508-compliance of electronic documents can be found at http://www.hhs.gov/web/508/index.html

3. Required Reports

1. Contract Management

Contract management reports consist of the Quality Management Plan (QMP), Health and Safety Plan (HASP), IT Security Plan (SSP) Standard Operating Procedures (SOPs), Chemical Inventory, and the Annual Water report.

2. Periodic Status

Periodic status reports, including a Monthly Status Report (MSR) that describes all chemicals or samples shipped or received; all reports issued and their status (draft or final); health and safety, quality assurance, information and data management, and IT security activities during the month; the status of all active assignments; and current costs for active assignments, cumulative costs for the contract, including direct and administrative costs; an Annual Report consisting of a compilation of all reports completed during the just ended contract year; and a Final Report consisting of the annual report for the last year of the contract.

3. Functional Activity (Chemistry)

Chemistry reports consist of the following report types.

1. Interim Reports consisting of preliminary results of an assignment in electronic format, usually as a data table. Interim reports are considered draft and do not need to be 508-compliant. The format for interim data reports can be found in Appendix 4.2. Data Submission Requirements.
2. Formal Reports of all work performed for each assignment for each Functional Activity. These reports consist of a Draft Final report, submitted for review and approval of the COR and a Final report, which is the COR-approved version of the report.

3. Letter Reports, which may be issued in lieu of a formal Draft Final or Final report at the direction of the COR. Letter reports are typically issued for Special Studies assignments, or canceled assignments for which work was performed and are formatted as a letter to the COR describing the work performed.

4. *Data Sheets*

   Data sheets consist of a one- or two-page summary report that lists in tabular form, the results of all analyses performed on a given chemical, test article, formulation, or sample.

5. *Other Reports*

   1. Microfiche, consisting of certified copies of all formal reports, letter reports, and data sheets; and all of the raw data supporting the information presented in the report. A PDF copy of the microfiched data must accompany the microfiche submittal. The PDF document is not required to be Section 508 compliant at this time.

   2. Spreadsheets, consisting of the final QA'd results of all biosample analyses. Typically issued for Biological Sample Analysis and Special Chemical Analysis assignments involving biosample analysis. Labeling, formatting, and data inclusion requirements for data spreadsheets can be found in Appendix 4.2. Data Submission Requirements.

   3. Any incident or unforeseeable occurrences not listed in this document, or any physical modifications to the laboratory facilities, as well as any change in personnel that might have an impact on the conduct and results of studies, shall be reported immediately to the DTT.

2. General Reporting Requirements

1. The Contractor shall ensure that the reporting timeframes given below and for each Functional Activity are met.
2. All reports submitted under this contract shall reference the contract number, the title and type of report, any applicable DTT ChemTask number, and the represented period on the first page of the report.
3. Chemistry reports shall include a Header, an Executive Summary, a signed statement from the QAU, a GLP compliance statement (where applicable), and copies of representative instrumental output to support the data presented.

1. Chemistry reports shall be signed and dated by the Principal Investigator and the responsible Task Leader.
2. Chemistry reports shall include the name of the relevant Functional Activity in the report header. See Appendix 4.1. Report Header and Cover Page Formats for more detailed information.
3. Part 4.5. Chemistry Reports gives requirements regarding report format, content and submission deadlines.

4. The Principle Investigator and the person who prepared the report shall sign financial reports and status reports.
5. All final deliverables in electronic format must be Section 508 compliant. Currently Section 508 compliance for Portable Document Format (PDF) files is defined as passing the full compliance check found in Adobe Acrobat X or above with no reported errors and meets the requirements found in the PDF checklist specified at http://www.hhs.gov./web/508/accessiblefiles/checklists.html.
6. *Posting Electronic Reports*
    1. Electronic copies of all approved final chemistry reports and data sheets shall be submitted to the DTT IMS Drop box at a URL specified by the COR.
    2. Electronic copies of contract management and status reports shall be submitted to the DTT IMS. The COR will designate a forum for these reports.
    3. Electronic copies of financial reports shall be emailed to the Contracting Officer. The Contracting Officer will provide the email address to the Contractor.
7. *Report Mailing Addresses*
    1. When required, hard copies of fiscal, status, or functional activity reports required, shall be delivered to the COR at following address and within the times specified below.

        COR

        National Institute of Environmental Health Sciences

        111 T.W. Alexander Drive

        P.O. Box 12233

        Research Triangle Park, NC 27709-2233

2. When required, hard copies of reports required for the Contracting Officer shall be addressed and delivered to the Contracting Officer at the following address:

   Contracting Officer

   National Institute of Environmental Health Sciences

   Research Contracts Branch

   111 T.W. Alexander Dr.

   P.O. Box 12233

   Research Triangle Park, NC 27709-2233

8. *Reporting Subcontracted Work*

   When reporting subcontracted work, the Contractor shall summarize the work in a report to the DTT and attach as an appendix the original report submitted to the Contractor by the Subcontractor.

3. Contract Management Reports

1. *Quality Management Plan (QMP)*

   1. The contractor shall submit a Quality Management Plan (QMP) that addresses the Quality requirements found in the DTT Chemistry Specifications, Section 1. Project Management. The QMP shall be submitted to the COR within 60 calendar days of the start of the contract.
   2. The contractor shall update the QMP on a biannual basis and resubmit the updated QMP to the COR.

2. *Health and Safety Plan (HASP)*

   The contractor shall submit a copy of their Health and Safety plan (HASP) to the COR within 60 days of the award of the Contract.

3. *IT Security Plan (SSP)*

   The contractor shall submit a copy of their IT Security (SSP) plan to the COR within 60 days of the award of the Contract

4. *Standard Operating Procedures (SOPs)*

   1. Within six (6) months of the start of the contract, the contractor shall post electronic copies of the general SOPs applicable to all of the Functional Activities covered by the DTT Chemistry Specifications, Section 2. Technical

Requirements, into the DTT IMS.

2. Subsequently, the contractor shall submit copies of these SOPs whenever they are changed.

3. It is not necessary for the contractor to submit copies of chemical-specific SOPs within 6 months of the start of the contract, as those SOPs will be submitted to the DTT IMS as needed for individual assignments.

5. *Chemical Inventory*

1. On the 15th day of each month of this contract, beginning with the second month after award, the Contractor shall provide an electronic version of the inventory of chemicals stored at their facility under this contract.

2. *Report Contents*

1. An electronic file listing the chemicals stored at the contractor's facility, including the CASRN and lot number of each chemical, and the amount on hand.

2. The electronic file format shall be tab-delimited or .xls (Excel).

3. *Delivery Requirements*

The contractor shall post a copy of the electronic file to the DTT IMS. The COR shall designate a forum to receive the electronic chemical inventory.

6. *Annual Water Analysis (AWA) Report*

1. The Contractor shall post an electronic copy of their AWA report to the DTT IMS within 30 days of the start of the contract and annually thereafter.

2. *Report Contents*

1. Report the results of the analysis, including at minimum, values for each parameter required by the AWA Functional Activity (see DTT Chemistry Specifications, Section 2, Part 6.3).

2. Include a reference to the entity performing the analysis, or to the relevant lab notebooks if performed by the contractor.

4. Periodic Status Reports

1. *Monthly Status Report (MSR)*

1. On the 15th day of the second month after the start of the contract, and each month thereafter, the Contractor shall provide a monthly status report of the

activities on the contract during the previous calendar month. The format of this status report shall conform to that given in Appendix 1 and shall include the following information:

1. A cover page listing the Report Date, the Report Title "Monthly Status Report" followed by the Contractor's contract number, and the date of the report. The middle of the page shall contain the phrase "Status Report –" followed by a number that indicates in sequential order for each month, the number of the current report; followed below by the reporting period; the contract title; the NIH contract number; and 'approved by' sign-off areas. At the bottom of the page the Contractor shall include the phrase "Submitted To:" followed below by the COR mailing address given in Part 4.2, above.
2. The report shall have page headers indicating the report title, number, date and page number.
3. MSR Section 1. Introduction shall contain an introduction stating the period of the report and the definitions of the status flags used by the Contractor in the report. For example, if the status flag "STARTED" is used in the report it could be defined as: "Work initiated during the reporting period but not completed." In addition, MSR Section 1 shall include tables that serve as keys to the program and funding codes (Table 1.1) and assignment acronyms (Table 1.2) used in the report. Refer to Part 4.8. Special Data Tables for Selected Reports, for a list of Program and Funding codes, and Functional Activity acronyms.
4. MSR Section 2. Reports Issued, shall consist of tables for the base and option years, and each exercised option listing all reports issued during the reporting period sorted by funding source and then by program supported (Tables 1 and 2). The table shall include the functional activity, chemical name, a short description of the work, the species/strain of any biosamples analyzed or toxicokinetic study performed, the report status code (Final or Interim), the Contractor's internal tracking number, and the DTT ChemTask number.
5. MSR Section 3. Materials Handling, shall consist of tables for the base and option years, and each exercised option listing all materials handling activities that have occurred during the reporting period sorted funding source, and then by program supported (Tables 1 and 2). MSR Section 3 is to be divided into subsections by activity i.e., Sample Receipt, Sample

Processing, and Shipment. The table is specific to the subsection being reported, but in general it should include the following: sample or aliquot type, species/strain (for biosamples), a brief sample description, lab assigned sample codes, lab assigned work assignment number or code, and the associated DTT ChemTask number.

6. MSR Section 4. Safety Program, describes all accidents and/or injuries, industrial hygiene, and training activities involving contract staff during the reporting period.

    1. Chemical Exposure Monitoring

        When sampling is performed, the data (e.g., sites and/or personnel sampled, strategy, methodology, duration, and results) shall be included in the MSR for that reporting period.

    2. Injury and Incident Records and Reports

        The MSR shall include a discussion of any project-related health and safety problem areas that arose during the reporting period, including copies of injury and incident records and reports. Subsequent MSRs shall include descriptions of follow-up actions taken to prevent recurrence of accidents.

    3. Hoods and Vented Enclosures

        Ventilation system evaluations performed during the reporting period shall be included in the MSR for that reporting period. Floor plan diagrams shall be included (when applicable) that indicate airflow direction by arrows with deviant directions circled

    4. Hazardous Chemical Disposal

        1. Activities and costs associated with hazardous waste disposal are also reported in this section. If surplus chemicals are disposed of, the lot number, supplier and amount shall be listed in a table in this section of the report.

7. MSR Section 5. Quality Assurance, is a summary of the activities of the QAU along with a table that summarizes the work performed on individual assignments for the base contract and all exercised options during the reporting period. MSR Section 5 includes a discussion of any project-related QA problem areas that arose during the reporting period.

8. MSR Section 6. Information Management, describes activities relating to computer facilities, software, and equipment used under the Contract, including work performed on the contractors information management system and databases. Activities include routine maintenance, software and hardware upgrades, and software development projects related to the contract. MSR Section 6 also reports project-related electronic data collection, processing, and transmission problem areas that arose during the reporting period.
9. MSR Section 7. Status Summary, consists of two subsections, sorted by funding source and program. The first subsection consists of a table that reports the status of all the work started, continued, reported, or completed during the reporting period. The table shall include columns for the following: DTT ChemTask number, Contractor assigned work number, chemical name, functional activity, species/strain or matrix for biosample analysis or toxicokinetic studies, or vehicle for formulation work; a status code, due date, and date completed.
10. MSR Section 8. Fiscal Data, reports monthly and cumulative summaries of total expenditures, direct costs, and labor incurred on the Contract during the reporting period. MSR Section 8 consists of five subsections.
    1. MSR Sections 8.1 and 8.2 report monthly and cumulative direct, administrative and total costs for the base and option years, and each active option, respectively.
        1. Direct costs are defined as labor and materials costs applied directly to completion of assignments.
        2. Administrative costs are defined as labor and materials costs applied to management of the workload, e.g., QC, QA, etc.
        3. Total cost is defined as invoiced cost.
    2. MSR Section 8.3. Active Assignment Costs, reports the costs of all the work started, continued, reported, or completed during the reporting period for the base and each exercised option in tabular form (Table 8.3.1) meeting the following criteria:
        1. Columns: DTT ChemTask number, Contractor assigned work number, chemical name, CAS number, functional activity, estimated cost for the assignment, costs incurred for the assignment during the

reporting period, and cumulative cost for the assignment since its inception.

2. Subtables: The table is split into subtables sorted by funding source and then by program.
3. Cost Data:
    1. Data in cost columns may be footnoted to clarify issues related to the cost of a particular assignment.
    2. Any assignment whose cumulative cost exceeds 150% of its estimated cost shall be flagged and footnoted.
    3. Any assignment with a cumulative cost 80% of its estimated cost shall be flagged using a flag different from the cost exceeded flag.
    4. Total costs for each program shall be reported after each subtable. Total costs for each funding source shall be reported after the last subtable for each funding source.
    5. Footnotes shall describe the reason(s) for any cost overrun.

3. MSR Section 8.4. Cost Summary, presents invoiced monthly costs for the current contract year for the base contract and each exercised option (Table 8.4.1) and for each program and funding code (Table 8.4.2). Program and Funding codes to be used are specified in Part 4.8, below.
    1. Table 8.4.1. shall include a line listing the cumulative total for the base and each exercised option along with a line listing the annual awarded amount for the base and each exercised option.
    2. Table 8.4.2. Shall include three columns for each program and funding code: Direct Costs, Administrative Costs, and Total Costs. The cost summary shall be broken out by Contract Year and each row in the table shall correspond to 1 month. The last row in each annual table shall contain the cumulative totals for each column.
    3. MSR Section 8.5. Graphs, shall present plots showing dollars and person-hours expended for a running year, which are cumulative for the contract. The plots shall be furnished for the base, all active options, and the total contract.

11. MSR Section 9. IT Security

    1. MSR Section 9 shall report on all activities specified in the Contractor's submitted System Security Plan (SSP). This information would typically include, but is not limited to the following information for the reporting period.

        1. Staff training performed
        2. Results of routine system scans
        3. Software updates/rollouts related to DTT work
        4. Reports of any IT incursions or suspicious activities
        5. Documentation of backups of DTT data performed

12. The Monthly Status Report may include other information deemed pertinent as directed by the COR.

2. Delivery Requirements

1. One copy posted to the DTT IMS.
2. Reporting Timeframe

   The Monthly Status Report shall be submitted during each month of the contract, beginning during the second month after award. The report is due within 15 calendar days following the end of each reporting period.

2. Annual Report

1. Within 60 calendar days of the end of each year of this contract, the Contractor shall submit an annual report, except for the final contract year. This report shall include the following information:

    1. A compilation of all reports completed during the just ended contract year in PDF format on electronic media. The electronic media shall be indexed and shall include PDF readers for Windows, Macintosh, and other relevant operating systems, designated by the COR, at the time of compilation.
    2. The annual report shall include a paper copy table of contents for each electronic media.
    3. Reports may include other information as directed by the COR.

2. Delivery Requirements

1. One electronic copy to the COR and one electronic copy to the Contract

Specialist.

2. Addresses to which electronic media shall be sent are given in Part 4.2.7. Report Mailing Addresses.

3. Reporting Timeframe

1. Once a year for the Base contract and Option years.
2. The first annual report shall cover the period comprising the first full 12 calendar months following the effective start date of this contract in addition to any fractional part of the initial month.
3. The annual report must be received within 60 calendar days following each reporting period.

3. Final Report

1. The Contractor shall submit a final report, which shall consist of the Annual Report for the last year of the contract.

2. Delivery Requirements

1. One electronic copy of the final report shall be sent to the COR and one electronic copy to the Contract Specialist.
2. Addresses to which electronic media shall be sent are given in Part 4.2.7. Report Mailing Addresses.

3. Reporting Timeframe

The contract final report is due on or before the expiration date of the contract.

5. Functional Activity (Chemistry) Reports

1. General Requirements

1. For all assignments performed under the contract that generate data, the contractor shall issue interim reports consisting of preliminary results of an assignment in electronic format, usually as a data table. Interim reports may be sent by email to the COR, but must be posted into the designated DTT Information Management System (DTT IMS, currently Innotas) as soon as the data becomes available. NOTE: Interim reports are considered draft and do not need to be 508-compliant.
    1. Interim data and/or reports provided by the contractor do not have to be formally quality checked by the QAU, but must be reviewed by the

laboratory staff and the Principal Investigator prior to release.

2. Interim data and/or reports shall be posted to the DTT IMS as attachments to the relevant Action Item, or copied and pasted into the description field of a DTT IMS forum topic as a reply to the relevant Action Item.

2. For all assignments performed the contractor shall issue a Draft Final Report upon completion of an assignment that describes the work performed for the assignment and details the results obtained as required herein, and in the specific report requirements for each functional activity.

    1. The draft final report shall include all the information required in Part 5.2. Content Requirements and following.

    2. Draft Final reports shall be posted to the DTT IMS as review documents attached to the relevant Action Item.

    3. If a review of the Draft Final Report by the COR results in changes to the report, the Contractor shall submit a new version of the Draft Final Report to the COR that reflects the required changes, prior to submission of the Final Report.

3. After the COR approves the Draft Final report, the Contractor shall issue a Final Report consisting of the approved Draft Final report, with a signed Quality Assurance statement, which is uploaded as a Section 508-compliant electronic document in PDF format to an Innotas project specified by the COR.

4. The COR may request that the Contractor post a PDF copy of the Final report to the DTT IMS as a document attached to the relevant assignment.

2. *Content Requirements*

1. Reports shall contain a header with information about the sample(s) being analyzed. All report headers shall contain the contract number, sample name or descriptor, lot/batch numbers, all assigned sample codes, the sample source, and the date the sample was obtained or received. Other information that may be included in the report header depends on the assignment being reported and may include any or all of the following:

    1. Analysis date(s)

    2. Shipping date

    3. Archival date

4. Archival mass
5. Number of samples collected
6. Person(s) responsible for sample collection
7. See Appendix 4.1. Report Header and Cover Page Formats in the DTT Chemistry Specifications for additional information.

2. The report shall include an Executive Summary that summarizes the work performed and the results obtained.
3. The report shall include all contractor-assigned codes, presented so that they are traceable to the original source material.
4. When analysis results for samples are reported, and whenever the contractor reports test article(s), chemical(s), or samples shipped or received, the report shall include a table identifying all of the samples shipped, received and/or analyzed. The table shall list all sample identification codes, including animal numbers, color codes, dose group codes, contractor-assigned log numbers, and/or sample source-assigned codes, etc.; and other identifying information e.g.: nominal concentrations, species/strain information, lot numbers, and/or dose route, etc.
5. The contractor shall report all procedures developed or used, including (for method development activities) the process leading up to the final method(s) and references to all applicable development report(s), substance-specific analysis protocol(s), dose analysis and/or characterization reports.
6. Analysis reports shall include a description summarizing all methods used for sampling (when applicable) and analysis, the results of the assignment, normally in tabular form, a discussion of the results of each analysis performed, including the measurement limits of the method; the mean and an estimate of sample variability (e.g. %RSD) for all replicate analyses, including replicate QC standards; a tentative identification (when the method used allows for such) for each substance measured, a written results summary, data tables, and relevant figures.
7. Analysis reports shall include a reference to the report that describes the analysis method validation. Biological Sample Analysis reports shall also include a reference to any Extended Stability Study reports performed on the target analyte in a similar matrix.

8. *Special Content Requirements for Selected Reports*

    1. Protocols Development (PD)

        1. PD reports shall include references to the formulation and/or characterization reports that are the source of the method described in the protocol.

        2. Typical analytical output of the method performed shall be included in the PD report.

    2. Chemical Reanalysis (CRA)

        1. CRA reports shall include a plot of the results for all previous analyses of the same lot, formatted as % Relative purity vs. Time.

    3. Preliminary Formulation Studies (PFS)

        1. The Contractor shall report the maximum concentration (mg/mL) at which the test article was soluble in the vehicles tested. Include the Merck Index or other reference solubility when available.

        2. The Contractor shall report the results of storing the maximum concentration solution in the refrigerator for 24 hours.

        3. For each vehicle tested, the Contractor shall report the maximum concentration (mg/mL) of test article solution, which was shown to be syringeable through an 18-, 20-, or 22-gauge gavage needle.

        4. When a solution is syringeable with an 18-gauge gavage needle, the Contractor shall report whether it is also syringeable with a 22-gauge needle.

        5. Report the observed stability of the suspension/emulsion with respect to homogeneity and test article settling rate.

        6. Use the format given in Table 3.5.1 to report the results electronically.

    4. Formulation Development (FD), Formulation Development & Validation (FDV)

        1. The effective range of the method must be specified in the report along with method validation data.

        2. FD and FDV report contents

            - Cover
            - Header

- Executive Summary
- GLP Compliance page (not required for FD reports)
- QA Statement
- Table of Contents
- Method Section
- Introduction
- Method development notes
- Description of method
- Method validation (not required for FD reports)
- Homogeneity and stability results
- Summary and Conclusion
- Acknowledgments/References
- Appendices (as required)

5. Formulation Analysis (FA, FPA)

The results of analysis for feed formulations shall be reported as milligram test article per gram vehicle. All other formulations shall be reported as milligram test article per milliliter vehicle.

Table 4.1. Formulation Analysis Results Format

Sample	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	Mean Determined Concentration ± s (%RSD)	Mean % Target	Mean %RE
0-1 0-2 0-3	0 0 0	ND ND ND	NA	NA	NA
75-1 75-2 75-3	75 75 75	75.83 75.60 75.03	75.82±0.22 (0.3%)	101.1	1.1
150-1 150-2 150-3	150 150 150	151.3 151.4 153.2	152.0±1.1 (0.7%)	101.3	1.3
300-1 300-2 300-3	300 300 300	301.8 302.7 305.9	303.5±2.2 (0.7%)	101.2	1.2
450-1 450-2 450-3	450 450 450	454.5 449.9 463.6	456.0±7.0 (1.5%)	101.3	1.3

6. Biosample Method Development and Validation (BMDV)

    1. A report of the method development activities conducted including a presentation of the validation and stability results, a conclusion regarding the acceptability of the method, and a discussion of the sample storage requirements.

    2. BMDV report contents

        - Cover
        - Header
        - Executive summary
        - GLP Compliance page
        - QA Statement
        - Table of Contents
        - Introduction/Objectives
        - Method development notes
        - Experimental design
        - Definitions
        - Method validation
            - Validation Data
            - Analysis period stability
            - Method verification (if needed to extend the standard curve range)
            - Specificity testing (if needed)
        - Storage stability
        - Acknowledgment/References
        - Appendices (as required)

7. Biological Sample Analysis (BSA)

    (Also applies to other Functional Activities for which GLP biosample analysis was performed). In addition to the formal report, the Contractor shall submit a spreadsheet to the DTT IMS, which meets the following

requirements.

1. The spreadsheet must be in Microsoft Excel, or an Excel-compatible file format.
2. The spreadsheet data shall be a true and accurate copy of the data in the final report and shall have been reviewed by the Contractor's QAU.
3. One spreadsheet shall be issued for each tissue from one species covered by the BSA assignment.
4. Within a tissue, one spreadsheet tab shall be allotted for each sex, e.g. male rat.
5. Each tab shall contain header information describing the study from which the samples to be analyzed, came. At minimum, the header shall specify:
    1. The animal species, strain and sex of sample results reported.
    2. The name of the study from which the samples came, e.g., toxicokinetic study, 2-year bioassay, etc.
    3. The date(s) the samples were received.
    4. The date(s) the samples were analyzed.
6. All individual sample data reported in any spreadsheet shall be clearly identifiable and traceable to the animal from which the sample data came; and shall be clearly labeled as to dose group. A dose is defined as a specific administered formulation concentration, and the animal's sex, and life stage, e.g., 25 mg/kg bwt, adult, non-pregnant female.
7. BSA reports shall include a reference to the study and/or source from which the samples analyzed came.

8. <u>Palatability Study (PAL)</u>
    1. The results of the palatability study including a presentation of the food and/or water consumption and body weight gains at each dose and a discussion of the implications of the data for the palatability of the dose.
    2. PAL report contents
        - Cover
        - Header

- Executive summary
- GLP Compliance page
- QA Statement
- Table of Contents
- Introduction/Objectives
    - Description of study
- Methods
    - Test article
    - Animals
    - Experimental design
- Discussion/Conclusion
- Acknowledgments/References
- Appendices (as required)

9. Preliminary Toxicokinetic Studies (PTKS)
    1. The results of the PTKS, including the resulting toxicokinetic modeling parameters and a discussion of the data, including a comparison between species, sexes, doses, and dose routes, as applicable.
    2. PTKS report contents
        - Cover
        - Header
        - Executive Summary
        - QA Statement
        - Table of Contents
        - Introduction (Objectives)
            - Description of study
        - Methods
            - Test article
            - Animals

        - Experimental design
        - Chemical analysis
        - Toxicokinetic evaluation
    - Results of the preliminary biological sample analysis (summary table)
    - Discussion/Conclusion
    - Acknowledgments/References
    - Appendices (as required)

10. Toxicokinetic Study (TKS)

    1. The results of TKS, including the resulting toxicokinetic modeling parameters and a discussion of the data, including a comparison between species, sexes, doses, and dose routes, as applicable.
    2. TKS report contents
        - Cover
        - Header
        - Executive Summary
        - GLP Compliance page
        - QA Statement
        - Table of Contents
        - Introduction/Objectives
            - Description of study
        - Methods
            - Test article
            - Animals
            - Experimental design
            - Chemical analysis
            - Toxicokinetic evaluation
        - Results
            - Chemical purity results

- Formulation analysis results
- Biological sample analysis results (summary table)

- Toxicokinetic evaluation
- Discussion/Conclusion
- Acknowledgments/References
- Appendices (as required)

11. Absorption, Distribution, Metabolism, and Excretion Study (ADMES)

1. The results of ADMES by phase. Each phase shall include discussion of the data, including a comparison between species, sexes, doses, and dose routes, as applicable.
2. ADMES report contents

- Cover
- Header
- Executive Summary
- GLP Compliance page
- QA Statement
- Table of Contents
- Introduction
- Study Objectives/Outline of Phases
  - *Phase Objective(s)*
    - *Description of phase*
  - *Methods*
    - *Test article*
      - *Radiochemical purity*
    - *Animals*
    - *Experimental design*
    - *Chemical analysis*
    - *Data evaluation*

- *Results*
    - *Chemical purity results*
    - *Formulation analysis results (when applicable)*
    - *Biological sample analysis results (summary table)*

{Repeat italicized section for each phase}

- Discussion/Conclusion
- Acknowledgments/References
- Appendices (as required)

12. Special Studies (SCA, SIS, AWA)
    1. Report titles for Special Studies reports shall include a reference to the functional activity(s) from which the report was derived when applicable, e.g., the title of a special dose formulation development report would be "Special Chemical Activity: Dose Formulation Development" followed by a short subtitle describing the work
13. HTS Chemical Procurement (HCP)
    - Cover
    - Header/Chemical Information
    - Introduction/Objectives
    - Quality Statement
    - List of all suppliers with addresses, contact phone numbers, and web addresses
    - Table 1: Supplier Order Information (Landscape)
        - Column 1: DTT Chemical name
        - Column 2: CASRN
        - Column 3: Supplier Name
        - Column 4: Supplier Lot No.
        - Column 5: Supplier Unit Size (e.g., 100 mg, 5 g, 1 kg)
        - Column 6: Amount Ordered
        - Column 7: Supplier CoA Purity

    - Column 8: Method of CoA Analysis
- Table 2: Chemicals not Ordered
    - Column 1: DTT Chemical Name
    - Column 2: CASRN
    - Column 3: Reason for not ordering, e.g., rare, not available, insoluble in DMSO, gas at 25ºC, explosive, degrades, expensive
- Conclusion
- Table 3: Summary Table
    - Column 1: Type
    - Column 2: Number
    - Row 1: "Type", "Number"
    - Row 2: "Chemicals Ordered", ##[1]
    - Row 3: "Chemicals not Ordered", ##
    - Row 4 (Sub R3): "Insoluble", ##
    - Row 5 (Sub R3): "Gas @25ºC", ##
    - Row 6 (Sub R3): "Explosive", ##
    - Row 7-nn (Sub R3)" {*Additional Conditions*}, ##
    - Final Row: "Total", ## (total of Rows 1 and 2)
- Acknowledgements/References
- Appendices (as needed)
    - Appendix 1: Supplier information for chemicals whose supplier information differs from DTT information, e.g., different name or CASRN.
        - Table A-1: Supplier Information Differs from DTT
            - Column 1: DTT Chemical name

[1] ## is the number of chemicals that fall into the specific category, e.g., the number of chemicals prepared.

- Column 2: DTT CASRN
- Column 3: Supplier
- Column 4: Supplier Chemical name
- Column 5: Supplier CASRN

14. HTS Chemical Handling (HCH)

- Cover
- Header/Chemical Information
- Executive Summary
- Quality Statement
- Table of Contents
- Introduction/Objectives
- List of equipment/solvents/reagents used
- Table 1: Chemicals Prepared and Concentrations[2]
    - Column 1: DTT Chemical name
    - Column 2: CASRN
    - Column 3: Supplier
    - Column 4: Lot Number
    - Column 5: CoA Purity
    - Column 6: DMSO Concentration
    - Column 7: Plate Address (Plate number, row and column ID)[3]
- Table 2: Chemicals Not Prepared (if necessary)
    - Column 1: DTT Chemical name
    - Column 2: CASRN
    - Column 3: Reason for not preparing (e.g., insoluble in DMSO,

[2] If multiple researchers are receiving the same chemicals, one table is appropriate, if chemicals to be prepared are different, a separate table for each researcher is required.
[3] When micro-plates (96- or 384-well) are prepared.

physical change upon dissolving, gas generation upon dissolving, etc.

- Conclusion
- Table 3: Summary Table
    - Column 1: Type
    - Column 2: Number
    - Row 1: "Type", "Number"
    - Row 2: "Chemicals Prepared", ##[4]
    - Row 3: "Chemicals not Prepared", ##
    - Row 4 (Sub R3): "Insoluble", ##
    - Row 5 (Sub R3): "Solution Change", ##
    - Row 6: (Sub R3): "Gas Generation", ##
    - Rows 7-nn (Sub R3): {*Additional Conditions*}, ##
    - Final Row: "Total", ## (total of Rows 1 and 2)

15. HTS Chemical Identification and Purity (HIPS)

- Cover
- Header/Chemical Information
    - Citation of Tables
- Executive Summary
- Quality Statement
- Table of Contents
- Introduction/Objectives
- List of equipment/chemicals/solvents/reagents used
- Method Development notes
- Experimental Design

[4] ## is the number of chemicals that fall into the specific category, e.g., the number of chemicals prepared.

- Include all analysis methods
- Table 1: Summary Table outlining chemical types

Type	Number
Mixture	
Flame Retardant	
Ionic liquid	
Etc.	
Total	1408

- Table 2: Chemical Analysis Results
  - Column 1: Tox21_ID
  - Column 2: DTT Chemical name
  - Column 3: CASRN
  - Column 4: Supplier
  - Column 5: Lot
  - Column 6: COA Purity
  - Column 7: HIPS Purity
  - Column 8: Purity Method (GC/MS, LC/MS, NMR, etc.)
- Acknowledgement/References
- Appendices (As Needed)
  - Appendix 1: Definitions of Terms used in tables, e.g., Tox21_ID, STRUCTURE_Formula, etc.
  - Appendix 2: Structure File (Due to the size of the structure file, it must be broken into multiple tables. The tables will be presented in landscape; font no smaller than Arial 10. The first 3 columns of each table will be: Tox21_ID, DTT Chemical Name, and CASRN. Columns for each table are given below:
    - Table A-1: Tox21_ID, DTT Chemical Name, CASRN, Tox21_RID, DSSTox_CID, DSSTox_Generic_SID, Tox21_Solution_ID, CoA Purity, HIPS Purity

- Table A-2: Tox21_ID, DTT Chemical Name, CAS number, STRUCTURE_Formula, STRUCTURE_MolecularWeight, STRUCTURE_ChemicalType, STRUCTURE_TestedForm_DefinedOrganic
- Table A-3: Tox21_ID, DTT Chemical Name, CAS number, STRUCTURE_Shown, Source_ChemcialName
- Table A-4: Tox21_ID, DTT Chemical Name, CAS number, TestSubstance_Description, ChemicalNote, STRUCTURE_ChemicalName_IUPAC, STRUCTURE_SMILES
- Table A-5: Tox21_ID, DTT Chemical Name, CAS number, STRUCTURE_Parent_SMILES, STRUCTURE_InChI, STRUCTURE_InChIKey, PUBCHEM_ID
- Table A-6: Tox21_ID, DTT Chemical Name, CAS number, Substance_modify_yyymmdd, Note_DTTHTS, Aliquot_Conc_(mM), Supplier, Lot_Number
- Table A-7: Tox21_ID, DTT Chemical Name, CAS number, Purity (%), DTT_Set1, DTT_SetB, DTT_SetC, Tox21_duplicate

16. Shipment (SHIP) of Multiple Chemicals or HTS Chemicals

1. In addition to the report header (see Report Formats) information, shipping reports for multiple chemicals shall contain a table (Table 1) with the following information:
   - Column 1: Code (if required)
   - Column 2: DTT-CID No. (for HTS-chemicals)
   - Column 3: Chemical Name
   - Column 4: CASRN
   - Column 5: Supplier
   - Column 6: Lot No.
   - Column 7: CoA Purity (%)
   - Column 8: Determined Purity (%) (CIPS, CCA, HIPS, etc)

- Column 9: Storage Conditions (abbreviate: RT, RF, FR, PFL (protect from light), IG (inert gas), etc.)
- Column 10: Amount Shipped (e.g., aliquot weight)

9. *Required Chemistry Report Appendices*

When appropriate, reports may include appendices containing, for example, a Substance Specific Analysis Protocol (SSAP), a method summary, a study protocol, a mixing protocol, raw data tables, computer modeling and/or simulation outputs, or other chemistry reports that support the work being reported.

1. Biological Sample Analysis reports shall include an appendix with tables of all of the raw, individual animal results, with associated animal numbers, with one table for each dose group and controls.
2. Palatability Study reports shall include appendices for the study tables and any associated chemistry reports. The study tables shall include all comply with the following:
    1. The Contractor shall provide separate tables for rat and mouse data. Each table shall include columns for:
        1. Survival, the number of animals in each dose group surviving on the last day of the study ÷ number of animals in that dose group at the start of the study. Survival shall be expressed as a fraction i.e., 4/5.
        2. Weight gain (for days 1, 7, and 14 at minimum)
        3. Mean weight change at the end of the study relative to day 0.
        4. Percent weight change at the end of the study relative to controls.
        5. Food and water consumption (g/day).
        6. Compound consumption (mg chemical/kg bwt/day, based on dose concentration and daily food or water consumption data.
    2. Tables shall contain a separate line for each dose group and controls.
3. Preliminary Toxicokinetic Study reports must include appendices for the study protocol (with all amendments and deviations); all associated chemistry reports (formulation preparation and analysis and biological sample analysis); individual animal data including biosample analysis results, food and water consumption (when applicable), and body weights;

and toxicokinetic evaluation supporting documentation e.g. output from modeling programs, etc.

4. Toxicokinetic Study reports must include appendices for the study protocol (with all amendments and deviations); all associated chemistry reports (chemical characterization, formulation preparation and analysis, and biological sample analysis); individual animal data including biosample analysis results, food and water consumption (when applicable), and body weights; and toxicokinetic evaluation supporting documentation e.g. output from modeling programs, etc.
5. ADME Study reports must include appendices for the study protocol (with all amendments and deviations); individual animal data including biosample analysis results, food and water consumption (when applicable) and body weights; and supporting documentation for all data evaluations e.g. output from modeling programs, etc.

3. *Reporting Results*

1. Reports shall present results in tabular form whenever practical.
2. Discussions of the results of any analyses shall reference accepted literature values when applicable.
3. Results of all analyses of samples, standard curves, and QC standards shall be reported. These results may be presented as summary information in the body of the report, but in that case, the raw data must be included in an appendix.
    1. Chromatographic purity assays shall report all peaks with integrated areas ≥ 0.1% of the total area and include the Contractor's best information (from literature, synthesis routes, manufacturer, etc.) on what these peaks represent.
    2. Formulation analyses reports shall flag any result that is outside the specified acceptability criteria, typically ± 10% of nominal.
    3. Vehicle analysis reports shall flag any result that exceeds the specified limit value for that vehicle.
    4. Raw data includes but is not limited to standard concentrations (nominal or prepared), responses, and found concentrations, sample responses and found concentrations, and modeling program outputs.
4. Plots of analytical results shall be reported when appropriate (e.g., standard

curves, dose-response curves, time-course data, QC plots, etc.).

5. Reports shall include representative instrument or other analytical output, which support the reported results of the analysis. This data includes chromatograms, spectra, plots or other output, which may be presented as figures, photos, tables, principle component analysis (PCA) plots, and/or heat maps, etc. All reported instrument output figures, including photographs and photomicrographs, spectra, chromatograms, etc., supplied as supporting documentation in any report, shall be clear, in focus and unambiguously labeled to allow trace-back to the source bulk chemical, test article, dose formulation, or sample from which they were produced.
6. When system suitability is performed for any analysis the report shall include a table of the results.

4. Letter Reports

Reports of Special Studies or canceled assignments for which work was performed, may be reported as letter reports, at the direction of the COR.

1. The Contractor shall describe the work performed, including (when applicable), samples received, sample and standards preparation, analytical method parameters, including instrument settings, and any calculations performed.
2. Letter reports shall be formatted as a letter to the COR describing the work performed.
    1. The Contractor shall present the results obtained from the work (if any), including summary tables, graphs, and/or figures as appropriate to illustrate the results.
    2. Letter reports are not required to have a cover page, report header, GLP compliance page, Quality Assurance Statement, Executive Summary, or Table of Contents unless specifically requested by the COR.
    3. Letter reports must be dated with their date of issuance, include the chemical name or study which they were done, the CASRN, and the ChemTask number for which the work was performed.
    4. The Contractor's Principal Investigator must sign letter reports.
3. Letter reports shall be considered Draft Final reports until they are approved by the COR and follow the same reporting process as formal Draft Final reports.

5. *Draft Final Reports*

    1. The Contractor shall provide a draft final report a specified number of calendar days after all laboratory work is completed depending on the report category (see below).
    2. Draft Final reports shall be considered final by the Contractor, but shall not be signed.
    3. The Contractor shall post electronic copies of Draft Final reports to the DTT IMS for review by the COR. If the COR requests revisions to a Draft Final report, the Contractor shall submit a new version of the Draft Final report to the DTT IMS reflecting the requested changes, prior to the submission of a Final Report.

6. *Final Reports*

    1. Once the COR approves the Draft Final report, a certified electronic copy of the final report shall be uploaded to the DTT IMS drop box.
    2. Final reports must be posted to the DTT IMS drop box folder within 1 week from the date of COR approval.

7. *Amending Reports*

    1. When an error is found in an approved Final Report, the report shall be amended to correct the error at the direction of the COR.
    2. When an error is found in an approved Final Report, the report shall be amended to correct the error at the direction of the COR. An appendix shall be included in the amended report, which indicates all of the changes made in the report, by page number.
    3. The revised final report shall be submitted to the COR for review and approval.
    4. Once the revisions are approved by the COR, the report shall be reissued as an Amended Final Report. The report date of the amended report shall reflect the date of COR approval for the revisions and the title page shall reflect its amended status. The report title shall clearly indicate that the report has been amended.
    5. Amended Final reports shall be uploaded to the DTT IMS drop box as certified electronic copies within 1 week from the date of COR approval.

8. *Reporting Deadlines*

    1. Chemistry Report deadlines for each assignment category are given below.

Deadline exceptions may be granted on a case-by-case basis with the approval of the COR.

1. Logistics and Handling: 4 weeks after all laboratory work is completed
2. Characterization: 8 weeks after all laboratory work is completed
3. Formulation: 8 weeks after all laboratory work is completed
4. Biosample Analysis: 12 weeks after all laboratory work is completed
5. Animal Studies: 8 weeks after receipt of the final biosample analysis data
6. Special Studies: 8 weeks after all laboratory work is completed
7. Letter reports: 8 weeks after the cancellation of the assignment or completion of all laboratory work.
8. HTS reports: Up to 6 months after the all laboratory work is completed, at the discretion of the COR.

6. Data Sheet Reports

1. A data sheet report consists of a one- or two-page report that lists in tabular form, the results of all analyses performed on a given bulk chemical, test article, formulation, or sample.
2. The data sheet shall include an abbreviated report header that shall minimally include the chemical or sample name, CAS number, lot number and/or source- and contractor-supplied sample codes, sample source, and sample receipt or mixing date. See Appendix 4.1. Report Header and Cover Page Formats for more information.
3. The reported results shall include:
    1. A table listing the instrument and instrument parameters used to measure the sample.
    2. For characterization activities, a table listing all substances found in the sample at an apparent concentration of ≥ 0.1%.
        1. For chromatographic-mass spectrometric data, the table shall include a peak identification number, the determined molecular mass, the retention time (in minutes), and the % Total Area value for that peak.
        2. For non-chromatographic data, the table shall include identification numbers, determined values (e.g., chemical shifts), and a % of sample

estimate, for each substance reported.

3. Figures of instrument output for the sample and reference (library or reference standard).
    1. For chromatographic non-mass spectrometric data, the figures shall include the chromatogram of the sample and the reference standard run with the samples, along with any applicable standard curves.
    2. For chromatographic-mass spectrometric data, the figures shall include the total ion chromatogram, and the sample, standard reference (if applicable) and library reference mass spectra, along with any applicable standard curves.
    3. For NMR data, the figures shall include the sample spectrum and library reference, along with any 2-D NMR data plots produced.
4. A brief summary of the sample and standards (when applicable) preparation procedure.

4. Data Sheets will be issued as an additional deliverable for the following Functional Activities:
    1. Comprehensive Chemical Analysis (CCA)
    2. Low-Level Impurity Determination (LLID)
    3. Dose Formulation Development (DFD)
    4. Biosample Method Development and Validation (BMDV)
    5. Biological Sample Analysis (BSA)
    6. Preliminary Toxicokinetic Studies (PTKS)
    7. Toxicokinetic Studies (TKS)
    8. Aborption, Distribution, Metabolism, and Excretion Studies (ADMES)
    9. Special Inhalation Study (SIS)
5. Data Sheets may be submitted in lieu of a formal chemistry report for the CIPS, MIPS, and HIPS Functional Activities.
6. Stand-alone Data Sheets shall be submitted as Draft Final reports, and shall be subject to the same reporting requirements as Chemistry Reports (Parts 4.5.5 – 4.5.8, above).

7. Additional Reporting Requirements

1. Microfiching of Data

1. Two (2) copies of all chemistry reports and all raw data supporting the reports shall be submitted on microfiche to the COR semi-annually for all approved Chemistry Reports and Data.
2. The contractor shall verify and certify that the microfiche produced represent a clear, complete copy of the original data and final report.
3. The microfiche pages shall be labeled with the chemical name, laboratory identification number, DTT program and ChemTask number for which the work was done, and the date of the report.
4. A PDF document containing all of the microfiched data for each assignment (see above) submitted on a CD, DVD, or other media specified by the COR, must accompany the microfiche submittal. NOTE: The PDF document is not required to be Section 508 compliant at this time.

2. Electronic Data Submission

1. Copies of all approved chemistry reports, including the supporting raw data and all supporting instrument outputs shall be submitted to the DTT IMS forum library associated with the DTT IMS task entry for that work, or as specified by the COR, in accordance with the requirements described below.
2. The Contractor shall verify and certify that the data submitted, represents a clear, complete copy of the original data and final approved report.
3. The uploaded data shall be labeled with the contract number, and lab-assigned work number, DTT-assigned work number, for which the work was done, the species/strain and study codes associated with the work (if applicable), the functional activity(s) for which the report was generated, and the date of the report.
4. Additional information may be included at the discretion of the Contractor.
5. Data included on the upload must be readable on all commercially available operating systems at the time of issuance. The COR shall approve file types for particular categories of data.
6. Copies of approved reports and supporting raw data shall be uploaded once the report has been approved, but not less than semi-annually.

3. *GLP Compliance Statements in Reports*

    1. GLP Compliance statements are required to be present in reports of all work conducted in compliance with FDA GLP regulations.
    2. The GLP Compliance statement shall precede the Quality Assurance Statement in all reports for which it appears.
    3. Typically, reports for the following Functional Activities will require a GLP Compliance statement:
        1. PD
        2. CCA
        3. CRA (when done in support of an DTT GLP study)
        4. FDV
        5. FA including referee analysis (when done in support of an DTT GLP study)
        6. FP (when done in support of an DTT GLP study)
        7. FPA (when done in support of an DTT GLP study)
        8. BMDV
        9. BSA (when done in support of an DTT GLP study)
        10. TKS
        11. ADMES
        12. SCA (when done in support of an DTT GLP study)

8. Special Data Tables for Selected Reports

1. *Program and Funding Codes*

    Codes are used to track contract expenditures by funding source and program supported. Each assignment will be given funding and program codes prior to commencement of work. Status reports issued by the Contractor shall reference the funding and program codes when tabulating expenses.

    1. Funding Codes shall be as listed in Table 1. Additional funding codes may be added during the course of the contract at the discretion of the COR.

Table 1. Funding Codes

Funding Source	Funding Code
National Toxicology Program	DTT
NIH AIDS	AIDS
National Institute of Environmental Health Sciences (NIEHS not DTT)	DIR
Superfund	SPR
Other Government Agency	OGA

2. Program Codes shall be as listed in Table 2. Additional program codes may be added during the course of the contract at the discretion of the COR.

Table 2. Program Codes

Program/Initiative	Program Code
Nanotechnology	NTEC
High Throughput Screening	HTS
Toxicity Testing	TOX
NIEHS In-house not DTT	DIR
AIDS	AIDS
Mold	MOLD
Other Program	OTH

2. Required Report Formats

See Appendix 4.1. Report Format Requirements for more information regarding the formatting and content requirements for the monthly status report and chemistry report headers and cover pages.