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Final Report on the Safety Assessment of Cyclomethicone

Cyclomethicone is a mixture of cyclic dimethylpolysiloxane compounds used primarily as an emollient and solvent in cosmetic formulations at concentrations from < 0.1% to > 50%.

Cyclomethicone is not significantly absorbed through the skin. Small amounts of Cyclomethicone were absorbed by both humans and monkeys in oral feeding studies. The absorbed Cyclomethicone was detected in both the urine and expired air.

Acute oral dose of Cyclomethicone to rats produced no deaths nor any gross lesions. Short-term dermal studies produced no behavioral, local skin, gross, nor histopathological changes. In subchronic inhalation studies in monkeys, no significant differences were found between exposed and unexposed animals.

Undiluted Cyclomethicone applied to the intact and abraded skin of rabbits produced little or no irritation in two studies. Ocular studies indicated that Cyclomethicone produced only slight transient conjunctival irritation in washed and unwashed eyes. Cyclomethicone did not produce reproductive effects in rats. Cyclomethicone was not a mutagen when assayed in the Ames test.

Cyclomethicone was neither irritating nor sensitizing to human skin in two clinical studies.

On the basis of the available data, it is concluded that Cyclomethicone is safe as a cosmetic ingredient in present practices of use.

INTRODUCTION

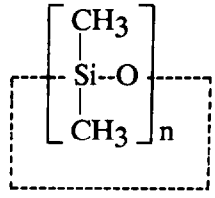
Cyclomethicone is a cyclic polysiloxane compound used primarily as an emollient and solvent in cosmetic formulations.

Cyclomethicone, as manufactured by Dow Corning, includes four fluids, two of which have the tetramer ($n = 4$) as the primary component and two that contain primarily the pentamer ($n = 5$). Since the particular properties for each of these four fluids are available (Table 1), reference as to the polymer composition (e.g., $n = 5$, $n = 4$) of Cyclomethicone has been included where appropriate. Because these fluids are so similar, references include not the specific fluid name but the general composition of the chemical.

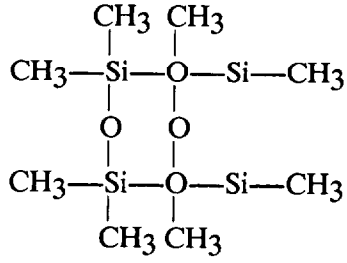
CHEMISTRY

Definition and Structure

Cyclomethicone (CAS No. 69430-24-6) is a mixture of cyclic dimethyl polysiloxane compounds that conform to the following formula:



where *n* has an average value that ranges from 3 to 6.[1] The tetramer ($n = 4$) and pentamer ($n = 5$) of Cyclomethicone are frequently the predominant polymers found in cosmetic formulations. The tetramer polymer ($n = 4$) is illustrated below.[2]



Tetramer (n=4)
Octamethylcyclotetrasiloxane

Another name for Cyclomethicone is Dimethyl Cyclosiloxane. Numerous trade names are available elsewhere.[2,3]

Chemical and Physical Properties

Cyclomethicone is a colorless, odorless, transparent, nongreasy, silicone fluid. It has a low viscosity and surface tension and a relatively high vapor pressure, which allows the majority of the silicone portion to evaporate from the surface to which it is applied. Variations in the volatility of Cyclomethicone can be achieved through the blending of its different polymers. Cyclomethicone is soluble in ethanol (99%), isopropanol (99%), mineral oil, paraffin wax, stearyl alcohol, stearic acid, and aliphatic, chlorinated, and fluorinated solvents. It is highly insoluble in water but hydrolytically stable as to be easily emulsified into most cosmetic preparations.[4]

Since the chemical name "Cyclomethicone" encompasses a number of different polymers, slight variations will exist in calculations of molecular weight, solubility, specific gravity, viscosity, and so on. Table 1 includes the physico-chemical properties of four Cyclomethicones as submitted by Dow Corning.

TABLE 1. PHYSICO-CHEMICAL PROPERTIES OF CYCLOMETHICONE

Property	*Dow Corning 244 Fluid*	*Dow Corning 245 Fluid*	*Dow Corning 344 Fluid*	*Dow Corning 345 Fluid*
Composition (polymer %)	90% $n = 4$	95% $n = 5$	90% $n = 4$ 10% $n = 5$	75% $n = 5$ 25% $n = 6$
Refractive index (25°C)	1.394	1.397	1.394	1.398
Viscosity (cs, 25°C)	2.5	4.2	2.5	5.0
Specific gravity (25°C)	0.953	0.956	0.950	0.956
Surface tension (25°C, dynes/cm)	17.8	18.0	19.0	20.8
Flash point (°C) (closed cup)	55	76	52	74
Boiling point (°C, 760 mm Hg)	172	205	178	217

Analytical Methods

A commonly used analytical method for the identification of Cyclomethicone is gas chromatography.[5,6]

Reactivity

Cyclomethicones are nondegradable, inert polymers. In normal cosmetic conditions and formulations, they are nonreactive. Cyclomethicone is compatible with many organic and other silicones.[4] The low volatility of Cyclomethicone allows the silicone portion to evaporate without cooling the skin like other volatile carrier fluids. By blending Cyclomethicones (mixtures of the n value in its structural formula), the volatility of the compound can be adjusted to correspond to the amount of time that the silicone portion is to contact the skin. At 22°C, the tetramer component ($n = 4$) evaporates nearly twice as slowly as water. The pentamer ($n = 5$) is much slower to evaporate than the tetramer.[2]

USE

Cosmetic Use

Cyclomethicone is used in cosmetic products primarily as a spreading or wetting agent. Because of its low viscosity, low surface tension, water repellency, and nongreasy texture, Cyclomethicone enhances spreading of highly viscous or waxy cosmetic systems. It is used to deposit or spread active ingredients, liquids, powders, or resins, and can provide light lubrication to hair and skin.[4]

Data obtained from the Food and Drug Administration (FDA) indicated that Cyclomethicone was used in a total of 168 product formulations. The FDA cosmetic product formulation computer printout[7] is compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.[8] Ingredients are listed in preset concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less

than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product. The actual concentration would be a fraction of that reported to the FDA. Data submitted within the framework of present concentration ranges provide the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to ten-fold error in the assumed ingredient concentration. Table 2 includes the product formulation data for Cyclomethicone as reported by the FDA.[7] Reported concentrations of Cyclomethicone in these products were present in all ranges of percentages.

Products containing Cyclomethicone are applied to all areas of the skin, hair, nails, and mucous membranes. They may be applied several times a day and remain in contact with the skin for variable periods of time following each application. Daily or occasional use may extend over many years. Cyclomethicone is formulated in eye and face makeup, manicuring preparations, skin creams and oils, foot powders and sprays, and other personal care products. The low vapor pressure of the chemical also makes it useful in cologne and odor products.

Noncosmetic Use

Noncosmetic applications of Cyclomethicone include glass and specialty cleaners, lubricants, and penetrating oils.[2] Other chemicals not specifically referred to as

TABLE 2. PRODUCT FORMULATION DATA FOR CYCLOMETHICONE[7]

Product category	Total no. containing ingredient	No. of product formulations within each concentration range (%)						
		>50	25-50	10-25	5-10	1-5	0.1-1	0-0.1
Bath oils/tablets/salts	1							1
Eyeliner	10						10	
Eye shadow	101		4	66	3	27	1	
Eye makeup remover	3				1		2	
Mascara	1						1	
Colognes/toilet waters	3					3		
Foundations	3				2	1		
Makeup bases	6			2	1	2		1
Rouges	1					1		
Other makeup preparations	1		1					
Manicuring basecoats/undercoats	2		1	1				
Nail polish and enamel	1			1				
Other manicuring preparations	3	2			1			
Other personal cleanliness products	19	10		2	4	3		
Face/body/hand (excluding shaving products)	1					1		
Foot powders/sprays	1					1		
Moisturizing products	8	1			1	3	1	2
Night preparations	2					2		
Paste masks (Mud packs)	1						1	
1984 Totals	168	13	6	72	13	44	16	4

nonvolatile silicones are reported as possible barriers in the prevention or recovery of skin damage.[4,9,10] Some siloxane oils are widely used for their lubricating properties and water repellency on walls, textiles, leather, in molds, and so on. Inhaled silicone oil vapor has acted as an antifoaming agent in the treatment of chronic bronchitis.[9] Polydimethylsiloxane, a specific silicone oil, also has been used in intraocular applications for the treatment of complicated retinal detachment.[11]

International Use

Cyclomethicone is an ingredient included in Japan's *Comprehensive Licensing Standards of Cosmetics by Category*.[5,6] This publication includes those ingredients not in *Japanese Standards of Cosmetic Ingredients* (JSCI), *Japanese Pharmacopoeia*, or *Japanese Standards of Food Additives* that may also be used in cosmetic products in Japan. As stated in the Chemical and Physical Properties section, Cyclomethicone contains different polymers depending on the value of *n* in its chemical structure. In the Japanese monographs, Cyclomethicone is listed as Decamethyl Cyclopentasiloxane ($n = 5$) and Octamethyl Cyclotetrasiloxane ($n = 4$) in Part 1 (1986) and Part 2 (1987), respectively.

BIOLOGY

Absorption

Data obtained in skin irritation studies indicated that Cyclomethicone (average $n = 4$) was not absorbed through the skin in toxic amounts.[12]

Metabolism

Two antifoam C-14 polydimethylsiloxane fluids were administered orally to rhesus monkeys to investigate metabolism of the fluids.[13] Antifoam A contained approximately 10% cyclic oligomers, and Antifoam M contained less than 0.022% of the lower molecular weight, cyclic components. Antifoam A was administered at 18 mg/kg, and 2.1 to 2.5% of the dose was recovered in expired air, bile, and urine. Blood concentrations were below the detection limit (1 ppm). Antifoam M was given at 41.8 mg/kg, and approximately 0.25% of the test material was detected in expired air and urine. Less than 0.01% was found in the tissues 72 h after dosing, and 93 to 98% of the dose was recovered from the feces. No low molecular weight siloxanes were present in the feces.

Antifoam A and Antifoam M compounds along with 30% emulsions of each were administered to humans in single oral doses of 100 mg/kg.[13] No increased amounts of silicon (measured as Si) were found in the expired air of the subjects given the emulsion or compound of Antifoam M. With Antifoam A, 1.8% and 3.3% were recovered from the urine of the subjects following dosage with the compound and emulsion, respectively, over a 6 day period. The half-life of each was 24 h. Expired air of the subjects contained at least 0.5% of the dose (half-life = 8 h), and the material was identified as the lower weight (tetramer and pentamer) cyclosiloxanes. The urinary products were not identified but probably were more polar than the cyclic components. These results indicated that the lower molecular weight cyclosiloxanes could be absorbed to some

extent. Some of the material was eliminated without metabolic change in expired air. It was unclear to the investigators whether metabolic alteration had occurred in the material eliminated in the urine.

ANIMAL TOXICOLOGY

Oral Studies

Acute Oral Toxicity

A polydimethylsiloxane fluid ($n \geq 5$) was tested in an acute oral toxicity study in albino rats.[14] Ten rats were given a 34.6 g/kg dose of the Cyclomethicone mixture. Hypoactivity, oily fur, and labored breathing were observed. No rats died and no gross lesions were noted at necropsy.

In an acute oral toxicity study in rats, 10% Cyclomethicone (average $n = 4$) in corn oil was fed in 1.0 and 2.0 g/kg doses.[12] In both cases, each group of two rats had very slight initial weight loss and slight to moderate hepatic lesions. No deaths occurred.

Single undiluted 20 g/kg doses of Cyclomethicone ($n \geq 5$) were administered to two male and two female rats in a study of oral toxicity.[15] No deaths occurred, and no adverse reactions were noted.

Dermal Studies

Short-Term Dermal Toxicity

A 28-day dermal study was conducted using male albino rabbits.[16] An undiluted dose of Cyclomethicone was applied to the backs of 10 rabbits on a schedule of 1 g/kg/day. An untreated group of 10 rabbits served as the control. No behavioral or local skin reactions, no significant gross alterations of the tissues or organs (particular attention being given to the effects on the testes), and no significant changes of body or organ weights were noted in the treated or untreated animals.

Inhalation Studies

Acute Inhalation Toxicity

An acute inhalation study using Albino rats had no adverse effects. The 10 rats (5 male/5 female) were exposed to a 90 mg/L aerosol burst of 10% Cyclomethicone (average $n = 4$) every ½ h for 7½ h.[17] Physiological and pathological examinations were made of the animals, and no adverse effects were found.

An acute inhalation study in rats was conducted for a period of 7 h in two atmospheric saturations of Cyclomethicone (average $n = 4$).[12] In the three rats treated with an approximate atmospheric saturation of 200 ppm (from a 23°C test material bath temperature), very slight initial weight loss and moderate hepatic lesions were noted. Three rats treated at an approximate atmospheric saturation of 1000 ppm (from a 100°C bath temperature) also had slight initial weight loss. Fog was generated in the 1000 ppm setup.

Short-Term Inhalation Toxicity

A 28-day inhalation study of Octamethylcyclosiloxane ($n = 4$) was conducted in hamsters, guinea pigs, rabbits, and mice.[18] For each species, two groups of male and

female animals (number not specified) were exposed to 0 and 700 ppm 6 h each day for 4 weeks. The overall mean concentration of the test material was 697 ppm. No overt signs of toxicity or deaths occurred in any group. No significant changes in body weight, feed consumption, or gross or microscopic lesions were observed in any animal in test or control groups. Significant increases in mean absolute and relative liver weights of male and female mice and female hamsters for Cyclomethicone exposed groups were found. Liver weights of exposed and control groups of the remaining animals tested were comparable.

Subchronic Inhalation Toxicity

A 90-day aerosol inhalation study on cynomolgus monkeys was conducted with Cyclomethicone.[19] Two groups of 6 monkeys each (3 male/3 female) were exposed to 10% Cyclomethicone either predominantly tetramer with pentamer (designated $n = 4$) or predominantly pentamer with tetramer (designated $n = 5$) in freon. A third group of 6 served as the control (freon only). Each group was exposed to four 15-sec sprays every 5 min for a total of 20 min twice daily. The average amount of material released in the set of four 15-sec aerosol bursts was 78.9 ($n = 4$), 77.2 ($n = 5$), and 73.9 (the control) g. [The average daily nominal concentrations were 158.3 mg/L (DC 344 Fluid), 154.8 mg/L (DC 345 Fluid); average analytical concentrations were 0.005 mg/L (DC 344 Fluid) and 0.036 mg/L (DC 345 Fluid).] Data were collected with respect to mortality, behavior, body weight, hematological, ophthalmic, and other clinical profiles. In addition, the monkeys were subjected to tuberculin tests, EKGs and x-rays. Complete pathological examinations were conducted on day 91. Results were compared to that of the control group, and statistical evaluation of numerical values was conducted where applicable. No deaths occurred, and no significant differences were found between the exposed and unexposed animals. In one of the Cyclomethicone-exposed groups ($n = 5$), the presence of some macrophages in the alveolar spaces and lumens of the terminal bronchioles in the lungs was noted on histopathological evaluation of the tissues. These "aggregates of alveolar macrophages" were limited in number and were not widespread in the lungs. Also in the same group ($n = 5$), "single, mild, physiologic abnormalities" were noted in 4 of the 6 animals in the group; these abnormalities were described as transient in nature. No such changes were noted in the other Cyclomethicone-exposed group ($n = 4$).

A 90-day inhalation study of Octamethylcyclotetrasiloxane was conducted in Sprague-Dawley rats.[20] Four groups of 10 male and female rats were exposed to 0, 50, 300, and 700 ppm 6 h each day for 13 weeks. Rats were observed and were killed for evidence of changes in blood and urine, tissue alterations, and changes in organ weights. Two additional groups of 10 rats were concurrently exposed to 0 and 700 ppm for 13 weeks. These rats were observed for the reversibility, persistence, or occurrence of toxic effects for 4 weeks after exposure before they were killed. The mean concentrations of the test material in the test groups were 51, 301, 700, and 703 (recovery group) ppm. Reductions of body weight gains were observed in females of the 700 ppm group. After the recovery period, however, the body weights were comparable to the controls. No significant changes were observed in blood, urinary, or clinical chemistry values. Increases in liver weights at two high doses were statistically significant. From these data, the investigators determined that Cyclomethicone ($n = 4$) has an effect on the liver. During a recovery period, the increase in hepatic weights did not change in females, but hepatic weights returned to normal in the males. Significant decreases in ovarian weights were found in the 700 ppm group. No gross or

histopathological changes were observed in the organs or tissues of treated and control animals.

DERMAL IRRITATION STUDIES

Undiluted Cyclomethicone (average $n = 4$) applied to the intact skin of the ear and abdomen of the rabbit produced little or no response after 10 applications.[12] Three applications of the ingredient to abraded skin of the abdomen produced slight transitory irritation.

Undiluted Cyclomethicone ($n \geq 5$) was applied to the ear and abdomen of rabbits in a skin irritation study.[15] Ten applications of the test material to the intact skin of the ear produced no skin reactions. The application of Cyclomethicone to the intact and abraded skin of the abdomen for 10 and 3 times, respectively, produced no adverse responses. No data on number of animals, dose, or other test protocol were available.

OCULAR IRRITATION STUDIES

In two studies, undiluted Cyclomethicone (average $n = 4$ and $n \geq 5$) was applied to the eye of rabbits.[12,15] In both washed and unwashed sites, there was slight conjunctival irritation with no corneal injury. Signs completely subsided within 24 h. The dose and number of animals tested were unavailable.

REPRODUCTIVE STUDIES

A short-term study in male rats investigated reproductive effects of Cyclomethicone.[15] Thirty male rats, divided in three groups of 10 each, were given an oral 4 ml/kg dose of Cyclomethicone ($x \geq 5$), saline (the negative control), or another silicone fluid (the positive control). Initial and final body weight (BW, in grams) and a seminal vesicle weight (SVW, in milligrams) were recorded in the 5-day experimental period. The SVW/BW ratio (mg/g) for the control, positive control, and Cyclomethicone were 0.85 (± 0.08), 0.54 (± 0.10), and 0.74 (± 0.12), respectively. A statistical analysis of the data by *t*-test indicated that the "probability of group similarity to (the negative) control" was 0.022 for the positive control and 0.019 for Cyclomethicone. Based on the results of the study, the investigators determined that Cyclomethicone did "not have an effect on the reproductive system as do certain materials of similar chemical composition."

Cyclomethicone (average $n = 4$) was evaluated in an extended rodent dominant lethal assay.[21] Male rats received Cyclomethicone doses of 100, 500, and 1000 mg/kg/day by gavage for 5 days per week for a period of 8 weeks. Rats given an oral dose of 0.05 mg/kg/day of triethylenemelamine, a known clastogen, served as the positive control, and those given tap water served as the negative control. Fifteen male rats were used in each of the dose and control groups. A 2-week mating period followed (2 females were supplied each week to every male) to allow for the expression of any germinal cell damage in pregnant females. The numbers of corpora lutea and live and dead implantations were counted in females killed 14 days after the midweek of mating.

Male body weights were also measured over the dosing period. No statistically significant differences were found among the Cyclomethicone-dosed rats and the positive and negative control rats in male body weight. No significant reduction in fertility or prevalence of dead implants was found in the Cyclomethicone-dosed rats as compared to the negative control. In the positive control, statistically significant differences were noted in fertility over the 2-week test period and in the number of dead implants.

MUTAGENICITY

Ames assays with and without the addition of activation systems were conducted for Cyclomethicone ($n = 4$, $n = 5$).[22] The microbial strains used were *Salmonella typhimurium* TA1535, TA1537, TA1538, TA98, and TA100. The range of concentration of the test material was 0.5 to 500 μg/plate. In all the five strains employed, Cyclomethicone tested negatively with and without metabolic activation. Cyclomethicone was considered not to be mutagenic under the conditions of the test.

CLINICAL ASSESSMENT OF SAFETY

Dermal Irritation and Sensitization

Fifty human subjects participated in a repeated insult patch test of Cyclomethicone (average $n = 4$).[23] A series of nine occlusive test patches was placed on each subject over a period of 3 weeks, with a single challenge patch testing occurring 12 days later. The arm of the 28 male subjects and the shoulder area of the upper portion of the back of the 22 female subjects were used for testing. None of the 450 skin patch applications had irritation reactions (all irritation scores for edema or erythema were zero). The investigators determined Cyclomethicone to be neither irritating to the skin nor a sensitizer.

The irritation and sensitization potential of Cyclomethicone (average $n = 5$) was evaluated in 52 (28 male and 24 female) human subjects.[24] The repeated insult patch technique involved the application of a series of nine 24-h occlusive patches followed by a single challenge patch 12 days later. No skin irritating reactions were recorded for the series of induction applications or the challenge applications (all irritation scores were zero). Cyclomethicone was considered to be neither irritating nor sensitizing to the skin.

SUMMARY

Cyclomethicone is a mixture of cyclic dimethylpolysiloxane compounds used primarily as an emollient and solvent in cosmetic formulations. It is a colorless, odorless, silicone fluid that has a high vapor pressure and low surface tension and viscosity. Cyclomethicone is soluble in aliphatic, chlorinated, and fluorinated solvents and is very insoluble in water.

Cyclomethicone is used in cosmetic formulations to deposit or spread active

ingredients, liquids, powders, or resins, but also provides light lubrication and a silky feel to hair and skin. FDA data[7] indicate that Cyclomethicone is used in 168 product formulations in all ranges of percentages. Cyclomethicone is also approved for cosmetic use in Japan.

Noncosmetic use of Cyclomethicone includes its formulation in glass and specialty cleaners, lubricants, and penetrating oils.

There was no indication that Cyclomethicone was significantly absorbed through the skin. Oral doses of a formulation containing Cyclomethicone were given to monkeys and humans. A small amount of Cyclomethicone was absorbed and mostly recovered in the urine and expired air.

In two oral toxicity studies, an acute dose of Cyclomethicone to rats produced no deaths nor any gross lesions. In a third study involving 4 rats, slight initial weight loss and slight-to-moderate hepatic lesions were found.

A short-term dermal study using rabbits produced no behavioral, local skin, gross, nor histopathological changes.

In inhalation studies, the results of acute doses of Cyclomethicone in rats were from no adverse effects to slight initial weight loss and moderate hepatic lesions. A short-term study using guinea pigs and rabbits produced no evidence of toxicity. Significant increases in hepatic weights of mice and hamsters were found in short-term inhalation studies of Cyclomethicone-exposed groups.

In subchronic inhalation studies using cynomolgus monkeys, no significant differences were found between exposed and unexposed animals. One exposed group (n = 5) had some pulmonary lesions and a few single transient abnormalities. In a 90-day inhalation study using rats, investigators determined that Cyclomethicone (n = 4) produced hepatic toxicity.

Undiluted Cyclomethicone applied to the intact and abraded skin of rabbits produced little or no irritation in two studies. Two studies of Cyclomethicone applied to the eye of the rabbit resulted in slight, transient conjunctival irritation in washed and unwashed sites.

Cyclomethicone did not produce reproductive effects in a short-term study in male rats. In an Ames assay using *S. typhimurium,* Cyclomethicone was not a mutagen.

Cyclomethicone was neither irritating nor sensitizing to human skin in two clinical dermal irritation studies using the repeated insult patch technique.

DISCUSSION

In two human sensitization studies conducted with 50 and 52 subjects, Cyclomethicone was not a sensitizer. The Panel generally would require each test to include over 150 subjects. However, the available data were considered sufficient to conclude that the ingredient is not a sensitizer. Additional studies were, therefore, not requested.

Certain phenylmethylcyclosilosaxes have produced adverse reproductive effects. Data included in this report indicate that Cyclomethicones (polydimethylsiloxanes) did not produce such similar adverse effects. No significant reductions in fertility nor prevalence of dead embryos were found in female rats after mating with Cyclomethicone-dosed male rats. Although emphasis on reproductive studies is evident in the literature on Cyclomethicone, data support the opinion that the ingredient does not produce reproductive effects.

CONCLUSION

On the basis of the available data, the Expert Panel concludes that Cyclomethicone is safe as a cosmetic ingredient in present practices of use.

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* Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, N.W., Suite 310, Washington, D.C. 20036.