

## Environmental Protection Agency

## § 79.60

(D) Full reports for unpublished/in-house studies.

(ii) Emissions characterization appendices shall contain:

(A) Complete laboratory reports, including documentation of calibration and verification procedures;

(B) Documentation of the emissions generation procedures used; and

(C) Lists of speciated emission products and their emission rates reported in units of grams/mile.

(iii) [Reserved]

(iv) Tier 2 appendices shall contain, for each test performed:

(A) Complete protocol used;

(B) Documentation of emission generation procedures; and

(C) Complete laboratory report in compliance with the reporting standards in § 79.60, including detailed test results and conclusions, and descriptions of any problems encountered and their resolution.

(v) Laboratory certification/accreditation information, personnel credentials, and statements of compliance with the Good Laboratory Practices Standards specified in § 79.60 and the requirements in § 79.53(c)(1).

(d) *Tier 3 Report.* Subject to applicability as specified in § 79.54, each manufacturer of a designated fuel or fuel additive, or each group of such manufacturers pursuant to the provisions of § 79.56, shall submit the following information with respect to each Tier 3 test conducted for such fuels or fuel additives:

(1) The test objectives, including a summary of the reason(s) why such additional testing, beyond Tiers 1 and 2, was required;

(2) Name, address, and telephone number of each testing facility;

(3) Summary of test procedures, results and conclusions;

(4) Complete documentation of test protocols and emission generation procedures, complete laboratory reports in compliance with the reporting standards of § 79.60, detailed test results and conclusions, including references if used to support such results and conclusions, and descriptions of any problems encountered and their resolution; and

(5) Laboratory certification information, personnel credentials, and state-

ments of compliance with the Good Laboratory Practices Standards specified in § 79.60.

(e) *Availability of Information.* (1) All health and safety test data and other information concerning health and welfare effects which is submitted by any manufacturer or group pursuant to §§ 79.52(c), 79.53, or 79.54, shall be considered to be public information and shall be made available to the public by EPA upon request. A reasonable fee may be charged by EPA for copying such materials. Any manufacturer or group who claims that any information concerning the composition of a fuel or fuel additive product, or any other information, submitted under this subpart is confidential business information must state this claim in writing at the time of the submittal.

(2) To assert a business confidentiality claim concerning any information submitted under this subpart, the submitter must:

(i) Clearly mark the information as confidential at each location it appears in the submission; and

(ii) Submit with the information claimed as confidential a separate document setting forth the claim and listing each location at which the information appears in the submission.

(3) If any person subsequently requests access to information submitted under this subpart (other than health and safety test data and other information concerning health and welfare effects), and such information is subject to a claim of business confidentiality, the request and any subsequent disclosure shall be governed by the provisions of 40 CFR part 2.

[59 FR 33093, June 27, 1994, as amended at 62 FR 12572, 12576, Mar. 17, 1997]

### **§ 79.60 Good laboratory practices (GLP) standards for inhalation exposure health effects testing.**

(a) *General Provisions—(1) Scope.* (i) This section prescribes good laboratory practices (GLPs) for conducting inhalation exposure studies relating to motor vehicle emissions health effects testing under this part. These directions are intended to ensure the quality and integrity of health effects data submitted pursuant to registration regulations issued under sections 211(b) or 211(e) of

the Clean Air Act (CAA) (42 U.S.C. 7545).

(ii) This section applies to any study described by paragraph (a)(1)(i) of this section which any person conducts, initiates, or supports on or after May 27, 1994.

(iii) It is EPA's policy that all health effects data developed under sections 211(b) and (e) of CAA be in accordance with provisions of this section. If data are not developed in accordance with the provisions of this section, EPA may consider such data insufficient to evaluate the health effects of a motor vehicle's fuel or fuel additive emissions, unless the submitter provides additional information demonstrating that the data are reliable and adequate and EPA determines that the data are sufficient.

(2) *Definitions.* As used in this section, the following terms shall have the meanings specified:

*Batch* means a specific quantity or lot of a test fuel, additive/base fuel mixture, or reference substance that has been characterized according to § 79.60(f)(1)(i).

*CAA* means the Clean Air Act.

*Carrier* means any material which is combined with engine/motor vehicle emissions or a reference substance for administration to a test system. "Carrier" includes, but is not limited to, clean, filtered air, water, feed, and nutrient media.

*Control atmosphere* means clean, filtered air which is administered to the test system in the course of a study for the purpose of establishing a basis for comparison with the test atmosphere for chemical or biological measurements.

*Experimental start date* means the first date the test atmosphere is applied to the test system.

*Experimental termination date* means the last date on which data are collected directly from the study.

*Person* includes an individual, partnership, corporation, association, scientific or academic establishment, government agency, or organizational unit thereof, and any other legal entity.

*Quality assurance unit* means any person or organizational element, except the study director, designated by testing facility management to perform

the duties relating to quality assurance of the studies.

*Raw data* means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the exact copy or exact transcript may be substituted for the original source as raw data. "Raw data" may include photographs, videotape, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments.

*Reference substance* means any chemical substance or mixture, analytical standard, or material other than engine/motor vehicle emissions and/or its carrier, that is administered to or used in analyzing the test system in the course of a study. A "reference substance" is used to establish a basis for comparison with the test atmosphere for known chemical or biological measurements, *i.e.*, positive or negative control substance.

*Specimen* means any material derived from a test system for examination or analysis.

*Sponsor* means person who initiates and supports, by provision of financial or other resources, a study or a person who submits a study to EPA in response to the CAA Section 211(b) or 211(e) Fuels and Fuel Additives Registration Rule or a testing facility, if it both initiates and actually conducts the study.

*Study* means any experiment, at one or more test sites, in which a test system is exposed to a test atmosphere under laboratory conditions to determine or help predict the health effects of that exposure in humans, other living organisms, or media.

*Study completion date* means the date the final report is signed by the study director.

*Study director* means the individual responsible for the overall conduct of a study.

*Study initiation date* means the date the protocol is signed by the study director.

*Test substance* means a vapor and/or aerosol mixture composed of engine/motor vehicle emissions and clean, filtered air which is administered directly, or indirectly, by the inhalation route to a test system in a study which develops data to meet the registration requirements of CAA section 211(b) or (e).

*Test system* means any animal, micro-organism, chemical or physical matrix, to which the test, control, or reference substance is administered or added for study. This definition also includes appropriate groups or components of the system not treated with the test, control, or reference substance.

*Testing facility* means a person who actually conducts a study, *i.e.*, actually uses the test substance in a test system. "Testing facility" encompasses only those operational units that are being or have been used to conduct studies.

*TSCA* means the Toxic Substances Control Act (15 U.S.C. 2601 *et seq.*).

(3) *Applicability to studies performed under grants and contracts.* When a sponsor or other person utilizes the services of a consulting laboratory, contractor, or grantee to perform all or a part of a study to which this section applies, it shall notify the consulting laboratory, contractor, or grantee that the service is, or is part of, a study that must be conducted in compliance with the provisions of this section.

(4) *Statement of compliance or non-compliance.* Any person who submits to EPA a test in compliance with registration regulations issued under CAA section 211(b) or section 211(e) shall include in the submission a true and correct statement, signed by the sponsor and the study director, of one of the following types:

(i) A statement that the study was conducted in accordance with this section; or

(ii) A statement describing in detail all differences between the practices used in the study and those required by this section; or

(iii) A statement that the person was not a sponsor of the study, did not conduct the study, and does not know

whether the study was conducted in accordance with this section.

(5) *Inspection of a testing facility.* (i) A testing facility shall permit an authorized employee or duly designated representative of EPA, at reasonable times and in a reasonable manner, to inspect the facility and to inspect (and in the case of records also to copy) all records and specimens required to be maintained regarding studies to which this section applies. The records inspection and copying requirements shall not apply to quality assurance unit records of findings and problems, or to actions recommended and taken, except the EPA may seek production of these records in litigation or formal adjudicatory hearings.

(ii) EPA will not consider reliable for purposes of showing that a test substance does or does not present a risk of injury to health or the environment any data developed by a testing facility or sponsor that refuses to permit inspection in accordance with this section. The determination that a study will not be considered reliable does not, however, relieve the sponsor of a required test of any obligation under any applicable statute or regulation to submit the results of the study to EPA.

(6) *Effects of non-compliance.* (i) Pursuant to sections 114, 208, and 211(d) of the CAA, it shall be a violation of this section and a violation of this rule (40 CFR part 79, subpart F) if:

(A) The test is not being or was not conducted in accordance with any requirement of this part; or

(B) Data or information submitted to EPA under part 79, including the statement required by § 79.60(a)(4), include information or data that are false or misleading, contain significant omissions, or otherwise do not fulfill the requirements of this part; or

(C) Entry in accordance with § 79.60(a)(5) for the purpose of auditing test data is denied.

(ii) EPA, at its discretion, may not consider reliable for purposes of showing that a chemical substance or mixture does not present a risk of injury to health any study which was not conducted in accordance with this part. EPA, at its discretion, may rely upon such studies for purposes of showing adverse effects. The determination that

**§ 79.60**

**40 CFR Ch. I (7-1-14 Edition)**

a study will not be considered reliable does not, however, relieve the sponsor of a required test of the obligation under any applicable statute or regulation to submit the results of the study to EPA.

(iii) If data submitted in compliance with registration regulations issued under CAA section 211(b) or section 211(e) are not developed in accordance with this section, EPA may determine that the sponsor has not fulfilled its obligations under 40 CFR part 79 and may require the sponsor to develop data in accordance with the requirements of this section in order to satisfy such obligations.

(b) *Organization and Personnel*—(1) *Personnel.* (i) Each individual engaged in the conduct of or responsible for the supervision of a study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned functions.

(ii) Each testing facility shall maintain a current summary of training and experience and job description for each individual engaged in or supervising the conduct of a study.

(iii) There shall be a sufficient number of personnel for the timely and proper conduct of the study according to the protocol.

(iv) Personnel shall take necessary personal sanitation and health precautions designed to avoid contamination of test fuel and additive/base fuel mixtures, test and reference substances, and test systems.

(v) Personnel engaged in a study shall wear clothing appropriate for the duties they perform. Such clothing shall be changed as often as necessary to prevent microbiological, radiological, or chemical contamination of test systems and test, control, and reference substances.

(vi) Any individual found at any time to have an illness that may adversely affect the quality and integrity of the study shall be excluded from direct contact with test systems, fuel and fuel/additive mixtures, test and reference substances and any other operation or function that may adversely affect the study until the condition is corrected. All personnel shall be instructed to report to their immediate

supervisors any health or medical conditions that may reasonably be considered to have an adverse effect on a study.

(2) *Testing facility management.* For each study, testing facility management shall:

(i) Designate a study director as described in § 79.60(b)(3) before the study is initiated.

(ii) Replace the study director promptly if it becomes necessary to do so during the conduct of a study.

(iii) Assure that there is a quality assurance unit as described in § 79.60(b)(4).

(iv) Assure that test fuels and fuel/additive mixtures and test and reference substances have been identified as to content, strength, purity, stability, and uniformity, as applicable.

(v) Assure that personnel, resources, facilities, equipment, materials and methodologies are available as scheduled.

(vi) Assure that personnel clearly understand the functions they are to perform.

(vii) Assure that any deviations from these regulations reported by the quality assurance unit are communicated to the study director and corrective actions are taken and documented.

(3) *Study director.* For each study, a scientist or other professional person with a doctorate degree or equivalent in toxicology or other appropriate discipline shall be identified as the study director. The study director has overall responsibility for the technical conduct of the study, as well as for the interpretation, analysis, documentation, and reporting of results, and represents the single point of study control. The study director shall assure that:

(i) The protocol, including any changes, is approved as provided by § 79.60(g)(1)(i) and is followed;

(ii) All experimental data, including observations of unanticipated responses of the test system are accurately recorded and verified;

(iii) Unforeseen circumstances that may affect the quality and integrity of the study are noted when they occur, and corrective action is taken and documented;

(iv) Test systems are as specified in the protocol;

## Environmental Protection Agency

## § 79.60

(v) All applicable good laboratory practice regulations are followed; and

(vi) All raw data, documentation, protocols, specimens, and final reports are archived properly during or at the close of the study.

(4) *Quality assurance unit.* A testing facility shall have a quality assurance unit which shall be responsible for monitoring each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the regulations in this section. For any given study, the quality assurance unit shall be entirely separate from and independent of the personnel engaged in the direction and conduct of that study. The quality assurance unit shall conduct inspections and maintain records appropriate to the study.

(i) *Quality assurance unit duties.* (A) Maintain a copy of a master schedule sheet of all studies conducted at the testing facility indexed by test substance and containing the test system, nature of study, date study was initiated, current status of each study, identity of the sponsor, and name of the study director.

(B) Maintain copies of all protocols pertaining to all studies for which the unit is responsible.

(C) Inspect each study at intervals adequate to ensure the integrity of the study and maintain written and properly signed records of each periodic inspection showing the date of the inspection, the study inspected, the phase or segment of the study inspected, the person performing the inspection, findings and problems, action recommended and taken to resolve existing problems, and any scheduled date for re-inspection. Any problems which are likely to affect study integrity found during the course of an inspection shall be brought to the attention of the study director and management immediately.

(D) Periodically submit to management and the study director written status reports on each study, noting any problems and the corrective actions taken.

(E) Determine that no deviations from approved protocols or standard operating procedures were made with-

out proper authorization and documentation.

(F) Review the final study report to assure that such report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

(G) Prepare and sign a statement to be included with the final study report which shall specify the dates inspections were made and findings reported to management and to the study director.

(ii) The responsibilities and procedures applicable to the quality assurance unit, the records maintained by the quality assurance unit, and the method of indexing such records shall be in writing and shall be maintained. These items including inspection dates, the study inspected, the phase or segment of the study inspected, and the name of the individual performing the inspection shall be made available for inspection to authorized employees or duly designated representatives of EPA.

(iii) An authorized employee or a duly designated representative of EPA shall have access to the written procedures established for the inspection and may request test facility management to certify that inspections are being implemented, performed, documented, and followed up in accordance with this paragraph.

(c) *Facilities*—(1) *General.* Each testing facility shall be of suitable size and construction to facilitate the proper conduct of studies. Testing facilities which are not completely located within an indoor controlled environment shall be of suitable location/proximity to facilitate the proper conduct of studies. Testing facilities shall be designed so that there is a degree of separation that will prevent any function or activity from having an adverse effect on the study.

(2) *Test system care facilities.* (i) A testing facility shall have a sufficient number of animal rooms or other test system areas, as needed, to ensure proper separation of species or test systems, quarantine or isolation of animals or other test systems, and routine or specialized housing of animals or other test systems.

(ii) A testing facility shall have a number of animal rooms or other test system areas separate from those described in paragraph (a) of this section to ensure isolation of studies being done with test systems or test, control, and reference substances known to be biohazardous, including volatile atmospheres and aerosols, radioactive materials, and infectious agents. The animal handling facility must operate under the supervision of a veterinarian.

(iii) Separate areas shall be provided, as appropriate, for the diagnosis, treatment, and control of laboratory test system diseases. These areas shall provide effective isolation for the housing of test systems either known or suspected of being diseased, or of being carriers of disease, from other test systems.

(iv) Facilities shall have proper provisions for collection and disposal of contaminated air, water, or other spent materials. When animals are housed, facilities shall exist for the collection and disposal of all animal waste and refuse or for safe sanitary storage of waste before removal from the testing facility. Disposal facilities shall be so provided and operated as to minimize vermin infestation, odors, disease hazards, and environmental contamination.

(v) Facilities shall have provisions to regulate environmental conditions (e.g., temperature, humidity, day length, etc.) as specified in the protocol.

(3) *Test system supply/operation areas.*

(i) There shall be storage areas, as needed, for feed, bedding, supplies, and equipment. Storage areas for feed and bedding shall be separated from areas where the test systems are located and shall be protected against infestation or contamination. Perishable supplies shall be preserved by appropriate means.

(ii) Separate laboratory space and other space shall be provided, as needed, for the performance of the routine and specialized procedures required by studies.

(4) *Facilities for handling test fuels and fuel/additive mixtures and reference substances.* (i) As necessary to prevent contamination or mixups, there shall be separate areas for:

(A) Receipt and storage of the test fuels and fuel/additive mixtures and reference substances;

(B) Mixing of the test fuels, fuel/additive mixtures, and reference substances with a carrier, *i.e.*, liquid hydrocarbon; and

(C) Storage of the test fuels, fuel/additive mixtures, and reference substance/carrier mixtures.

(ii) Storage areas for test fuels and fuel/additive mixtures and reference substances and for reference mixtures shall be separate from areas housing the test systems and shall be adequate to preserve the identity, strength, purity, and stability of the substances and mixtures.

(5) *Specimen and data storage facilities.* Space shall be secured for archives for the storage and retrieval of all raw data and specimens from completed studies.

(d) *Equipment—(1) Equipment design.* Equipment used in the generation, measurement, or assessment of data and equipment used for facility environmental control shall be of appropriate design and adequate capacity to function according to the protocol and shall be suitably located for operation, inspection, cleaning, and maintenance.

(2) *Maintenance and calibration of equipment.* (i) Equipment shall be adequately inspected, cleaned, and maintained. Equipment used for the generation, measurement, or assessment of data shall be adequately tested, calibrated, and/or standardized.

(ii) The written standard operating procedures required under § 79.60(e)(1)(ii)(K) shall set forth in sufficient detail the methods, materials, and schedules to be used in the routine inspection, cleaning, maintenance, testing, calibration, and/or standardization of equipment, and shall specify, when appropriate, remedial action to be taken in the event of failure or malfunction of equipment. The written standard operating procedures shall designate the person responsible for the performance of each operation.

(iii) Written records shall be maintained of all inspection, maintenance, testing, calibrating, and/or standardizing operations. These records, containing the date of the operation, shall

describe whether the maintenance operations were routine and followed the written standard operating procedures. Written records shall be kept of non-routine repairs performed on equipment as a result of failure and malfunction. Such records shall document the nature of the defect, how and when the defect was discovered, and any remedial action taken in response to the defect.

(e) *Testing Facilities Operation*—(1) *Standard operating procedures.* (i) A testing facility shall have standard operating procedures in writing, setting forth study methods that management is satisfied are adequate to insure the quality and integrity of the data generated in the course of a study. All deviations in a study from standard operating procedures shall be authorized by the study director and shall be documented in the raw data. Significant changes in established standard operating procedures shall be properly authorized in writing by management.

(ii) Standard operating procedures shall be established for, but not limited to, the following:

- (A) Test system room preparation;
- (B) Test system care;
- (C) Receipt, identification, storage, handling, mixing, and method of sampling of test fuels and fuel/additive mixtures and reference substances;
- (D) Test system observations;
- (E) Laboratory or other tests;
- (F) Handling of test animals found moribund or dead during study;
- (G) Necropsy or postmortem examination of test animals;
- (H) Collection and identification of specimens;
- (I) Histopathology
- (J) Data handling, storage and retrieval.
- (K) Maintenance and calibration of equipment.
- (L) Transfer, proper placement, and identification of test systems.

(iii) Each laboratory or other study area shall have immediately available manuals and standard operating procedures relative to the laboratory procedures being performed. Published literature may be used as a supplement to standard operating procedures.

(iv) A historical file of standard operating procedures, and all revisions

thereof, including the dates of such revisions, shall be maintained.

(2) *Reagents and solutions.* All reagents and solutions in the laboratory areas shall be labeled to indicate identity, titer or concentration, storage requirements, and expiration date. Deteriorated or outdated reagents and solutions shall not be used.

(3) *Animal and other test system care.* (i) There shall be standard operating procedures for the housing, feeding, handling, and care of animals and other test systems.

(ii) All newly received test systems from outside sources shall be isolated and their health status or appropriateness for the study shall be evaluated. This evaluation shall be in accordance with acceptable veterinary medical practice or scientific methods.

(iii) At the initiation of a study, test systems shall be free of any disease or condition that might interfere with the purpose or conduct of the study. If during the course of the study, the test systems contract such a disease or condition, the diseased test systems shall be isolated, if necessary. These test systems may be treated for disease or signs of disease provided that such treatment does not interfere with the study. The diagnosis, authorization of treatment, description of treatment, and each date of treatment shall be documented and shall be retained.

(iv) When laboratory procedures require test animals to be manipulated and observed over an extended period of time or when studies require test animals to be removed from and returned to their housing units for any reason (e.g., cage cleaning, treatment, etc.), these test systems shall receive appropriate identification (e.g., tattoo, color code, etc.). Test system identification shall conform with current laboratory animal handling practice. All information needed to specifically identify each test system within the test system-housing unit shall appear on the outside of that unit. Suckling animals are excluded from the requirement of individual identification unless otherwise specified in the protocol.

(v) Except as specified in paragraph (e)(3)(v)(A) of this section, test animals of different species shall be housed in separate rooms when necessary. Test

animals of the same species, but used in different studies, shall not ordinarily be housed in the same room when inadvertent exposure to the test or reference substances or test system mixup could affect the outcome of either study. If such mixed housing is necessary, adequate differentiation by space and identification shall be made.

(A) Test systems that may be used in multispecies tests need not be housed in separate rooms, provided that they are adequately segregated to avoid mixup and cross-contamination.

(B) [Reserved]

(vi) Cages, racks, pens, enclosures, and other holding, rearing, and breeding areas, and accessory equipment, shall be cleaned and sanitized at appropriate intervals.

(vii) Feed and water used for the test animals shall be analyzed periodically to ensure that contaminants known to be capable of interfering with the study and reasonably expected to be present in such feed or water are not present at greater than trace levels. Documentation of such analyses shall be maintained as raw data.

(viii) Bedding used in animal cages or pens shall not interfere with the purpose or conduct of the study and shall be changed as often as necessary to keep the animals dry and clean.

(ix) If any pest control materials are used, the use shall be documented. Cleaning and pest control materials that interfere with the study shall not be used.

(x) All test systems shall be acclimatized to the environmental conditions of the test, prior to their use in a study.

(f) *Test fuels, additive/base fuel mixtures, and reference substances*—(1) *Test fuel, fuel/additive mixture, and reference substance identity.* (i) The product brand name/service mark, strength, purity, content, or other characteristics which appropriately define the test fuel, fuel/additive mixture, or reference substance shall be reported for each batch and shall be documented before its use in a study. Methods of synthesis, fabrication, or derivation, as appropriate, of the test fuel, fuel/additive mixture, or reference substance shall be documented by the sponsor or the testing

facility, and such location of documentation shall be specified.

(ii) The stability of test fuel, fuel/additive mixture, and reference substances under storage conditions at the test site shall be known for all studies.

(2) *Test fuel, additive/base fuel mixture, and reference substance handling.* Procedures shall be established for a system for the handling of the test fuel, fuel/additive mixture, and reference substance(s) to ensure that:

(i) There is proper storage.

(ii) Distribution is made in a manner designed to preclude the possibility of contamination, deterioration, or damage.

(iii) Proper identification is maintained throughout the distribution process.

(iv) The receipt and distribution of each batch is documented. Such documentation shall include the date and quantity of each batch distributed or returned.

(3) Mixtures of test emissions or reference solutions with carriers.

(i) For test emissions or each reference substance mixed with a carrier, tests by appropriate analytical methods shall be conducted:

(A) To determine the uniformity of the test substance and to determine, periodically, the concentration of the test emissions or reference substance in the mixture;

(B) When relevant to the conduct of the experiment, to determine the solubility of each reference substance in the carrier mixture before the experimental start date; and

(C) To determine the stability of test emissions or a reference solution in the test substance before the experimental start date or concomitantly according to written standard operating procedures, which provide for periodic analysis of each batch.

(ii) Where any of the components of the reference substance/carrier mixture has an expiration date, that date shall be clearly shown on the container. If more than one component has an expiration date, the earliest date shall be shown.

(iii) If a chemical or physical agent is used to facilitate the mixing of a test substance with a carrier, assurance shall be provided that the agent does

## Environmental Protection Agency

## § 79.60

not interfere with the integrity of the test.

(g) *Protocol for and conduct of a study*—(1) *Protocol*. (i) Each study shall have a written protocol that clearly indicates the objectives and all methods for the conduct of the study. The protocol shall contain but shall not be limited to the following information:

(A) A descriptive title and statement of the purpose of the study.

(B) Identification of the test fuel, fuel/additive mixture, and reference substance by name, chemical abstracts service (CAS) number or code number, as applicable.

(C) The name and address of the sponsor and the name and address of the testing facility at which the study is being conducted.

(D) The proposed experimental start and termination dates.

(E) Justification for selection of the test system, as necessary.

(F) Where applicable, the number, body weight, sex, source of supply, species, strain, substrain, and age of the test system.

(G) The procedure for identification of the test system.

(H) A description of the experimental design, including methods for the control of bias.

(I) Where applicable, a description and/or identification of the diet used in the study. The description shall include specifications for acceptable levels of contaminants that are reasonably expected to be present in the dietary materials and are known to be capable of interfering with the purpose or conduct of the study if present at levels greater than established by the specifications.

(J) Each concentration level, expressed in milligrams per cubic meter of air or other appropriate units, of the test or reference substance to be administered and the frequency of administration.

(K) The type and frequency of tests, analyses, and measurements to be made.

(L) The records to be maintained.

(M) The date of approval of the protocol by the sponsor and the dated signature of the study director.

(N) A statement of the proposed statistical method.

(ii) All changes in or revisions of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol.

(2) *Conduct of a study*. (i) The study shall be conducted in accordance with the protocol.

(ii) The test systems shall be monitored in conformity with the protocol.

(iii) Specimens shall be identified by test system, study, nature, and date of collection. This information shall be located on the specimen container or shall accompany the specimen in a manner that precludes error in the recording and storage of data.

(iv) In animal studies where histopathology is required, records of gross findings for a specimen from postmortem observations shall be available to a pathologist when examining that specimen histopathologically.

(v) All data generated during the conduct of a study, except those that are generated by automated data collection systems, shall be recorded directly, promptly, and legibly in ink. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change. In automated data collection systems, the individual responsible for direct data input shall be identified at the time of data input. Any change in automated data entries shall be made so as not to obscure the original entry, shall indicate the reason for change, shall be dated, and the responsible individual shall be identified.

(h) *Records and Reports*—(1) *Reporting of study results*. (i) A final report shall be prepared for each study and shall include, but not necessarily be limited to, the following:

(A) Name and address of the facility performing the study and the dates on which the study was initiated and was completed, terminated, or discontinued.

(B) Objectives and procedures stated in the approved protocol, including any changes in the original protocol.

(C) Statistical methods employed for analyzing the data.

(D) The test fuel, additive/base fuel mixture, and test and reference substances identified by name, chemical abstracts service (CAS) number or code number, strength, purity, content, or other appropriate characteristics.

(E) Stability, and when relevant to the conduct of the study, the solubility of the test emissions and reference substances under the conditions of administration.

(F) A description of the methods used.

(G) A description of the test system used. Where applicable, the final report shall include the number of animals or other test organisms used, sex, body weight range, source of supply, species, strain and substrain, age, and procedure used for identification.

(H) A description of the concentration regimen as daily exposure period, *i.e.*, number of hours, and exposure duration, *i.e.*, number of days.

(I) A description of all circumstances that may have affected the quality or integrity of the data.

(J) The name of the study director, the names of other scientists or professionals and the names of all supervisory personnel, involved in the study.

(K) A description of the transformations, calculations, or operations performed on the data, a summary and analysis of the data, and a statement of the conclusions drawn from the analysis.

(L) The signed and dated reports of each of the individual scientists or other professionals involved in the study, including each person who, at the request or direction of the testing facility or sponsor, conducted an analysis or evaluation of data or specimens from the study after data generation was completed.

(M) The locations where all specimens, raw data, and the final report are to be kept or stored.

(N) The statement, prepared and signed by the quality assurance unit, as described in § 79.60(b)(4)(i)(G).

(ii) The final report shall be signed and dated by the study director.

(iii) Corrections or additions to a final report shall be in the form of an amendment by the study director. The

amendment shall clearly identify that part of the final report that is being added to or corrected and the reasons for the correction or addition, and shall be signed and dated by the person responsible. Modification of a final report to comply with the submission requirements of EPA does not constitute a correction, addition, or amendment to a final report.

(iv) A copy of the final report and of any amendment to it shall be maintained by the sponsor and the test facility.

(2) *Storage and retrieval of records and data.* (i) All raw data, documentation, records, protocols, specimens, and final reports generated as a result of a study shall be retained. Specimens obtained from mutagenicity tests, wet specimens of blood, urine, feces, and biological fluids, do not need to be retained after quality assurance verification. Correspondence and other documents relating to interpretation and evaluation of data, other than those documents contained in the final report, also shall be retained.

(ii) All raw data, documentation, protocols, specimens, and interim and final reports shall be archived for orderly storage and expedient retrieval. Conditions of storage shall minimize deterioration of the documents or specimens in accordance with the requirements for the time period of their retention and the nature of the documents of specimens. A testing facility may contract with commercial archives to provide a repository for all material to be retained. Raw data and specimens may be retained elsewhere provided that the archives have specific reference to those other locations.

(iii) An individual shall be identified as responsible for the archiving of records.

(iv) Access to archived material shall require authorization and documentation.

(v) Archived material shall be indexed to permit expedient retrieval.

(3) *Retention of records.* (i) Record retention requirements set forth in this section do not supersede the record retention requirements of any other regulations in this subchapter.

(ii) Except as provided in paragraph (h)(3)(iii) of this section, documentation records, raw data, and specimens pertaining to a study and required to be retained by this part shall be archived for a period of at least ten years following the completion of the study.

(iii) Wet specimens, samples of test fuel, additive/base fuel mixtures, or reference substances, and specially prepared material which are relatively fragile and differ markedly in stability and quality during storage, shall be retained only as long as the quality of the preparation affords evaluation. Specimens obtained from mutagenicity tests, wet specimens of blood, urine, feces, biological fluids, do not need to be retained after quality assurance verification. In no case shall retention be required for a longer period than that set forth in paragraph (h)(3)(ii) of this section.

(iv) The master schedule sheet, copies of protocols, and records of quality assurance inspections, as required by § 79.60(b)(4)(iii) shall be maintained by the quality assurance unit as an easily accessible system of records for the period of time specified in paragraph (h)(3)(ii) of this section.

(v) Summaries of training and experience and job descriptions required to be maintained by § 79.60(b)(1)(ii) may be retained along with all other testing facility employment records for the length of time specified in paragraph (h)(3)(ii) of this section.

(vi) Records and reports of the maintenance and calibration and inspection of equipment, as required by § 79.60(d)(2) (ii) and (iii), shall be retained for the length of time specified in paragraph (h)(3)(ii) of this section.

(vii) If a facility conducting testing or an archive contracting facility goes out of business, all raw data, documentation, and other material specified in this section shall be transferred to the sponsor of the study for archival.

(viii) Records required by this section may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records.

#### § 79.61 Vehicle emissions inhalation exposure guideline.

(a) *Purpose.* This guideline provides additional information on methodologies required to conduct health effects tests involving inhalation exposures to vehicle combustion emissions from fuels or fuel/additive mixtures. Where this guideline and the other health effects testing guidelines in 40 CFR 79.62 through 79.68 specify differing values for the same test parameter, the specifications in the individual health test guideline shall prevail for that health effect endpoint.

(b) *Definitions.* For the purposes of this section the following definitions apply.

*Acute inhalation study* means a short-term toxicity test characterized by a single exposure by inhalation over a short period of time (at least 4 hours and less than 24 hours), followed by at least 14 days of observation.

*Aerodynamic diameter* means the diameter of a sphere of unit density that has the same settling velocity as the particle of the test substance. It is used to compare particles of different sizes, densities and shapes, and to predict where in the respiratory tract such particles may be deposited. It applies to the size of aerosol particles.

*Chronic inhalation study* means a prolonged and repeated exposure by inhalation for the life span of the test animal; technically, two years in the rat.

*Concentration* means an exposure level. Exposure is expressed as weight or volume of test aerosol/substance per volume of air, usually  $\text{mg}/\text{m}^3$  or as parts per million (ppm) over a given time period. Micrograms per cubic meter ( $\mu\text{g}/\text{m}^3$ ) or parts per billion may be appropriate, as well.

*Cumulative toxicity* means the adverse effects of repeated exposures occurring as a result of prolonged action or increased concentration of the administered test substance or its metabolites in the susceptible tissues.

*Inhalable diameter* means that aerodynamic diameter of a particle which is considered to be inhalable for the organism. It is used to refer to particles which are capable of being inhaled and may be deposited anywhere within the respiratory tract from the trachea to the alveoli.