(6) Spencer, P.S., Bischoff, M., and chaumburg, H.H. "Neuropathological ethods for the detection of neuro-xic disease." In: "Experimental and linical Neurotoxicology." Spencer, .S. and Schaumburg, H.H., eds. Balti-ore, MD: Williams and Wilkins, pp. 3–757 (1980).

(7) Hafez, E.S., ed., "Reproduction id Breeding Techniques for Labora-ry Animals." Chapter 10. Philadel-ia: Lea and Febiger. (1970).

(e) *Effective dates.* (1) The effective ate of this final rule is October 27, 89.

(2) The guidelines and other test ethods cited in this section are ref-enced here as they exist on October , 1989.

4 FR 37808, Sept. 13, 1989, as amended at 58 R 34205, June 23, 1993]

799.3175 Oleylamine.

(a) *Identification of test substance.* (1) Octadecenylamine (hereafter ODA) AS Number 112–90–3) shall be tested accordance with this section.

(2) The ODA test substance shall be least 90 percent ODA. The vehicle all be one such as mineral oil for hich there are adequate historical xicological data and which will not terfere in the test results.

(b) *Persons required to submit study lans, conduct tests, and submit data.* (1) ll persons who manufacture or proc-ss ODA (other than as an impurity) om October 7, 1987 to the end of the eimbursement period shall submit let-ers of intent to conduct testing or ex-mption applications, study plans, and/ r shall conduct tests in accordance ith part 792 of this chapter, and sub-it data as specified in this section, ubpart A and part 790 of this chapter.

(2) Persons subject to this section are ot subject to the requirements 790.50(a)(2), (5), and (6) and (b) and 790.87(a)(1)(ii) of this chapter.

(3) Persons who notify EPA of their ntent to conduct tests in compliance ith the requirements of this section ust submit plans for those tests no ater than 45 days before the initiation f each of those tests.

(4) In addition to the requirements of 790.87 (a)(2) and (3) of this chapter, PA will conditionally approve exemp-ion applications for this rule if EPA has received a letter of intent to conduct the testing from which exemption is sought and EPA has adopted test standards and schedules in a final Phase II test rule.

(c) *Health effects testing*—(1) *Developmental toxicity—(i) Required testing.* An oral developmental toxicity study shall be conducted with ODA in two mammalian species, rat and rabbit.

(ii) *Test standard.* (A) The developmental toxicity study shall be conducted with ODA in accordance with §798.4900 of this chapter except the provisions of paragraphs (e) (1)(i) and (5) of §798.4900.

(B) For purposes of this section, the following provisions also apply:

(*1*) *Species and strain.* The rat and rabbit shall be the test species. The strain shall not have low fecundity and shall preferably be characterized for its sensitivity to developmental toxins.

(*2*) *Administration of the test substance.* The route of administration shall be oral by gavage. The test substance shall be administered at approximately the same time each day.

(iii) *Reporting requirements.* (A) The developmental toxicity testing shall be completed and the final report submitted to EPA within 12 months of the date specified in paragraph (d)(1) of this section.

(B) An interim progress report shall be provided to EPA 6 months after the date specified in paragraph (d)(1) of this section.

(2) *Mutagenic effects—chromosomal aberrations*—(i) *Required testing.* (A) An oral *in vivo* mammalian bone marrow cytogenetics test: Chromosomal analysis shall be conducted for ODA.

(B) An oral rodent dominant lethal assay shall be conducted for ODA if it produces a positive result in the *in vivo* mammalian bone marrow cytogenetics test conducted pursuant to paragraph (c)(2)(i)(A) of this section.

(C) An oral rodent heritable translocation assay shall be conducted for ODA if it produces a positive result in the rodent dominant lethal assay conducted pursuant to paragraph (c)(2)(i)(B) of this section and if so required in a FEDERAL REGISTER notice or certified letter sent to test sponsors.

(ii) *Test standard.* (A)(*1*) The *in vivo* mammalian bone marrow cytogenetics

test: Chromosomal analysis shall be conducted with ODA in accordance with §798.5385 of this chapter except the provisions of paragraphs (d) (3)(i) and (5)(iii) of §798.5385.

(*2*) For purposes of this section, the following provisions also apply.

(*i*) *Species and strain.* Mice shall be used.

(*ii*) *Route of administration.* The route of exposure shall be oral by gavage.

(B)(*1*) The rodent dominant lethal assay shall be conducted with ODA in accordance with §798.5450 of this chapter except the provisions of paragraphs (d) (3)(i) and (5)(iii) of §798.5450.

(*2*) For purposes of this section, the following provisions also apply:

(*i*) *Species.* Mice shall be used as the test species. Strains with low background dominant lethality, high pregnancy frequency, and high implant numbers are recommended.

(*ii*) *Route of administration.* The route of administration shall be oral by gavage.

(C)(*1*) The rodent heritable translocation assay shall be conducted with ODA is accordance with §798.5460 of this chapter, except for the provisions of paragraphs (d) (3)(i) and (5)(iii) of §798.5460.

(*2*) For purposes of this section, the following provisions also apply.

(*i*) *Species.* Mice shall be used as the test species.

(*ii*) *Route of administration.* The route of administration shall be oral by gavage.

(iii) *Reporting requirements.* (A) The chromosomal aberration tests shall be completed and the final reports submitted to EPA as follows:

(*1*) The *in vivo* mammalian bone marrow cytogenetics test shall be completed within 14 months of the date specified in paragraph (d)(1) of this section.

(*2*) The rodent dominant lethal assay (if required) shall be completed within 26 months of the date specified in paragraph (d)(1) of this section.

(*3*) The rodent heritable translocation assay shall be completed (if required) within 25 months of EPA's notification of the test sponsor by certified letter or FEDERAL REGISTER notice under paragraph (c)(2)(i)(C) of this section that testing should be initiated.

(B) Interim progress reports shall be provided to EPA at 6-month intervals for each test beginning 6 months after the date specified in paragraph (d)(1) of this section or notification that testing should be initiated under paragraph (c)(2)(i)(C) of this section, until submission of the final report.

(3) *Mutagenic effects—gene mutations*—(i) *Required testing.* (A) A detection of gene mutation in somatic cells in culture assay shall be conducted with ODA.

(B) An oral sex linked recessive lethal test in *Drosophila melanogaster* shall be conducted for ODA if it produces a positive result in the detection of gene mutation assay in somatic cells in culture conducted pursuant to paragraph (c)(3)(i)(A) of this section.

(C) A mouse visible specific locus test (MVSL) or a mouse biochemical specific locus test (MBSL) shall be conducted for ODA if it produces a positive result in the sex-linked recessive lethal test in *Drosophila melanogaster* conducted pursuant to paragraph (c)(3)(i)(B) of this section and if so required in a FEDERAL REGISTER notice or certified letter sent to test sponsors.

(ii) *Test standard.* (A) (*1*) The detection of gene mutations in somatic cells in culture shall be conducted with ODA in accordance with §798.5300 of this chapter, except for the provisions of paragraphs (d)(3) (i), (ii) and (4) of §798.5300.

(*2*) For purposes of this section, the following provisions also apply:

(*i*) *Types of cells used in the assay.* ODA shall be tested in L5178Y mouse lymphoma cells. Cells should be checked for *Mycoplasma* contamination and may be periodically checked for karyotype stability.

(*ii*) *Cell growth and maintenance.* Alternative dosing procedures consisting of suspension cultures or roller-bottle incubation shall be used. Appropriate incubation conditions (CO_2 concentrations, temperature, and humidity) shall be used.

(*iii*) *Metabolic activation.* The metabolic activation system shall be derived from the postmitochondrial fraction (S–9) of livers from rats pretreated with Aroclor 1254. Cells shall be ex-

)sed to test substance both in the 'esence and absence of an appropriate etabolic activation system.

(B) (*1*) The sex-linked recessive lethal st in *Drosophila melanogaster* shall be)nducted with ODA in accordance ith §798.5275 of this chapter except for ıe provisions of paragraph (d)(5)(iii) of 798.5275.

(*2*) For purposes of this section, the llowing provisions also apply:

(*i*) *Route of administration.* The route administration shall be oral.

(*ii*) [Reserved]

(C)(*1*) If required, the MVSL or MBSL ıall be conducted with ODA in accordıce with §§798.5200 or 798.5195 of this ıapter, respectively, except for the ovisions of paragraph (d)(5)(iii) of ıch of these sections.

(*2*) For purposes of this section, the llowing provision also applies.

(*i*) *Route of administration.* The route exposure shall be oral by gavage.

(*ii*) [Reserved]

(iii) *Reporting requirements.* (A) Gene ıutation tests shall be completed and ıe final reports submitted to EPA as)llows:

(*1*) The detection of gene mutations ı somatic cells in culture shall be ompleted within 10 months of the date pecified in paragraph (d)(1) of this sec- ion.

(*2*) The sex-linked recessive lethal est in *Drosophila melanogaster* (if reuired) shall be completed within 22 ıonths of the date specified in pararaph (d)(1) of this section.

(*3*) The MVSL or MBSL shall be comleted and the final report submitted o EPA within 51 months of EPA's noification of the test sponsor by certified letter or FEDERAL REGISTER notice that testing shall be initiated.

(B) Interim progress reports shall be rovided to EPA at 6-month intervals or each test beginning 6 months after he date specified in paragraph (d)(1) of his section until submission of the inal report.

(C) Progress reports shall be submitted to EPA for the MVSL or the MBSL t 6-month intervals, the first of which s due within 6 months of EPA's notifiation of the test sponsor that testing hall be initiated.

(4) *Oncogenicity*—(i) *Required testing.* ın oncogenicity bioassay shall be conducted orally for ODA if positive results occur in any of the following tests and if so required in a FEDERAL REGISTER notice or certified letter sent to test sponsors.

(A) *In vivo* mammalian bone marrow cytogenetics tests conducted pursuant to paragraph (c)(2)(i)(A) of this section.

(B) Detection of gene mutation in somatic cells in culture assay conducted pursuant to paragraph (c)(3)(i)(A) of this section.

(C) Sex linked recessive lethal test in *Drosophila melanogaster,* conducted pursuant to paragraph (c)(3)(i)(B) of this section.

(ii) *Test standard.* (A)(*1*) The oncogenicity bioassay shall be conducted with ODA in accordance with §798.3300 of this chapter, except for the provisions of paragraphs (b)(1)(i) and (6) of §798.3300.

(*2*) For purposes of this section, the following provisions also apply:

(*i*) *Species and strain.* ODA shall be tested in both rats and mice. Commonly used laboratory strains shall be employed.

(*ii*) *Administration of the test substance.* The route of administration shall be oral by gavage.

(iii) *Reporting requirements.* (A) The oncogenicity bioassay shall be completed and the final report submitted to EPA within 53 months of EPA's notification of the test sponsor by certified letter or FEDERAL REGISTER notice under paragraph (c)(4)(i) of this section that testing should be initiated.

(B) Interim progress reports shall be provided at 6-month intervals beginning 6 months after the notification under paragraph (c)(4)(i) of this section until submission of the final report.

(d) *Effective dates.* (1) The effective date of this rule is October 7, 1987, except for the provisions of paragraphs (c)(1)(ii) and (c)(1)(iii), (c)(2)(ii) and (c)(2)(iii); (c)(3)(ii)(A), and (c)(3)(ii)(B), (c)(3)(iii)(A)(*1*), (c)(3)(iii)(A)(*2*), (c)(3)(iii)(B), (c)(4)(ii) and (c)(4)(iii), which are effective on January 17, 1989.

(2) Paragraphs (c)(3)(i)(C), (c)(3)(ii)(C), (c)(3)(iii)(A)(*3*), and (c)(3)(iii)(C) of this section are effective May 21, 1990.

(3) The guidelines and other test methods cited in this section are ref-

erenced as they exist on the effective date of the final rule.

[52 FR 31969, Aug. 24, 1987, as amended at 53 FR 48546, Dec. 1, 1988; 55 FR 12643, Apr. 5, 1990; 58 FR 34205, June 23, 1993]

§ 799.3300 Unsubstituted phenylenediamines.

(a) *Identification of test substance.* (1) The unsubstituted phenylenediamines (pda's), *para*-phenylenediamine (*p*-pda, CAS No. 106–50–3), or its sulfate salt (*p*-pda.H_2SO_4, CAS No. 1624–57–75), *meta*-phenylenediamine (*m*-pda, CAS No. 108–45–2), or its sulfate salt (*m*-pda.H_2SO_4, CAS No. 54–17–08), and *ortho*-phenylenediamine (*o*-pda, CAS No. 95–54–5) shall be tested in accordance with this section.

(2) *p*-Pda, *m*-pda, and *o*-pda of at least 98 percent purity shall be used as the test substances. Either the hydrochloride or sulfate salt of *m*-pda shall be used as the test substances. Either the hydrochloride or sulfate salt of *m*-pda shall be used as a test substance in the oncogenicity test in paragraph (c)(2) of this section if the free base proves to be unstable under the conditions of this study. Either the hydrochloride or sulfate salt of *o*-pda, *p*-pda, or *m*-pda shall be used as a test substance in the 90-day subchronic neurotoxicity studies in paragraph (c)(3)(B) of this section if the free base proves to be unstable under the conditions of these studies. The salt(s) shall be of at least 98 percent purity.

(b) *Persons required to submit study plans, conduct tests, and submit data.* (1) All persons who manufacture (including import or by-product manufacture) or process *m*-pda or *m*-pda.H_2SO_4, or intend to manufacture or process *m*-pda or *m*-pda.H_2SO_4, after the effective date of this rule to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in paragraphs (c), (d), and (e) of this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(2) All persons who manufacture (including import or by-product manufacture) or process *p*-pda, or *p*-pda.H_2SO_4, or intend to manufacture or process *p*-pda, or *p*-pda H_2SO_4, after the effective date of this rule to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in paragraphs (c)(3), (d), and (e) of this section, subpart A of this part and parts 790 and 792 of this chapter for single-phase rulemaking.

(3) All persons who manufacture (including import or by-product manufacture) or process *o*-pda, or intend to manufacture or process *o*-pda after the effective date of this rule to the end of the reimbursement period shall submit letters of intent to test, submit study plans, conduct tests, and submit data, or submit exemption applications as specified in paragraphs (c)(3), (d), and (e) of this section, subpart A of this part, and parts 790 and 792 of this chapter for single-phase rulemaking.

(c) *Health effects testing*—(1) *Mutagenicity testing*—(i) *Required testing.* (A) The sex-linked recessive lethal (SLRL) assay shall be conducted, by injection, in *Drosophila melanogaster* with *m*-pda in accordance with § 798.5275 of this chapter.

(B) If the SLRL assay conducted pursuant to paragraph (c)(1)(i)(A) of this section is positive, either the mouse visible specific locus test (MVSL) or the mouse biochemical specific locus test (MBSL) shall be conducted for *m*-pda by gavage in accordance with §§ 798.5200 or 798.5195 of this chapter, if after public program review, EPA issues a FEDERAL REGISTER notice or sends a certified letter to the test sponsor(s) specifying that testing shall be initiated. The test sponsor shall notify EPA of its choice in writing in its first interim report.

(C) The mouse bone marrow cytogenetics: micronucleus (MBMC) assay shall be conducted on *m*-pda in accordance with § 798.5395 of this chapter.

(D) If the MBMC assay conducted pursuant to paragraph (c)(1)(i)(C) of this section is positive, the dominant lethal assay (DL) in mice shall be conducted on *m*-pda pursuant to § 798.5450 of this chapter.

(E) If the DL conducted pursuant to paragraph (c)(1)(i)(D) of this section is positive, heritable translocation (HT) testing in the mouse on *m*-pda shall be conducted pursuant to § 798.5460 of this