

## Appendix II: Testing and Toxicology Studies in FY 2019

The NTP testing program evaluates substances for a variety of health-related effects, generally using rodent models. For each test article, a study team develops an appropriate testing strategy to address the identified research needs, and a project review committee evaluates the strategy. Reports and summaries of NTP toxicity studies, including carcinogenicity and effects on development and reproduction, are available on the NTP website.

The following Division of NTP branches at NIEHS are involved in the testing program: Biomolecular Screening Branch, led by acting chief Warren Casey, Ph.D.; Cellular and Molecular Pathology Branch, led by Robert Sills, D.V.M., Ph.D.; NTP Laboratory, led by acting chief B A. Merrick, Ph.D.; Program Operations Branch, led by Michelle Hooth, Ph.D.; and Toxicology Branch, led by Nigel Walker, Ph.D.

Studies initiated, ongoing, or completed in 2019 are listed in this section.

### Disposition, Metabolism, and Toxicokinetic Studies

Complete dosimetry of a chemical or physical agent describes its [absorption, distribution, metabolism, and excretion](#) in the body of both humans and test animals at differing levels of exposure, of all ages, via several routes of exposure, and under varying genetic backgrounds. Substances evaluated during FY 2019 are listed below.

#### *Disposition, Metabolism, and Toxicokinetics Studies during FY 2019*

Test Article	CASRN*	Species	Route	Status	Study Scientist
2-((1-(4-Phenoxyphenoxy)propan-2-yl)oxy)pyridine	95737-68-1	Rats	Gavage	Ongoing	Barry McIntyre
2-((1-(4-Phenoxyphenoxy)propan-2-yl)oxy)pyridine	95737-68-1	Rabbits	Gavage	Ongoing	Barry McIntyre
2-Ethylhexyl p-Methoxycinnamate	5466-77-3	Rats	Dosed-feed	Completed	Suramya Waidyanatha
alpha-Pinene	80-56-8	Rats, mice	Inhalation	Planned	Cynthia Rider
Bisphenol AF	1478-61-1	Rats, mice	Gavage	Ongoing	Vicki Sutherland
Bisphenol AF	1478-61-1	Rats, mice	Intravenous	Ongoing	Vicki Sutherland
Bisphenol AF	1478-61-1	Rats, mice	Gavage	Completed	Suramya Waidyanatha
Bisphenol AF	1478-61-1	Rats, mice	Intravenous	Completed	Suramya Waidyanatha
Bisphenol AF	1478-61-1	Rats, mice	Dosed-feed	Ongoing	Suramya Waidyanatha
Bisphenol S	80-09-1	Rats, mice	Gavage	Completed	Suramya Waidyanatha

Test Article	CASRN*	Species	Route	Status	Study Scientist
Bisphenol S	80-09-1	Rats, mice	Intravenous	Completed	Suramya Waidyanatha
Bisphenol S	80-09-1	Rats, mice	Dosed-feed	Completed	Suramya Waidyanatha
Ginkgo biloba extract	90045-36-6	Rats	Gavage	Ongoing	Suramya Waidyanatha
Microcystin LR	101043-37-2	Rats, mice	Gavage	Ongoing	Suramya Waidyanatha
Microcystin LR	101043-37-2	Rats, mice	Intravenous	Ongoing	Suramya Waidyanatha
NTP Systematic Evaluation of the Application of Zebrafish in Toxicology	N/A	Fish	N/A	Initiated	Kristen Ryan
Phenolic benzotriazoles (2-(2H-benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl)phenol)	70321-86-7	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (2-(2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylpropyl)phenol)	25973-55-1	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (2-(2H-Benzotriazol-2-yl)-4-tert-butylphenol)	3147-76-0	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (2-(2H-Benzotriazol-2-yl)phenol)	10096-91-0	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (2-(5-chloro-2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylethyl)phenol)	3864-99-1	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (3-(2H-benzotriazol-2-yl)-5-(1,1-dimethylethyl)-4-hydroxybenzenepropanoic acid, octyl ester)	84268-23-5	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (Bumetrizole)	3896-11-5	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (Drometrizole)	2440-22-4	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Phenolic benzotriazoles (Octrizole)	3147-75-9	Rats	Gavage, intravenous	Ongoing	Suramya Waidyanatha
Polyethylene glycol monomethyl ether	9004-74-4	Rats	Subcutaneous injection	Initiated	Jia-Long Fang
Resveratrol	501-36-0	Rats, mice	Gavage	Completed	Suramya Waidyanatha
Resveratrol	501-36-0	Rats, mice	Intravenous	Completed	Suramya Waidyanatha

Test Article	CASRN*	Species	Route	Status	Study Scientist
Sodium arsenite	7784-46-5	Rats	Dosed-feed	Ongoing	Vicki Sutherland
Sodium arsenite	7784-46-5	Mice	Dosed-water	Ongoing	Vicki Sutherland
Sodium arsenite	7784-46-5	Monkey	Gavage	Ongoing	Vicki Sutherland
Sulfolane	126-33-0	Rats, mice	Gavage	Completed	Chad Blystone
Sulfolane	126-33-0	Rats, mice	Intravenous	Completed	Chad Blystone

\*CASRN = Chemical Abstracts Service Registry Number

## Genetic Toxicity Studies

Genetic toxicity test results are used to help interpret general toxicity, carcinogenicity, or other in vivo test results and to provide a database for use in structure-activity relationship analysis. Substances evaluated during FY 2019 are listed below.

### *Genetic Toxicity Studies in FY 2019*

Test Article	CASRN*	Species/C ell Line	Testing Battery	Status	Study Scientist
1,2-bis(pentabromophenyl)ethane	84852-53-9	N/A	Salmonella	Ongoing	Kristine Witt
2-(Thiocyanomethylthio)benzothiazole	21564-17-0	N/A	Salmonella	Ongoing	Kristine Witt
2-(Thiocyanomethylthio)benzothiazole	21564-17-0	TK6 cells	Micronucleus	Ongoing	Kristine Witt
2-Chloro-N-(2-methyl-4-bromophenyl) acetamide	96686-51-0	N/A	Salmonella	Ongoing	Kristine Witt
2-Chloro-N-(2-methyl-4-bromophenyl) acetamide	96686-51-0	TK6 cells	Micronucleus	Ongoing	Kristine Witt
2-ethylhexyl-2,3,4,5-tetrabromobenzoate	183658-27-7	N/A	Salmonella	Ongoing	Kristine Witt
2-Hydroxy-4-methoxybenzophenone	131-57-7	N/A	Salmonella	Ongoing	Kristine Witt
4-(Hexyloxy)phenol	18979-55-0	N/A	Salmonella	Ongoing	Kristine Witt
4-(Hexyloxy)phenol	18979-55-0	TK6 cells	Micronucleus	Ongoing	Kristine Witt
(Aminomethyl)phosphonic acid	1066-51-9	N/A	Salmonella	Ongoing	Kristine Witt

Test Article	CASRN*	Species/Cell Line	Testing Battery	Status	Study Scientist
(Aminomethyl)phosphonic acid	1066-51-9	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Benzo[a]pyrene	50-32-8	Rats	Pig-a gene mutation	Ongoing	Kristine Witt
Benzo[a]pyrene	50-32-8	Rats	Comet assay	Completed	Kristine Witt
Bisphenol S	80-09-1	Rats	Micronucleus	Ongoing	Kristine Witt
Bisphenol S	80-09-1	Rats	Micronucleus	Ongoing	Kristine Witt
Buccaneer Plus	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Buccaneer Plus	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Cornerstone Plus	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Cornerstone Plus	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Deionized water	7732-18-5	Mice	Micronucleus	Ongoing	Kristine Witt
Deionized water	7732-18-5	Mice	Micronucleus	Ongoing	Kristine Witt
Deionized water	7732-18-5	Mice	Micronucleus	Ongoing	Kristine Witt
Deionized water	7732-18-5	Mice	Micronucleus	Ongoing	Kristine Witt
Dipentaerythritol pentaacrylate	60506-81-2	N/A	Salmonella	Ongoing	Kristine Witt
Dipentaerythritol pentaacrylate	60506-81-2	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Dipyrrithione	3696-28-4	N/A	Salmonella	Ongoing	Kristine Witt
Dipyrrithione	3696-28-4	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Diquat dibromide monohydrate	6385-62-2	N/A	Salmonella	Ongoing	Kristine Witt
Diquat dibromide monohydrate	6385-62-2	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Durango DMA	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Durango DMA	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Echinacea purpurea	90028-20-9	Rats	Micronucleus	Ongoing	Kristine Witt
Garcinia cambogia	90045-23-1	Rats	Micronucleus	Ongoing	Kristine Witt
Garcinia cambogia	90045-23-1	Mice	Micronucleus	Ongoing	Kristine Witt

Test Article	CASRN*	Species/Cell Line	Testing Battery	Status	Study Scientist
Glyphosate acid	1071-83-6	N/A	Salmonella	Ongoing	Kristine Witt
Glyphosate acid	1071-83-6	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Glyphosate isopropyl amine	38641-94-0	N/A	Salmonella	Ongoing	Kristine Witt
Glyphosate isopropyl amine	38641-94-0	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Glystar Plus	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Glystar Plus	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Halex GT	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Halex GT	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Hexachlorocyclopentadienyl-dibromocyclooctane	51936-55-1	N/A	Salmonella	Ongoing	Kristine Witt
H-Isoindole-1,3(2H)-diimine	3468-11-9	N/A	Salmonella	Ongoing	Kristine Witt
H-Isoindole-1,3(2H)-diimine	3468-11-9	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Kill-Zall	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Kill-Zall	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Mesotrione	104206-82-8	N/A	Salmonella	Ongoing	Kristine Witt
Mesotrione	104206-82-8	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Methylcellulose	9004-67-5	Mice	Micronucleus	Ongoing	Kristine Witt
Methylcellulose	9004-67-5	Mice	Micronucleus	Ongoing	Kristine Witt
Methylcellulose	9004-67-5	Mice	Micronucleus	Ongoing	Kristine Witt
Methylcellulose	9004-67-5	Mice	Micronucleus	Ongoing	Kristine Witt
Microcystin	101043-37-2	Mice	Pig-a gene mutation	Ongoing	Kristine Witt
Microcystin	101043-37-2	Mice	Pig-a gene mutation	Ongoing	Kristine Witt
Microcystin LR	101043-37-2	Mice	Micronucleus	Ongoing	Kristine Witt
Microcystin LR	101043-37-2	Mice	Micronucleus	Ongoing	Kristine Witt
N-Ethyl-N-nitrosourea	759-73-9	Rats	Micronucleus	Ongoing	Kristine Witt
N-Ethyl-N-nitrosourea	759-73-9	Rats	Micronucleus	Ongoing	Kristine Witt

Test Article	CASRN*	Species/C ell Line	Testing Battery	Status	Study Scientist
N-Ethyl-N-nitrosourea	759-73-9	Rats	Pig-a gene mutation	Ongoing	Kristine Witt
N-Ethyl-N-nitrosourea	759-73-9	Rats	Pig-a gene mutation	Ongoing	Kristine Witt
N-Ethyl-N-nitrosourea	759-73-9	Rats	Pig-a gene mutation	Ongoing	Kristine Witt
N-Ethyl-N-nitrosourea	759-73-9	Rats	Comet assay	Completed	Kristine Witt
N-Ethyl-N-nitrosourea	759-73-9	Rats	Comet assay	Completed	Kristine Witt
Potassium dicyanoaurate	13967-50-5	N/A	Salmonella	Ongoing	Kristine Witt
Potassium dicyanoaurate	13967-50-5	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Remuda Full Strength	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Remuda Full Strength	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Roundup Concentrate Plus	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Roundup Concentrate Plus	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Roundup Custom	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Roundup Custom	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Roundup PowerMax	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Roundup PowerMax	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Roundup Super Concentrate	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Roundup Super Concentrate	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Roundup WeatherMax	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Roundup WeatherMax	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
S-Metolachlor	51218-45-2	N/A	Salmonella	Ongoing	Kristine Witt
S-Metolachlor	51218-45-2	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Sodium metavanadate	13718-26-8	Mice	Comet assay	Completed	Kristine Witt
Sodium metavanadate	13718-26-8	Rats	Comet assay	Completed	Kristine Witt
Thallium (I) sulfate	7446-18-6	Rats	Micronucleus	Initiated	Kristine Witt
Thallium (I) sulfate	7446-18-6	Mice	Micronucleus	Initiated	Kristine Witt

Test Article	CASRN*	Species/C ell Line	Testing Battery	Status	Study Scientist
Thallium (I) sulfate	7446-18-6	Rats	Pig-a gene mutation	Initiated	Kristine Witt
Thallium (I) sulfate	7446-18-6	Mice	Pig-a gene mutation	Initiated	Kristine Witt
Touchdown total	N/A	N/A	Salmonella	Ongoing	Kristine Witt
Touchdown total	N/A	TK6 cells	Micronucleus	Ongoing	Kristine Witt
Triclosan	3380-34-5	Rats	Micronucleus	Ongoing	Kristine Witt
Triclosan	3380-34-5	Rats	Micronucleus	Ongoing	Kristine Witt
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	Micronucleus	Ongoing	Kristine Witt
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	Micronucleus	Ongoing	Kristine Witt
Tricombination ABC:DTG:3TC	N/A	Rats	Micronucleus	Ongoing	Kristine Witt
Tricombination ABC:DTG:3TC	N/A	Rats	Micronucleus	Ongoing	Kristine Witt
Tris(4-chlorophenyl)methane	275754-78-6	Rats	Micronucleus	Ongoing	Kristine Witt
Vanadyl sulfate	27774-13-6	Mice	Comet assay	Completed	Kristine Witt
Vanadyl sulfate	27774-13-6	Rats	Comet assay	Completed	Kristine Witt

\*CASRN = Chemical Abstracts Service Registry Number

## Organ System Toxicity Studies

NTP studies toxicity of environmental substances on development, reproduction, and on the nervous and immune systems. Organ systems toxicity studies conducted during FY 2019 are listed below.

### *Neurotoxicity, Developmental Toxicity, and Reproductive Toxicity Studies during FY 2019*

Test Article	CASRN*	Species	Testing Battery	Length	Route	Status	Study Scientist
1020 Long multiwalled carbon nanotube	N/A	Rats, mice	Immunotoxicity	30 days	Inhalation	Ongoing	Dori Germolec, Nigel Walker
1020 Long multiwalled carbon nanotube	N/A	Mice	Immunotoxicity	90 days	Inhalation	Ongoing	Dori Germolec
2-((1-(4- Phenoxyphenoxy)pr	95737-68-1	Rats	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec

Test Article	CASRN*	Species	Testing Battery	Length	Route	Status	Study Scientist
opropan-2-yl)oxy)pyridine							
2-((1-(4-Phenoxyphenoxy)propoxy)pyridine	95737-68-1	Rats	Conventional teratology	GD 6-21	Gavage	Ongoing	Barry McIntyre
2-((1-(4-Phenoxyphenoxy)propoxy)pyridine	95737-68-1	Rabbits	Conventional teratology, teratology pilot	GD 7-28	Gavage	Ongoing	Barry McIntyre
2,3-Butanedione	431-03-8	Mice	Immunotoxicity	28 days	Inhalation	Ongoing	Dori Germolec
2-Hydroxy-4-methoxybenzophenone	131-57-7	Rats	Developmental toxicity	GD 6 to PND 21	Dosed-feed	Completed	Vicki Sutherland
3,3',4,4'-Tetrachloroazobenzene	14047-09-7	Rats	Immunotoxicity	28 days	Gavage	Ongoing	William Gwinn
4-Methylcyclohexane methanol	34885-03-5	Mice	Immunotoxicity	7 days	Topical application	Ongoing	Chad Blystone
4-Methylcyclohexane methanol	34885-03-5	Rats	Conventional teratology, teratology pilot	GD 6 to GD 20	Gavage	Ongoing	Chad Blystone
4-Methylimidazole	822-36-6	Rats	Continuous breeding	Continuous	Dosed-feed	Ongoing	Mamta Behl
Acenaphthenequinone	82-86-0	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Cynthia Rider
Arsenic	7440-38-2	Rats	Developmental toxicity	Pregnant dams through PND21	Gavage & dosed-water	Ongoing	Vicki Sutherland
Benz(j)aceanthrylene	202-33-5	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Benzo(a)pyrene	50-32-8	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Cynthia Rider
Benzo(b)fluoranthene	205-99-2	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Benzo(c)fluorene	205-12-9	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Benzo(k)fluoranthene	207-08-9	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Bisphenol AF	1478-61-1	Rats	Immunotoxicity	GD 6 - PND 96	Dosed-feed	Ongoing	Dori Germolec
Black cohosh	84776-26-1	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Chad Blystone



Test Article	CASRN*	Species	Testing Battery	Length	Route	Status	Study Scientist
Black cohosh	84776-26-1	Rats	Continuous breeding	N/A	Gavage	Ongoing	Chad Blystone
Butyl paraben	94-26-8	Rats	Continuous breeding	N/A	Dosed-feed	Ongoing	Chad Blystone
Chrysene	218-01-9	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Crude 4-Methylcyclohexane methanol	N/A	Mice	Immunotoxicity	7 days	Topical application	Ongoing	Scott Auerbach
Dibenz(a,h)anthracene	53-70-3	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Cynthia Rider
dibenzo(a,l)pyrene	191-30-0	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Dibenzothiophene	132-65-0	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Diisobutyl phthalate	84-69-5	Rats	Continuous breeding	Continuous	Dosed-feed	Ongoing	Chad Blystone
DMAE bitartrate	5988-51-2	Rats	Conventional teratology, teratology pilot	GD 6 to GD 20	Gavage	Ongoing	Vicki Sutherland
Echinacea purpurea root extract	90028-20-9	Rats	Immunotoxicity	28 days	Gavage	Initiated	Dori Germolec
Effective dose producing 50% response mixture	N/A	Mice	Immunotoxicity	28 days	Gavage	Planned	Dori Germolec
Gum guggul extract	N/A	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Indeno(1,2,3-cd)pyrene	193-39-5	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
N-Butylbenzenesulfonamide	3622-84-2	Mice	Immunotoxicity	28 days	Dosed-feed	Ongoing	Cynthia Rider
N-Butylbenzenesulfonamide	3622-84-2	Rats	Immunotoxicity	GD 6 - PND 42	Dosed-feed	Ongoing	Dori Germolec
Nelfinavir mesylate	159989-65-8	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec
Phenanthrene	85-01-8	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Cynthia Rider
Pyrene	129-00-0	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Cynthia Rider
Resveratrol	501-36-0	Mice	Immunotoxicity	180 days	Gavage	Ongoing	Dori Germolec
Resveratrol	501-36-0	Mice	Immunotoxicity	28 days	Gavage	Ongoing	Dori Germolec

Test Article	CASRN*	Species	Testing Battery	Length	Route	Status	Study Scientist
Sodium metavanadate	13718-26-8	Mice	Immunotoxicity	28 days	Dosed-water	Ongoing	Georgia Roberts
Sodium tungstate dihydrate	10213-10-2	Mice	Immunotoxicity	28 days	Dosed-water	Ongoing	Dori Germolec
Sulfolane	126-33-0	Rats, mice	Immunotoxicity	13 weeks	Gavage	Ongoing	Chad Blystone, Dori Germolec
Tenofovir disoproxil fumarate	202138-50-9	Mice	Teratology pilot	GD 5 - PND 21	Gavage	Ongoing	Barry McIntyre
tert-Butylphenyl diphenyl phosphate	56803-37-3	Rats	Immunotoxicity	N/A	N/A	Planned	Dori Germolec
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	Teratology pilot	GD 5 - GD 18	Gavage	Ongoing	Vicki Sutherland
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	Maternal transfer	GD 5-15	Gavage	Ongoing	Vicki Sutherland
Tris(Chloropropyl) phosphate	13674-84-5	Rats	Immunotoxicity	GD 6 - PND 127	Dosed-feed	Ongoing	Dori Germolec
Tris(Chloropropyl) phosphate	13674-84-5	Rats	Conventional teratology, teratology pilot	GD 6 to GD 20	Gavage	Ongoing	Kristen Ryan
Vinclozolin	50471-44-8	Rats	Continuous breeding	9 months	Gavage	Ongoing	Barry McIntyre
Vinpocetine	42971-09-5	Rats	Conventional teratology, teratology pilot	GD 6 to GD 20	Gavage	Ongoing	Vicki Sutherland
Vinpocetine	42971-09-5	Rabbits	Teratology pilot	GD 7 to GD 28	Gavage	Ongoing	Vicki Sutherland

\*CASRN = Chemical Abstracts Service Registry Number

## Modified One-Generation Reproduction Studies

NTP modified one-generation study design emphasizes a full evaluation of the first-generation offspring of animals and uses fewer animals than the classical multigenerational study design. These studies generate information on the effects of substances on prenatal development, postnatal development, and reproduction. Planned or ongoing modified one-generation studies are listed below.

### *Modified One-Generation Studies in FY 2019*

Test Article	CASRN*	Species	Testing battery	Status	Study Scientist
2,2'-Dimorpholinodiethyl ether	6425-39-4	Rats	Dose range finding	Ongoing	Georgia Roberts
2-Ethylhexyl p-methoxycinnamate	5466-77-3	Rats	Developmental toxicity, fertility	Ongoing	Barry McIntyre

Test Article	CASRN*	Species	Testing battery	Status	Study Scientist
			assessment, F0 generation		
2-Ethylhexyl p-methoxycinnamate	5466-77-3	Rats	Subchronic	Ongoing	Barry McIntyre
2-Hydroxy-4-methoxybenzophenone	131-57-7	Rats	Dose range finding	Ongoing	Barry McIntyre
2-Hydroxy-4-methoxybenzophenone	131-57-7	Rats	Developmental toxicity, fertility assessment, F0 generation	Ongoing	Barry McIntyre
Bisphenol AF	1478-61-1	Rats	Dose range finding	Ongoing	Vicki Sutherland
Bisphenol AF	1478-61-1	Rats	Developmental toxicity, fertility assessment, F0 generation, maternal transfer	Ongoing	Vicki Sutherland
Bisphenol AF	1478-61-1	Rats	Subchronic	Ongoing	Vicki Sutherland
Bisphenol S	80-09-1	Rats	Dose range finding	Ongoing	Vicki Sutherland
Bisphenol S	80-09-1	Rats	F0 generation	Planned	Vicki Sutherland
Boric acid	10043-35-3	Rats	Dose range finding	Initiated	Atlee Watson
Boric acid	10043-35-3	Rats	F0 generation	Initiated	Atlee Watson
Deoxynivalenol	51481-10-8	Rats	Dose range finding	Ongoing	Dori Germolec
Echinacea purpurea root extract	90028-20-9	Rats	Dose range finding	Ongoing	Kristen Ryan
Echinacea purpurea root extract	90028-20-9	Rats	Conventional teratology, fertility assessment	Ongoing	Kristen Ryan
Echinacea purpurea root extract	90028-20-9	Rats	Subchronic	Ongoing	Kristen Ryan
Ethylene glycol 2-ethylhexyl ether	1559-35-9	Rats	Dose range finding	Ongoing	Chad Blystone
Ethylene glycol 2-ethylhexyl ether	1559-35-9	Rats	Dose range finding, fertility assessment, F0 generation, maternal transfer, neurotoxicology assessment, subchronic	Planned	Chad Blystone
Hydroquinone	123-31-9	Rats	Developmental toxicity, dose range finding, fertility assessment, F0 generation, neurotoxicology assessment	Planned	Vicki Sutherland

Test Article	CASRN*	Species	Testing battery	Status	Study Scientist
Isopropylated phenol phosphate	68937-41-7	Rats	Dose range finding	Ongoing	Mamta Behl
Isopropylated phenol phosphate	68937-41-7	Rats	F0 generation, neurotoxicology assessment	Planned	Mamta Behl
Microcystin LR	101043-37-2	Mice	Dose range finding	Ongoing	Vicki Sutherland
N-Butylbenzenesulfonamide	3622-84-2	Rats	Developmental toxicity, fertility assessment, F0 generation, maternal transfer, neurotoxicology assessment	Ongoing	Cynthia Rider
N-Butylbenzenesulfonamide	3622-84-2	Rats	Subchronic	Ongoing	Cynthia Rider
Resveratrol	501-36-0	Rats	Developmental toxicity, fertility assessment, F0 generation	Ongoing	Dori Germolec
Simvastatin	79902-63-9	Rats	Dose range finding	Ongoing	Barry McIntyre
Triclosan	3380-34-5	Rats	Dose range finding	Ongoing	Vicki Sutherland
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	F0 generation	Ongoing	Vicki Sutherland
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	Subchronic	Initiated	Vicki Sutherland
Tricombination FTC:TDF:EFV (1:1.5:3)	N/A	Mice	Maternal transfer	Initiated	Vicki Sutherland
Tricombination ABC:DTG:3TC	N/A	Rats	Dose range finding	Initiated	Vicki Sutherland
Triphenyl phosphate	115-86-6	Rats	Dose range finding	Ongoing	Mamta Behl
Triphenyl phosphate	115-86-6	Rats	F0 generation, neurotoxicology assessment	Planned	Mamta Behl
Tris(4-chlorophenyl)methane	27575-78-6	Rats	Dose range finding	Ongoing	Troy Hubbard
Valerian (Valeriana officinalis L.) root extract	8057-49-6	Rats	Dose range finding	Ongoing	Georgia Roberts

\*CASRN = Chemical Abstracts Service Registry Number

## Toxicology and Carcinogenicity Studies

NTP performs toxicity studies to provide dose-setting information for chronic studies and to address specific deficiencies in the toxicology database for the chemical. Toxicology and carcinogenicity studies fall into two categories: prechronic toxicity studies and chronic two-year toxicology and carcinogenicity studies. Studies are generally conducted in rats and mice.

Each study type is performed according to the [Specifications for the Conduct of Studies to Evaluate the Reproductive and Developmental Toxicity of Chemical, Biological and Physical Agents in](#)

Laboratory Animals for the National Toxicology Program (NTP) (May 2011). Prechronic and chronic toxicity studies and carcinogenicity studies, that were initiated, ongoing, or completed during FY 2019, are listed below.

*Prechronic Toxicology and Carcinogenicity Studies FY 2019*

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
1,2,4-trimethylbenzene	95-63-6	Rats, mice	13 weeks	Inhalation	Ongoing	Kristen Ryan
1,2-Bis(2,4,6-tribromophenoxy)ethane	37853-59-1	Rats	5 days	Gavage	Ongoing	June Dunnick
1,2-Bis(pentabromophenyl)ethane	84852-53-9	Rats	5 days	Gavage	Ongoing	June Dunnick
1,3,5,7,9,11-Hexabromocyclododecane	25637-99-4	Rats	5 days	Gavage	Ongoing	June Dunnick
1020 Long multiwalled carbon nanotube	N/A	Rats, mice	Inhalation	Chronic	Ongoing	Nigel Walker
1020 Long multiwalled carbon nanotube	N/A	Rats, mice	Inhalation	Prechronic	Ongoing	Nigel Walker
2,2',4,4'-Tetrabromodiphenyl ether	5436-43-1	Rats	Gavage	Prechronic	Ongoing	June Dunnick
2,2'-Dimorpholinodiethyl ether	6425-39-4	Mice	Gavage	Prechronic	Ongoing	Georgia Roberts
2,3-Pentanedione	600-14-6	Rats, mice	Inhalation	Subchronic	Ongoing	Nigel Walker
2-Ethylhexyl-2,3,4,5-tetrabromobenzoate	183658-27-7	Rats	5 days	Gavage	Ongoing	June Dunnick
2-Ethyltoluene	611-14-3	Rats, mice	2 weeks	Inhalation	Ongoing	Madelyn Huang
2-Ethyltoluene	611-14-3	Rats, mice	3 months	Inhalation	Planned	Madelyn Huang
2-Hydroxy-4-methoxybenzophenone	131-57-7	Rats, mice	2 years	Dosed-feed	Ongoing	Barry McIntyre
3,3',4,4'-Tetrachloroazobenzene	14047-09-7	Rats	5 days	Gavage	Ongoing	William Gwinn
3,3',4,4'-Tetrachloroazobenzene	14047-09-7	Rats	5 days	Gavage	Initiated	William Gwinn
Abrasive blasting agents: blasting sand	N/A	Rats	14 days	Inhalation	Ongoing	William Gwinn
Abrasive blasting agents: blasting sand	N/A	Rats	39 weeks	Inhalation	Ongoing	William Gwinn
Abrasive blasting agents: specular hematite	N/A	Rats	14 days	Inhalation	Ongoing	William Gwinn
Abrasive blasting agents: specular hematite	N/A	Rats	39 weeks	Inhalation	Ongoing	William Gwinn
Acetaminophen (4-hydroxyacetanilide)	103-90-2	Rats	90 days	Gavage	Ongoing	Vicki Sutherland
Acetoin	513-86-0	Rats, mice	14 days	Inhalation	Ongoing	Nigel Walker

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
Acetoin	513-86-0	Rats, mice	90 days	Inhalation	Ongoing	Nigel Walker
Acrylamide	79-06-1	Rats	5 days	Gavage	Ongoing	William Gwinn
Aging cohort study: 12951/SvlmJ mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: A/J mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: B6C3F1J mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: C3H/HeJ mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: C57/BL/6J mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: CAST/EiJ mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: NOD. B10Sn-H2(b)/J	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: NZO/HiLtJ mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: PWK/PhJ mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Aging cohort study: WSB/EiJ mouse	N/A	Mice	2 years	N/A	Ongoing	June Dunnick
Air-lung interface model	N/A	N/A	N/A	N/A	Ongoing	Xuefei Cao
alpha/beta Thujone mixture	76231-76-0	Rats	5 days	Gavage	Ongoing	William Gwinn
alpha-Pinene	80-56-8	Rats, mice	2 years	Inhalation	Ongoing	Cynthia Rider
alpha-Pinene	80-56-8	Rats	90 days	Inhalation	Ongoing	Cynthia Rider
alpha-Pinene	80-56-8	Rats, mice	14 days	Inhalation	Ongoing	Cynthia Rider
Aqueous film forming foams (C20017)	N/A	Rats	14 days	Gavage	Planned	Mimi Huang
Aqueous film forming foams (C20017B)	N/A	Rats	14 days	Gavage	Planned	Mimi Huang
Arsenic	7440-38-2	Rats	Acute	Gavage & dosed-water	Ongoing	Daniel Doerge
Arsenic	7440-38-2	Mice	Acute	Gavage & dosed-water	Ongoing	Daniel Doerge
Arsenic	7440-38-2	Monkey	Acute	Gavage	Ongoing	Daniel Doerge
Asbestos, amosite	12172-73-5	Rats	N/A	Inhalation	Planned	Matt Stout
Aspergillus fumigatus mold	N/A	Mice	13 weeks	Inhalation	Ongoing	Dori Germolec

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
Bis(2-ethylhexyl) tetrabromophthalate	26040-51-7	Rats	5 days	Gavage	Ongoing	June Dunnick
Bisphenol AF (Start date: 04/05/2017)	1478-61-1	Rats	5 days	Gavage	Ongoing	William Gwinn
Bisphenol AF (Start date: 03/28/2019)	1478-61-1	Rats	5 days	Gavage	Initiated	William Gwinn
Bisphenol S	80-09-1	Mice	14 days	Dosed-feed	Ongoing	Vicki Sutherland
Black cohosh	84776-26-1	Rats, mice	2 years	Gavage	Ongoing	Chad Blystone
Black cohosh	84776-26-1	Rats	14 days	Gavage	Ongoing	Chad Blystone
Black cohosh	84776-26-1	N/A	N/A	N/A	Ongoing	Chad Blystone
Brominated vegetable oil	8016-94-2	Rats	90 days	Dosed-feed	Ongoing	Vicki Sutherland
Coumarin	91-64-5	Rats	5 days	Gavage	Ongoing	June Dunnick
Crumb rubber	N/A	Mice	14 days	N/A	Completed	Georgia Roberts
Damp building mold mixture	N/A	Mice	90 days	Inhalation	Planned	Dori Germolec
Decabromodiphenyl ether	1163-19-5	Rats	5 days	Gavage	Ongoing	June Dunnick
Di(2-ethylhexyl) phthalate	117-81-7	Rats	Perinatal + 2 years	Dosed-feed	Ongoing	Troy Hubbard
Di(2-ethylhexyl) phthalate	117-81-7	Rats	2 years	Dosed-feed	Ongoing	Troy Hubbard
Di(2-ethylhexyl) phthalate	117-81-7	Rats	5 days	Gavage	Ongoing	William Gwinn
Dibutyl phthalate	84-74-2	Rats, mice	2 years	Dosed-feed	Ongoing	Mimi Huang
Dimethylamine borane	74-94-2	Rats, mice	2 weeks	Dermal	Ongoing	AtLee Watson
Ethinyl estradiol	57-63-6	Rats	5 days	Gavage	Ongoing	William Gwinn
Ethinyl estradiol	57-63-6	Rats	5 days	Gavage	Initiated	William Gwinn
Fenofibrate	49562-28-9	Rats	5 days	Gavage	Ongoing	William Gwinn
Furan (Start Date: 08/01/2017)	110-00-9	Rats	5 days	Gavage	Ongoing	William Gwinn
Furan (Start Date: 03/21/2019)	110-00-9	Rats	5 days	Gavage	Initiated	William Gwinn
Furan (Start Date: 05/16/2019)	110-00-9	Rats	5 days	Gavage	Initiated	William Gwinn
Garcinia cambogia extract (C20611)	90045-23-1	Rats, mice	14 days	Dosed-feed	Ongoing	Cynthia Rider
Garcinia cambogia extract (C05016)	90045-23-1	Rats	N/A	Dosed-feed	Initiated	Cynthia Rider
Garcinia cambogia extract (C05016)	90045-23-1	Mice	NA	Dosed-feed	Initiated	Cynthia Rider

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
Ginkgo biloba extract (Start Date: 12/16/2015)	90045-36-6	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Ginkgo biloba extract (Start Date: 12/23/2015)	90045-36-6	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Ginkgo biloba extract (Start Date: 12/17/2015)	90045-36-6	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Ginkgo biloba extract (Start Date: 12/18/2015)	90045-36-6	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Ginkgo biloba extract (Start Date: 12/30/2015)	90045-36-6	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Ginseng	50647-08-0	Rats	5 days	Gavage	Ongoing	William Gwinn
Goldenseal extract	84603-60-1	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Green tea extract	N/A	Rats	5 days	Gavage	Ongoing	Scott Auerbach
Gum guggul extract	N/A	Rats, mice	13 weeks	Gavage	Ongoing	Troy Hubbard
Hexachlorobenzene	118-74-1	Rats	13 weeks	Gavage	Ongoing	Michelle Hooth
Hexachlorobenzene	118-74-1	Rats	5 days	Gavage	Ongoing	William Gwinn
Hexachlorocyclopentadienyl-dibromocyclooctane	51936-55-1	Rats	5 days	Gavage	Ongoing	June Dunnick
Insertional mutagenesis - definitive vector study (Cohort 1)	N/A	Mice	14 months	Intravenous	Ongoing	Dori Germolec
Insertional mutagenesis - definitive vector study (Cohort 2)	N/A	Mice	14 months	Intravenous	Ongoing	Dori Germolec
Insertional mutagenesis - definitive vector study (Cohort 3)	N/A	Mice	14 months	Intravenous	Ongoing	Dori Germolec
Insertional mutagenesis - definitive vector study (Cohort 4)	N/A	Mice	14 months	Intravenous	Ongoing	Dori Germolec
Insertional mutagenesis - definitive vector study (Cohort 5)	N/A	Mice	14 months	Intravenous	Ongoing	Dori Germolec
Ionic liquid: 1-Butyl-1-methylpyrrolidinium chloride	479500-35-1	Rats, mice	90 days	Dosed-water	Ongoing	Kristen Ryan
Ionic liquid: 1-Butyl-3-methylimidazolium chloride	79917-90-1	Rats, mice	90 days	Dosed-water	Ongoing	Kristen Ryan
Ionic liquid: 1-Ethyl-3-methylimidazolium chloride	65039-09-0	Rats, mice	90 days	Dosed-water	Ongoing	Kristen Ryan
Ionic liquid: N-Butylpyridinium chloride	1124-64-7	Rats, mice	90 days	Dosed-water	Ongoing	Kristen Ryan



Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
Isopropylated phenol phosphate	68937-41-7	Mice	13 weeks	Dosed-feed	Planned	Mamta Behl
Isopropylated phenol phosphate	68937-41-7	Mice	2 weeks	Dosed-feed	Ongoing	Mamta Behl
Libby amphibole 2007	N/A	Rats	30 days	Inhalation	Initiated	Matt Stout
Melamine + cyanuric acid combination (C09074)	N/A	Rats	90 days	Gavage	Ongoing	Goncalo Gamboa da Costa
Melamine + cyanuric acid combination (C09074C)	N/A	Rats	90 days + recovery	Gavage	Ongoing	Goncalo Gamboa da Costa
Melamine + cyanuric acid combination (C09074D)	N/A	Rats	90 day	Gavage	Ongoing	Goncalo Gamboa da Costa
Methyleugenol	93-15-2	Rats	5 days	Gavage	Ongoing	William Gwinn
Microbiome	N/A	N/A	N/A	N/A	Ongoing	Sangeeta Khare
Milk thistle extract	84604-20-6	Rats	5 days	Gavage	Ongoing	June Dunnick
Mixed xylenes	N/A	Mice	30 days	Inhalation	Initiated	Kristen Ryan
Myristicin	607-91-0	Rats	13 weeks	Gavage	Completed	Anika Dzierlenga
Myristicin	607-91-0	Mice	13 weeks	Gavage	Completed	Anika Dzierlenga
Nanoscale material (Fullerene-C60 1 micron)	99685-96-8	Rats, mice	90 days	Inhalation	Ongoing	Dori Germolec
Nanoscale material (Fullerene-C60 50 nanometers)	99685-96-8	Rats, mice	90 days	Inhalation	Ongoing	Dori Germolec
Nattokinase and lumbrokinase	N/A	Rats	28 days	Gavage	Ongoing	Vicki Sutherland
N-Butylbenzenesulfonamide	3622-84-2	Mice	14 days	Dosed-feed	Ongoing	Cynthia Rider
N-Butylbenzenesulfonamide	3622-84-2	Rats, mice	13 weeks	Dosed-feed	Ongoing	Cynthia Rider
Pentabromodiphenyl ether mixture [DE-71 (Technical Grade)]	32534-81-9	Rats	5 days	Gavage	Ongoing	June Dunnick
Perfluorobutane sulfonic acid	375-73-5	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorodecanoic acid	335-76-2	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorohexane sulfonate potassium salt	3871-99-6	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorohexanoic acid	307-24-4	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorononanoic acid	375-95-1	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorooctane sulfonic acid	1763-23-1	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorooctanoic acid (C20614)	335-67-1	Rats	2 years	Dosed-feed	Ongoing	Chad Blystone

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
Perfluorooctanoic acid (C20614B)	335-67-1	Rats	2 years	Dosed-feed	Ongoing	Chad Blystone
Perfluorooctanoic acid	335-67-1	Rats	28 days	Gavage	Completed	Chad Blystone
Perfluorooctanoic acid (Start Date: 04/05/2017)	335-67-1	Rats	5 days	Gavage	Ongoing	William Gwinn
Perfluorooctanoic acid (Start Date: 03/21/2019)	335-67-1	Rats	5 days	Gavage	Initiated	William Gwinn
Perfluorooctanoic acid (Start Date: 05/16/2019)	335-67-1	Rats	5 days	Gavage	Initiated	William Gwinn
Phenolic benzotriazoles (2-(2H-benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl)phenol)	70321-86-7	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (2-(2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylpropyl)phenol)	25973-55-1	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (2-(2H-benzotriazol-2-yl)-4-tert-butylphenol)	3147-76-0	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (2-(2H-benzotriazol-2-yl)phenol)	10096-91-0	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (2-(5-chloro-2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylethyl)phenol)	3864-99-1	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (3-(2H-benzotriazol-2-yl)-5-(1,1-dimethylethyl)-4-hydroxybenzenepropanoic acid, octyl ester)	84268-23-5	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (Bumetrizole)	3896-11-5	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (Drometrizole)	2440-22-4	Rats	14 days	Gavage	Ongoing	Chad Blystone
Phenolic benzotriazoles (Octrizole)	3147-75-9	Rats	14 days	Gavage	Ongoing	Chad Blystone
Pulegone	89-82-7	Rats	5 days	Gavage	Ongoing	William Gwinn
QT drugs (bepridil hydrochloride)	74764-40-2	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (bepridil hydrochloride)	74764-40-2	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (diltiazem hydrochloride)	33286-22-5	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
QT drugs (diltiazem hydrochloride)	33286-22-5	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (Loratadine)	79794-75-5	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (Loratadine)	79794-75-5	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (Lovastatin)	75330-75-5	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (Lovastatin)	75330-75-5	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (sotalol hydrochloride)	959-24-0	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (sotalol hydrochloride)	959-24-0	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (terfenadine)	50679-08-8	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
QT drugs (terfenadine)	50679-08-8	Dogs	1 day	Per os (Capsule)	Ongoing	Michelle Hooth
Resveratrol	501-36-0	Rats, mice	2 years	Gavage	Ongoing	Anika Dzierlenga
Resveratrol	501-36-0	Rats, mice	2 weeks	Gavage	Ongoing	Anika Dzierlenga
Resveratrol	501-36-0	Rats, mice	13 weeks	Gavage	Ongoing	Anika Dzierlenga
Sodium metavanadate	13718-26-8	Rats, mice	90 days	Dosed-water	Ongoing	Georgia Roberts
Sodium tungstate dihydrate	10213-10-2	Rats, mice	2 years	Dosed-water	Ongoing	Mamta Behl
Sodium tungstate dihydrate	10213-10-2	Rats, mice	13 weeks	Dosed-water	Ongoing	Mamta Behl
Stachybotrys chartarum	67892-26-6	Mice	13 weeks	Inhalation	Ongoing	Dori Germolec
Stachybotrys chartarum strain 1 mold (macrocytic trichothecene chemotype)	N/A	Mice	90 days	Inhalation	Planned	Dori Germolec
Stachybotrys chartarum strain 2 mold (atranone chemotype)	N/A	Mice	90 days	Inhalation	Planned	Dori Germolec
Sulfolane	126-33-0	Rats, mice, guinea pigs	28 days	Gavage	Ongoing	Chad Blystone
Sulfolane (Rat Core; Mice interim & Core)	126-33-0	Rats, mice	2 years	Dosed-water	Ongoing	Chad Blystone
Sulfolane (Rat interim)	126-33-0	Rats, mice	2 years	Dosed-water	Ongoing	Chad Blystone
Tetrabromobisphenol A (Start Date: 11/17/2016)	79-94-7	Rats	5 days	Gavage	Ongoing	William Gwinn
Tetrabromobisphenol A	79-94-7	Rats	5 days	Gavage	Initiated	William Gwinn

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
(Start Date: 03/21/2019)						
Tetrabromobisphenol A (Start Date: 05/16/2019)	79-94-7	Rats	5 days	Gavage	Initiated	William Gwinn
Tetrabromobisphenol A (Start Date: 03/28/2019)	79-94-7	Rats	5 days	Gavage	Initiated	William Gwinn
Tetrabromobisphenol A-bis(2,3-dibromopropyl ether)	21850-44-2	Rats	N/A	Gavage	Ongoing	June Dunnick
Thallium (I) sulfate	7446-18-6	Rats	Gestation day 6 to postnatal day 28	Dosed-water	Ongoing	Troy Hubbard
Thallium (I) sulfate	7446-18-6	Mice	2 weeks	Dosed-water	Ongoing	Troy Hubbard
Thallium (I) sulfate	7446-18-6	Rats	90 days	Dosed-water	Initiated	Troy Hubbard
Thallium (I) sulfate	7446-18-6	Mice	90 days	Dosed-water	Initiated	Troy Hubbard
Triclosan	3380-34-5	Mice	90 days	Dermal	Ongoing	Jia-Long Fang
Triclosan	3380-34-5	Rats	5 days	Gavage	Ongoing	William Gwinn
Trimethylsilyldiazomethane	18107-18-1	Rats, mice	10 days	Inhalation	Ongoing	William Gwinn
Triphenyl phosphate	115-86-6	Mice	2 weeks	Dosed-feed	Ongoing	Mamta Behl
Tris(chloropropyl) phosphate	13674-84-5	Rats, mice	2 years	Dosed-feed	Ongoing	Kristen Ryan
Tris(chloropropyl) phosphate	13674-84-5	Rats, mice	90 days	Dosed-feed	Ongoing	Kristen Ryan
Tris(chloropropyl) phosphate	13674-84-5	Rats	5 days	Gavage	Ongoing	William Gwinn
Valerian (Valeriana officinalis L.) root extract	8057-49-6	Mice	90 days	Gavage	Ongoing	Troy Hubbard
Vanadyl sulfate	27774-13-6	Rats, mice	90 days	Dosed-water	Ongoing	Georgia Roberts
Water damaged building mold mixture	N/A	Rats	90 days	Inhalation	Planned	Dori Germolec
Water damaged building mold mixture	N/A	Mice	90 days	Inhalation	Planned	Dori Germolec
Water disinfection byproducts (bromodichloroacetic acid) (Start Date: 04/19/2017)	71133-14-7	Rats	5 days	Gavage	Ongoing	William Gwinn
Water disinfection byproducts (bromodichloroacetic acid) (Start Date: 03/21/2019)	71133-14-7	Rats	5 days	Gavage	Initiated	William Gwinn
Water disinfection byproducts (bromodichloroacetic acid) (Start Date: 05/16/2019)	71133-14-7	Rats	5 days	Gavage	Initiated	William Gwinn
Wyeth 14,643 (WY)	50892-23-4	Rats	28 days	Gavage	Completed	Chad Blystone

Test Article	CASRN*	Species	Length	Route	Status	Study Scientist
Zinc carbonate, basic	5263-02-5	Rats	2 years	Dosed-feed	Completed	Natasha Catlin

\*CASRN = Chemical Abstracts Service Registry Number

## Toxicogenomic Studies

NTP is incorporating the latest toxicogenomic technologies into its testing program to gain further insights into the toxicity of environmental substances. Toxicogenomics examines how the entire genetic structure, or genome, influences an organism's response to environmental toxicants. Microarray, proteomic, metabolomics analyses, and next-generation (NextGen) sequencing are among the advanced technologies that NTP is using to study how chemical exposures change the expression of genes, proteins, and metabolites in targeted cells and tissues.

One of the more common toxicogenomics approach for use in NTP is by transcriptional profiling of target organs. The conventional approach has used the microarray platform but this has been transitioned into RNA-Seq and through a specialized NextGen platform, high throughput transcriptomics. The NTP is considering standardized use cases and analysis for transcript profiling in NTP toxicology studies. Briefly, NTP standard uses can be 1) chemical-toxicity classification and grouping by genes/pathways; 2) forecasting toxicity prior to pathology; 3) quantification of biological effects for point of departure (PoD) 4) NAM qualification – new approach methodology for in vitro to in vivo comparisons 5) AOP development (adverse outcome pathway); and 6) transitioning from adaptive vs adverse effects – tipping points and time of exposure. The discovery potential is well-recognized as a cross-cutting capability of transcriptomics that will continue to be exploited within NTP studies.

Measuring genome-wide changes in affected tissues could be useful for identifying disease biomarkers, detecting exposure to toxic substances, and understanding individual genetic susceptibilities. Once validated, biomarkers can be repeatedly sampled during long-term NTP studies to determine if chemical exposures can be detected or if developing diseases (e.g., cancer) provide a genetic signature.

Several FY 2019 toxicogenomic studies used NextGen sequencing technologies, which improves gene expression analysis, including base pair-level resolution of accuracy and increased sensitivity compared to microarray platforms. Although microarray analysis is a stable and well-understood technology for assaying gene expression, NextGen sequencing methods like RNA-seq likely will become more common as sequencing costs decline and bioinformatic analyses become standardized and integrated with genomic sequencing. Another promising NextGen sequencing-related area in toxicogenomics is the S1500+ platform. This platform provides a way to use high-throughput transcriptomic screening for thousands of genes per sample and can be applied to both in vitro chemical toxicity screening and in vivo screening of RNA extracted from animal tissues.

One promising research area is the application of exome sequencing (Exome-Seq) to either frozen or formalin-fixed, paraffin-embedded tissues. DNA can be extracted from either frozen or archival tissues. Coding portions of DNA, or exons, are captured by libraries of hybridization-based probes targeting over 200,000 exons and transcriptionally active regions. Exon-enriched DNA can be sequenced by DNA-Seq and then genomically aligned to find mutation insertions or deletions and other genetic abnormalities associated with disease. Several NTP studies are using Exome-Seq for profiling mutations on a genome-wide scale to understand differences between spontaneous and chemically induced tumors. An additional area of development is the isolation of circulating, cell-free

DNA (ccfDNA). DNA released from apoptosis or cell turnover normally appears in plasma, but chemical exposure can increase levels of ccfDNA due to toxicity, inflammation, or tumor development. The NTP is investigating the use and sequencing of ccfDNA in toxicology studies to determine its use as a new marker of chemical exposure.

NTP continues to evaluate study conditions that could contribute to differential gene expression, such as animal and tissue variability, methods for tissue sampling, and standards for conducting toxicogenomic studies under laboratory conditions. Planned or ongoing NTP toxicogenomic studies from FY 2019 are listed below.

#### *Toxicogenomic Studies Planned or Ongoing in FY 2019*

<b>Chemical (CASRN*)</b>	<b>Species/Cell Line</b>	<b>Route</b>	<b>Duration</b>	<b>Test Type (Platform)</b>	<b>Study Scientist</b>
112-chemical compound test set (pharmaceuticals and environmental compounds)	Human hepatocyte cell line-HepaRG	In vitro	2 days	High-throughput transcriptomic screening	Stephen Ferguson, Sreenivasa Ramaiahgari
2,3-Butanedione (diacetyl) (431-03-8) 2,3-Hexanedione (3848-24-6)	Human airway epithelium cell line	In vitro	4 days	High-throughput transcriptomic screening	William Gwinn
20-chemical compound test set (environmental compounds)	Primary rat hepatocytes Human HepaRG cells	In vitro	3 days	S1500+ NextGen sequencing	William Gwinn, Mike DeVito
Acetaminophen (103-90-2)	Mice, lean and DIO strains	Oral	18,40-week high fat diets, 24 hours APAP	Microarray and miRNA	Arun Pandiri, Takeshi
Arsenite (7784-46-5)	Human prostate cell line	In vitro	30 weeks	NextGen sequencing (Illumina)	Alex Merrick
Bisphenol A and analogues (80-05-7)	Human hepatocyte cell line	In vitro	2 days	High-throughput transcriptomic screening	Mike DeVito
Bisphenol AF (1478-61-1) Tetrabromobisphenol A (79-94-7)	Rat	Gavage	5 days	S1500+ NextGen sequencing	Sue Fenton
Bromodichloroacetic acid (5589-96-8) Methyleugenol (93-15-2)	Mouse	Gavage	2 years	NextGen sequencing Exome-Seq (Illumina)	Arun Pandiri
Carcinogens (HCC100)	Mouse	In vivo	2 years	HCC RNA-seq, CNV array	Miaofei Xu, Arun Pandiri

Chemical (CASRN*)	Species/Cell Line	Route	Duration	Test Type (Platform)	Study Scientist
Dieldrin (60-57-1) Ethinyl estradiol (57-63-6) Methyl mercury (115-09-3) Rotenone (83-79-4) Phenol (68937-41-7) Isopropylated phosphate (3:1) (60348-60-9) Pentabromodiphenyl ether (60348-60-9)	Mouse	In vitro	1 day	S1500+, NextGen sequencing	Alison Harrill
EPA tapwater concentrates	HepaRG	In vitro	2 days	High-throughput transcriptomic screening	Mike DeVito, Marianna Rosentsvit
Ginkgo biloba extract (90045-36-6)	Rat	Gavage	5 days	Microarray (Affymetrix)	Cynthia Rider, Scott Auerbach
Induced pluripotent stem cells Embryoid bodies Embryonic stem cells	Human stem cell	N/A	N/A	High-throughput transcriptomic screening	Erik Tokar, Mike DeVito
N/A	HepaRG	In vitro	1-21 days	High-throughput transcriptomic screening	Katelyn Lavrich, Steve Feruguson
N/A (High fat diet)	DO Mice	Feed	13 weeks	RNA-Seq	Alison Harrill, Madelyn Huang
N-ethyl-N-nitrosourea (759-73-9)	Rat, Harlan Sprague Dawley	Tail vein, i.v.	Single injection; brain tumor model	RNA-Seq; miRNA-Seq; Exome-Seq	Arun Pandiri, Ramesh Kovi
PCB-11 (2050-67-1)	Rat Human hepatocyte cell line	In vitro	1 day	S1500+ NextGen sequencing	Mike DeVito
PFAS -REACT Program	3D Human HepaRG	In vitro	2 days	High-throughput transcriptomic screening	Mike DeVito
PFOA, GenX	Mouse liver, placenta	Gavage	E17.5 gestational exposure	Microarray	Sue Fenton

Chemical (CASRN*)	Species/Cell Line	Route	Duration	Test Type (Platform)	Study Scientist
Phosphate flame retardants: tert-Butylphenyl diphenyl phosphate (56803-37-3) 2-Ethylhexyl diphenyl phosphate (1241-94-7) Isodecyl diphenyl phosphate (29761-21-5) Isopropylated phenol phosphate (68937-41-7)	Rat	Gavage	5 days	Microarray (Affymetrix) metabolomics	Scott Auerbach
Polycyclic aromatic compounds: Acenaphthenequinone (82-86-0) Benzo[b]fluoranthene (205-99-2) Benzo(a)pyrene (50-32-8) Dibenz[a,h]anthracene (53-70-3) 9-Methylanthracene (779-02-2) 1-Methylfluorene (1730-37-6) Perinaphthenone (548-39-0) Phenanthrene (85-01-8) Pyrene (129-00-0)	Human hepatocyte cell line	In vitro	2 days	Cytotoxicity and gene expression by quantitative polymerase chain reaction	Cynthia Rider, Erik Tokar
Tetrabromobisphenol A (79-94-7) Pentabromodiphenyl oxide-technical (DE-71) (32534-81-9) Triclosan (3380-34-5) alpha, beta-Thujone (76231-76-0)	Rat	Gavage	5 days	High-throughput transcriptomic screening	Mike DeVito, William Gwinn

\*CASRN = Chemical Abstracts Service Registry Number