Safety Assessment of Nylon as Used in Cosmetics

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All interested persons are provided 60 days from the above release date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Director, Dr. F. Alan Andersen.

The 2012 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Christina Burnett, Scientific Analyst/Writer, and Bart Heldreth, Ph.D., Chemist CIR.

Cosmetic Ingredient Review

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ABSTRACT

The Cosmetic Ingredient Review Expert Panel (the Panel) reviewed the safety of nylon polymers, which function in cosmetics primarily as bulking and opacifying agents. The Panel reviewed relevant animal and human data related to these large polymers and determined that they are not likely to penetrate the skin. While residual monomer information was not available, whatever residual monomers may be present, were not present at a sufficient level to cause any reactions in test subjects at the maximum ingredient use concentration. Accordingly, the Panel concluded that these ingredients are safe in the present practices of use and concentration.

INTRODUCTION

In the 1930's, Carothers and co-workers pioneered the synthesis of the first commercially viable synthetic fibers, polyamides.[1] The initial commercial application of these polyamides, specifically nylon 6/6, was women's hosiery. These polymers found use during World War II for parachutes, tire cord, thread and rope.

In cosmetic formulations, nylon ingredients function primarily as bulking and opacifying agents. This safety assessment reviews the available scientific literature, including unpublished data provided by industry, for Nylon-6, Nylon-11, Nylon-12, Nylon 6/12, Nylon-66, Nylon-611, Nylon-10/10 and Nylon-12/6/66 Copolymer.

ThePanel has previously reviewed the safety of 2 of the monomers used in the production of Nylon: decanedioic acid (also known as sebacic acid) and adipic acid.[2] The Panel concluded that these ingredients are safe in the present practices of use and concentration.

CHEMISTRY

The definition and structure of these ingredients are presented in Table 1, and available information on the physical and chemical properties of nylon ingredients are presented in Table 2.

The trade name terminology, nylon, has been firmly established as applying only to polyamides polymerized from unsubstituted, non-branched aliphatic monomers. Unfortunately, variations of these names are dispersed throughout the literature, such as nylon-66; 66-nylon; 6,6-nylon; and 6-6-nylon, all indicating nylon 6/6. The numbers added to the word "nylon" are indicative of the number of methylene groups (wherein the acid carbonyl can be counted as a theoretical methylene) in a monomer. These nylon ingredients are commonly synthesized via one of three ways: 1) polymerization of linear ω-amino acids, 2) ring-opening polymerization of lactams, or 3) co-polymerization of a linear diacid and a linear diamine. For example, Nylon-6 is a polyamide that can be synthesized from the unsubstituted, non-branched, aliphatic monomer 6-aminocaproic acid (Figure 1). Therein, "n" is equal to the number of monomer units in the resulting polymer. Because manufacturers can control the polymerization process to produce virtually any size polymer desired, n and, thus, molecular weights of these nylon ingredients can vary greatly.

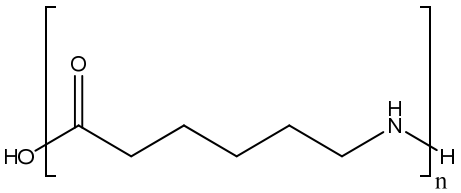
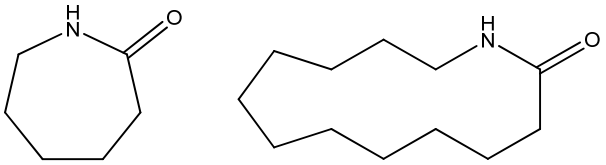


Figure 1. Nylon-6

In practice, however, Nylon-6 and other polyamides can also be synthesized from the ring-opening polymerization of the cyclic versions of these monomers, lactams. For instance, Nylon-6 and Nylon-12 can be synthesized from ε-caproplactam and dodecanolactam, respectively (Figure 2).[3] Ring-opening polymerization from the lactam monomer most likely occurs via a concerted ring-opening monomer addition. Essentially, this is a transamidation, converting from the amide of the lactam to the amide of a nylon product. The amide bond of a lactam (except in small, strained lactams that are not pertinent here) is

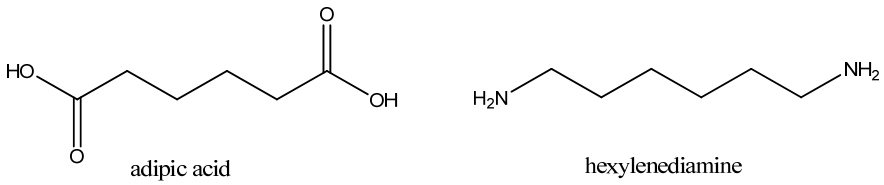
a fairly high energy bond, thus requiring reaction conditions above 500 Kelvin to initiate polymerization. However, this works in favor of processing and drawing the fibers, as they are ductile at this temperature.



caprolactam dodecanolactam

Figure 2. ε-caprolactam and dodecanolactam

Nylon analogues with two numbers added to the name represent polyamides synthesized from two distinct monomer units. Nylon 6/6 (INCI name Nylon-66), for example, is the polyamide synthesized from hexylenediamine and adipic acid (wherein each monomer has six methylene groups) (Figure 3).[3] This polymer is an ordered, alternating co-polymer of these monomers. As an example, starting with a molecule of adipic acid, the first step is the addition of one molecule of hexylenediamine. Therein, one of the nitrogens of hexylenediamine will form a bond with the carbon of one of the acid groups of adipic acid, releasing water (OH from the acid and H from the amine). This will result in a new molecule with the unreacted acid group of the adipic acid residue on one end, a newly formed amide in the middle, and the unreacted amine of the hexylenediamine at the other end. Next, either an additional molecule of adipic acid can be added to the unreacted amine of the hexylenediamine residue, or an additional molecule of hexylenediamine can react with the unreacted acid of the adipic acid residue. The polymerization will then continue in both directions, along the linear axis of the growing polymer, until one of the monomers is spent or a terminating group (eg, acetic acid) may be added to endcap the amines.



adipic acid hexylenediamine

Figure 3. Adipic acid and hexylenediamine

Traditionally, the first number listed in nylon nomenclature represents the diamine monomer and the second number represents the di-acid, but this is not strictly followed. Indeed, Nylon 6/12 is actually a polyamide synthesized via the co-polymerization of caprolactam and dodecanolactam (neither of which is a diamine or a diacid).

Nylon-6 and Nylon-66 can undergo photo-oxidative degradation, resulting in loss of strength, following long-term exposure to UV radiation.[3]

Method of Manufacture

The nylon analogues in this report, and polyamides in general, are typically manufactured by direct amidation of a diacid with a diamine, by self-amidation of amino acids, or by ring-opening transamidation of lactams.[3] For example, a supplier reports that Nylon-10/10 is obtained by melt polycondensation of sebacic acid (decanedioic acid) and decane diamine, and Nylon-12 is synthesized by ring-opening polymerization using laurolactam.[4] A stoichiometric balance, in the case of direct amidation of a diacid, is readily obtained by the preliminary formation of a diammonium salt (referred to as a "nylon salt"). This balance can be adjusted simply by adjusting pH. This aqueous salt solution is then concentrated to a slurry, and heated under pressure. The pressure is then slowly released to essentially perform a melt-polymerization. Molecular-weight control is often achieved by adding acetic acid as an end-capping unit.

Impurities

Nylon-6 may contain approximately 1% of the monomer, ε-caprolactam.[5] Additionally, Nylon-6 may contain 6-aminocaproic acid, as well as ε-caprolactam, if synthesized from the ω-amino acid.

A product description of Nylon-12 indicated that the maximum levels of heavy metals and arsenic were 10 ppm and 1 ppm, respectively; however, certificates of analysis for this product indicate that these substances were not detected (detection limits were not specified).[6-8] Polybrominated biphenyls (PBBs) and polybrominated diphenyl ethers (PDBEs) also were not detected (detection limits were not specified).[8] In further analyses of Nylon-12, the residual solvent levels of isoparaffinic hydrocarbon ranged from 0.08%-0.13% and the residual monomer of the Nylon-12 powder was 100 ppm or less, which meets USP 33/NF 28.[9-11] The initiator and catalyst in the manufacture of Nylon-12, potassium metal and phosphorus trichloride, were reported to be 2.0%-2.5% and 1.0%-2.0%, respectively.[11]

A supplier of Nylon-12 and Nylon-10/10 reported the residual monomer content after ethanolic extraction to be 0.14-0.18%.[4]

Nylon 6/12 is reported to have at least 85% (w/w) ε-caprolactam residue and not more than 15% (w/w) docecanolactam residue.[12]

Inclusion of a variety of chemicals (including volatile liquids and even gasses) is a common occurrence in polymer manufacture, especially in large-scale production. Most commercial polymers have at least some monomer, solvent, initiator, or catalyst. entrapped in the polymer superstructure, which may not be easily evaporated or released. The entrapment *may* be so inclusive that there is little concern of release under normal conditions of use, but time and solvents in a formulation *may* enable the escape/release of these non-polymeric materials.

To further complicate matters, the glass transition temperature (Tg) of Nylon-6 (25 ^{o}C) is just above room temperature but below body temperature. A Tg is a unique properties-changing temperature threshold exclusive to polymers. Above this temperature, the polymer is more pliable and plastic like. Below this temperature, the polymer is more brittle and "glass-like." Nylon-6 may be below the Tg in packaging, but on the skin it could rise above the Tg. Exceeding this threshold causes a change in the physical properties of the polymer, potentially increasing the rate of release of the monomer(s) or other non-polymeric materials from the polymer.

USE

Cosmetic

The nylon ingredients discussed in this safety assessment function primarily as bulking and opacifying agents in cosmetic formulations.[13] Additional functions may include absorbents (Nylon 6/12) and -611) and film formers (Nylon-12/6/66).

Table 3 presents the current product formulation data for the nylon ingredients. According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP), Nylon-12 has the most reported uses in cosmetic and personal care products, with a total of 980; 213 of those uses are in eye shadow formulations.[14] Nylon-6 has the second greatest number of overall uses reported, with a total of 61; 31 of those uses are in mascara formulations.

In a survey of use concentrations conducted by the Personal Care Products Council, Nylon-12 is reported to be used at a range of maximum concentrations of 0.001%-35%, with 35% reported in face powder formulations. For Nylon-6, the range of maximum concentrations was reported to be 0.01%-20%, with 20% reported in eyebrow pencil formulations. No uses or concentrations were reported for Nylon-611 or Nylon-12/6/66 Copolymer. Nylon-10/10 is a new cosmetic ingredient for which there are no reported uses to the VCRP and no reported use concentrations as of yet.

Nylon 12 was reported to be used in perfumes and other fragrance preparations and could possibly be inhaled. These ingredients are reportedly used at concentrations up to 8%. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm.[15-18] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[15,17]

The nylon ingredients in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union.[19]

Non-Cosmetic

Nylons, especially Nylon-6 and Nylon-66, have been used in textiles, such as hosiery, parachutes, tent cloth and other woven fabrics, thread, tire cord, fishing line, and rope, since the early 1940s.[1,20]

Nylon-6, Nylon-11, Nylon-12, Nylon 6/12, and Nylon-66 have been approved by the FDA as indirect food additives used for food contact surfaces (21 CFR §177.1500).

Nylon-6 and Nylon-66 are used in non-absorbable surgical sutures, which are FDA-approved medical devices (21 CFR §878.5020).

TOXICOKINETICS

Nylon-6 Monomer

The major metabolites of the monomer of Nylon-6 were studied in male Sprague-Dawley rats that received 3% caprolactam in their feed *ad libitum* for 2 to 3 weeks.[21] The metabolites were isolated by ion-exchange chromatography and characterized by infrared and nuclear magnetic resonance spectroscopy from urine samples collected at 24-h intervals during the final week of feed administration. The majority of the caprolactam (~16% of the dose) was excreted as 4-hydroxycaprolactam or the corresponding free acid, which rearranges in acidic solutions to yield an equilibrium mixture of 6-amino-γ-caprolactone and 6-amino-4-hydroxyhexanoic acid. In addition to these metabolites, a small amount of 6-aminohexanoic acid was excreted.

No other relevant studies on the toxicokinetics of the nylon ingredients were discovered in the published literature.

TOXICOLOGICAL STUDIES

Acute Toxicity

Oral – Non-Human

Nylon-12

The acute oral LD_{50} for Nylon-12 was reported to be 1 g/kg in rats, mice, guinea pigs, and rabbits.[22] In cats, the acute oral LD_{50} was about 0.25 g/kg.

Nylon 6/12

The acute oral LD_{50} for Nylon 6/12 in a corn oil suspension was reported to be greater than 10 g/kg in Sprague Dawley rats.[12]

Intraperitoneal – Non-Human

Nylon-6 Monomer

In a study from 1954, the monomer of Nylon-6, ε-caprolactam, caused convulsions in rats following intraperitoneal (i.p.) injection (frequency and duration not described) at doses starting at 500 mg/kg.[5] Deaths were observed at doses of 800 mg/kg and higher.

Nylon-11

In an acute study, groups of 25 male mice received i.p. injections (1.0 ml per 20 g of body weight) of Nylon-11 macerated in normal saline, cottonseed oil, or 30% ethyl alcohol.[23] The mice were closely observed for the first hour after injection and then periodically for the next seven days. No toxic responses were observed.

Nylon-12

The acute i.p. LD_{50} was reported to be 0.32-0.53 g/kg in rats.[22]

Intravenous – Non-Human

Nylon-6 Monomer

In a 1954 study, the monomer of Nylon-6, ε-caprolactam, caused convulsions in rabbits following intravenous (i.v.) injection (frequency and duration not described).[5] The animals were dosed with 100 to 300 mg/kg of the monomer, but the doses that caused the convulsions were not identified.

Nylon-11

The study described in the previous paragraph also tested mice with Nylon-11 through i.v. injection (1.0 ml per 20 g of animal weight).[23] No toxic responses were observed.

Rabbits were cannulated in the jugular vein with Nylon-11 macerated in normal saline, 30% ethyl alcohol, or harsh alcohol extract (HAE; the result of refluxing nylon pellets with absolute alcohol for 24 h).[23] The internal carotid artery was cannulated for blood pressure measurement and the trachea was

cannulated for differential respiratory measurement. No further details on doses or exposure durations were provided. A decrease in blood pressure was observed after dosing with the Nylon-11 in the ethyl alcohol extract. In some cases, there was a prolongation of the response to i.v. acetylcholine administered 4 minutes after the Nylon-11, but this effect could not always be duplicated. Negative effects were observed with the saline or HAE.

Repeated Dose Toxicity

Oral – Non-Human

Nylon-12 Monomer

In a subchronic study, male rats in groups of 10 were fed doses of 0, 0.06, 0.12, 0.25, or 0.5 g/kg of dodecanolactam, the monomer of Nylon-12, via stomach tube, 5 times per week for 12 weeks.[22] The no-effect level was 0.5 g/kg. No microscopic examination was performed on the major organs.

Dodecanolactam was evaluated for toxicity in a 90-day feeding study in Beagle dogs.[22] Groups of 4 males and 4 females received 44-49, 350-352, or 969-989 mg/kg dodecanolactam in feed (high dose group received capsules) 6 times per week. A positive control group received 306-353 mg/kg caprolactam in feed. (Results of the positive control group were not described.) A negative control group was also included in the study. The dogs were observed daily for ~ 8 h during the week and at least once daily on weekends. No abnormal behavior was observed during the treatment period in the controls and in the low and medium dose groups.

However, all dogs in the high dose group demonstrated an intense resistance to the administration of the capsules at times. On the second day, the dogs exhibited apathy, ataxia, trembling, and sialorrhea. Reactions to auditory and visual stimuli were observed. These signs occurred throughout the treatment period. One female dog of the high dose group died after 5 weeks. The death was preceded by severe lateral decubitus, extremely high respiratory frequency, and intense howling on occasion. Diarrhea was observed during the entire study in the high dose group and on occasion in the low and medium dose group. Vomiting was observed in all groups, except the positive control group, with the highest frequency occurring in the high dose group. Dogs in the high dose group exhibited loss of body weight ranging from 20-25%. Dogs in the remaining dose groups showed an increase in body weight. Feed consumption was decreased in the high dose group, but not in the remaining dose groups. Urine parameters were normal in all dogs. A decrease in erythrocyte number, hematocrit, and hemoglobin concentration was observed in one dog of the high dose group, the reticulocyte number was elevated after 3 months in another dog in the high dose group, and the leucocyte count decreased with a statistically significant difference from the negative controls in the high dose females after 1.5 months and in the high dose males after 3 months. A slight elevation in GPT activity in serum at 1.5 and 3 months was observed in the high dose group. Increased alkaline phosphatase activity was observed in the middle dose group at 1.5 months in females and at 3 months in males; these levels were elevated in the high dose group males and females after 1.5 months. Liver and kidney function tests in all dogs during the duration of the study were normal.

Ophthalmoscopic exams on all dogs yielded normal results. At necropsy, a statistically significant increase in the liver weights in the female high dose dogs was observed, as was a statistically significant increase in liver weight/brain weight ratio, when compared to the negative controls. A statistically significant increase in the liver weight/body weight ratio was observed in dogs in the middle and high dose groups. In high dose group males, statistically significant decreases in absolute testes weight, testes weight/body weight ratio, and testes weight/brain weight ratio were observed when compared to negative controls. Histopathological examination indicated changes in the prostate and testes in the high dose group. Interruption of spermatozoa maturation was observed in this group.

This 90 day study in Beagle dogs concluded that the no significant effect level was 44 mg/kg and the estimated maximum acceptable daily intake in food for man was calculated to be 2.6 mg/kg or 1.74 ppm.[22]

Intraperitoneal – Non-Human

Nylon-11

In a subchronic study, groups of 10 female Holtzman rats received daily i.p. injections (2 ml) of Nylon-11 macerated in HAE (doses not reported).[23] A control group of 10 rats received daily i.p. injections of normal saline solution. The injections were given 5 days a week for 6 weeks. A blood study was conducted on each rat at the beginning and end of the experiment. The animals were weighed weekly. At the end of the study, all animals were killed and underwent histopathological examination. The hematological values indicated a significantly higher white cell count for the rats that received Nylon-11

compared to the control group; however, the authors of this study could not attribute this observation directly to the test material "because the terminal count was elevated over the initial count as would be expected". No other signs of toxicity to Nylon-11 were observed in this study.

Tissue Implantation – Non-Human

Nylon-11

The potential toxicity of Nylon-11 in pellet form was studied for up to 3 months in rabbits.[23] Groups of 2-10 animals received implantation of the samples in the paravertebral muscle, the brain, and the intestinal mesentery. Positive and negative control samples were implanted into the same animals (materials used were not specified). Animals were observed for behavioral changes and "signs of growths" throughout the 3 month period. No toxicity to the exposed tissues was observed, even in a histopathological exam.

This study also used albino Holtzman female rats to study toxicity to Nylon-11.[23] The test article was implanted in the thigh, medial to the biceps femoris muscle and bounded by the adductor femoris, gastrocnemius, and the biceps femoris. In several additional rats, implants were placed in the nape of the neck into or between fascia or fatty tissue, lying near the dorsal surface of the levator auris muscle. At various post-implantation times, the rats were killed and the implant sites were examined for evidence of toxicity. No evidence of toxicity was observed.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

The potential for the Nylon-6 monomer, caprolactam, to cause developmental toxicity was evaluated in Fischer 344 rats and New Zealand White rabbits.[24] Groups of 20 rats received 0, 100, 500, or 1000 mg/kg bodyweight/d via gavage on days 6–15 of gestation. All surviving dams were killed on day 20 of gestation and the dams and fetuses were examined. The high-dose group dams had significantly decreased ($p \pm 0.05$) maternal survival rate and fetal viability. The remaining dose groups were comparable to controls. In the fetuses, no skeletal anomalies or major malformations were observed in any dose group.

Groups of 25 rabbits received 0, 50, 150, or 250 mg/kg bodyweight/d caprolactam via gavage on days 6–28 of gestation. An additional group of 21 rabbits received 3 mg/kg/d of the positive control, 6-aminonicotinamide, on gestation day 9. All surviving does were killed on day 29 of gestation and the does and fetuses were examined. No embryotoxicity or teratogenicity was observed. In the 150 and 250 mg/kg/d groups, fetal weights were decreased ($p < 0.05$ and $p < 0.01$, respectively), and in the 250 mg/kg/d group, an increased incidence of 13 ribs was observed ($p < 0.05$). The group that received 6-aminonicotinamide had significant loss of weight in the does ($p < 0.05$); decreased fetal weight ($p < 0.01$); and the fetuses all had major malformations. This study concluded that caprolactam did not induce embryotoxicity or teratogenicity in rats or rabbits.[24]

In a three-generation reproduction study, Fischer 344 albino rats received feed containing 0, 1000, 5000, or 10,000 ppm caprolactam.[25] The dose groups consisted of 10 male rats/group and 20 female rats/group, and each generation was treated over a 10-week period. Decreased body weights and feed consumption were observed in the 5000 and 10,000 ppm dose groups of both the parental generations and the offspring (from in utero through weaning). Significantly decreased body weights were observed in mature rats that received 5000 ppm caprolactam. Additionally, kidney toxicity, which consisted of slightly increased severity of spontaneous nephropathy accompanied by granular casts, was observed in the males of the 10,000 ppm group. No treatment-related effects on gross appearance, gross pathology, survival rate or number of pups were observed. The study concluded that the no-effect level for caprolactam toxicity was 1000 ppm and the minimum effect level was 5000 ppm. The reproductive toxicity no-effect level for caprolactam was 10,000 ppm.

GENOTOXICITY

No studies were found on the genotoxicity potential of the nylon polymer ingredients. However, the available genotoxicity data for caprolactam and dodecanolactam are summarized in Table 4. In a previous CIR safety assessment of dicarboxylic acids, adipic acid was not genotoxic in bacterial assays at concentrations up to 10,000 mg/plate, with or without metabolic activation, or in a yeast gene assay up at concentrations up to 200 mg/L.[2] In mammalian cells, adipic acid was not genotoxic at concentrations up to 200 mg/L in human embryonic lung fibroblast cells.

CARCINOGENICITY

Nylon-6 Monomer

The carcinogenic potential of the monomer of Nylon-6, ε-caprolactam, was studied in groups of 50 male or 50 female F344 rats and 50 male or 50 female B6C3F1 mice for 103 weeks.[26] In the feeding study, the rats received 3,750 or 7,500 ppm of the monomer and the mice received 7,500 or 15,000 ppm. Control groups consisted of 50 undosed rats and 50 undosed mice of each sex. During the study, mean body weight gains for dosed rats and mice of either sex were decreased when compared with those of the controls. No other treatment-related effects were observed. It was concluded that ε-caprolactam was not carcinogenic for F344 rats or B6C3F1 mice.

The International Agency for Research on Cancer (IARC) determined that caprolactam is probably not carcinogenic to humans (Group 4).[27]

Nylon-11 Monomer

The carcinogenic potential of the monomer of Nylon-11, 11-aminoundecanoic acid, was studied in groups of 50 male or 50 female F344 rats and 50 male or 50 female B6C3F1 mice for 103 weeks.[28] In the feeding study, the animals received 7,500 or 15,000 ppm of the test material. Control groups consisted of 50 undosed rats and 50 undosed mice of each sex. During the study, mean body weight gains for dosed male rats and mice of each sex were decreased when compared with those of the controls. A dose-related decrease in survival was also observed in these animal groups. Also noted was a dose-related increased incidence of hyperplasia of the transitional epithelium of the kidney and the urinary bladder in rats of both sexes. In the dosed mice, mineralization of the kidney was observed in both sexes. In high-dose male rats, neoplastic nodules of the liver and transitional-cell carcinomas of the urinary bladder were observed at significantly increased incidences ($p<0.01$) when compared with controls. Low-dose male mice had significantly increased incidences ($p<0.05$) of malignant lymphomas. It was concluded that 11-aminoundecanoic acid was carcinogenic in male F344 rats, but not carcinogenic in female F344 rats or female B6C3F1 mice. The results were equivocal for male B6C3F1 mice.

IARC determined that 11-aminoundecanoic acid is not classifiable as to its carcinogenicity to humans (Group 3).[29]

Nylon-66 Monomer

As previously reported by CIR, adipic acid was not carcinogenic in a 2-year study in rats fed diets containing up to 5% adipic acid.[2]

IRRITATION AND SENSITIZATION

Irritation

Human – Ocular

In an ophthalmological in-use safety evaluation of an eye shadow containing 5% Nylon-12, 33 female subjects were instructed to apply the product as they normally would at least once a day for 4 weeks.[30] Prior to the start of the study and at study completion, the subjects underwent a complete ophthalmic examination. The subjects kept a daily diary to record use. Approximately 50% of the panel wore hard or soft contact lenses. No adverse events were reported during the study. All ophthalmologic examinations found the subjects' eyes to be within normal limits throughout the study. It was concluded that an eye shadow containing 5% Nylon-12 did not produce ocular irritation and was considered safe for use by contact and non-contact lens wearers, individuals with self-perceived sensitive eyes, and individuals with normal eyes.

Non-Human - Other

Nylon-11

The intracutaneous toxicity of Nylon-11 macerated in normal saline, cottonseed oil, 30% ethyl alcohol, or HAE was evaluated in rabbits.[23] Approximately 0.2 ml of each eluate was injected in the back of shaved animals. (No further details were provided). The injection sites were observed for 48 h for signs of erythema or edema. A slight positive response was observed to the Nylon-11 in HAE. No tissue responses were noted in the remaining eluates.

Sensitization

Human

Nylon-12

A human repeat insult patch test (HRIPT) of a lip product containing 3% Nylon-12 was performed on 30 subjects.[31] The type of patch was not described. No dermal irritation or allergic hypersensitivity to the test material was observed.

A HRIPT was performed on 103 subjects using an eye shadow containing 5% Nylon-12.[32] The subjects received 0.2 g of the test material on a 1 squared inch pad. The treatment site was then semi-occluded. No adverse events were observed during the induction period or the challenge period. No dermal irritation or allergic contact sensitization was observed to the eye shadow.

In another HRIPT, a concealer containing 6% Nylon-12 was evaluated in 103 subjects.[33] The subjects received 0.2 g of the test material on a 1 squared inch pad, which was then semi-occluded. No adverse events were observed during the test period. No dermal irritation or allergic contact sensitization was observed to the concealer.

The sensitization potential of a solid perfume containing 5.24% Nylon-12 was studied in a HRIPT with 107 subjects.[34] The test material was applied as received under a semi-occlusive patch. The study concluded that the solid perfume containing 5.24% Nylon-12 did not demonstrate a clinically significant potential for eliciting dermal irritation or sensitization.

A HRIPT of a face powder containing 35% Nylon-12 was performed on 221 subjects.[35] The subjects received approximately 0.2 g of the test material on a ¾ inch squared pad and the treatment site was occluded. The study concluded that the face powder containing 35% Nylon-12 did not indicate a potential for dermal irritation or allergic contact sensitization.

Nylon 6/12

A HRIPT was performed on 103 subjects using a face powder containing 1.4% Nylon 6/12.[36] The subjects received 0.2 g of the test material on a 1 squared inch pad. The treatment site was then semi-occluded. No adverse events were observed during the induction period or the challenge period. No dermal irritation or allergic contact sensitization was observed to the face powder.

SUMMARY

The nylon ingredients evaluated in this safety assessment function primarily as bulking and opacifying agents in cosmetic formulations. Nylon-12 has the most reported uses in cosmetic and personal care products, with a total of 980; 213 of those uses are in eye shadow formulations. Nylon-6 has the second greatest number of overall uses reported, with a total of 61; 31 of those uses are in mascara formulations. Nylon-12 is reported to be used at a maximum concentration range of 0.001%-35%, with 35% reported in face powder formulations. In Nylon-6, the maximum concentration range was reported to be 0.01%-20%, with 20% reported in eyebrow pencil formulations. No uses or concentrations were reported for Nylon-611 or Nylon-12/6/66 Copolymer.

The nylon ingredients in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union.

Nylon has been used in textiles, such as hosiery, parachutes, tent cloth and other woven fabrics, thread, tire cord, fishing line, and rope, since the early 1940s. Nylon-6, Nylon-11, Nylon-12, Nylon 6/12, and Nylon-66 have been approved as indirect food additives as polymers used for food contact surfaces, and Nylon-6 and Nylon-66 are used in non-absorbable surgical sutures.

The acute oral LD_{50} for Nylon-12 was reported to be 1 g/kg in rats, mice, guinea pigs, and rabbits. In cats, the acute oral LD_{50} for Nylon-12 was about 0.25 mg/kg. The acute i.p. LD_{50} for Nylon-12 was reported to be 0.32-0.53 mg/kg in rats.

The acute oral LD_{50} for Nylon 6/12 in a corn oil suspension was reported to be greater than 10 g/kg in rats.

In acute studies, no toxic responses were observed in mice that received i.p. or i.v. injections of Nylon-11 macerated in normal saline, cottonseed oil, or 30% ethyl alcohol. A fall in blood pressure was observed after dosing rabbits in the jugular vein with the Nylon-11 in the ethyl alcohol extract.

The no-effect level for nylon-12 monomer was 0.5 g/kg in a subchronic study in male rats. The evaluation of the monomer for Nylon-12, dodecanolactam, in a 90-day feeding study in Beagle dogs

concluded that the no significant effect level was 44 mg/kg and the estimated maximum acceptable daily intake in food for man was calculated to be 2.6 mg/kg or 1.74 ppm.

In a subchronic study, rats that received daily i.p. injections of Nylon-11 macerated in HAE had significantly higher white cell count. No signs of toxicity were observed in rabbits and rats that received implant of Nylon-11 in pellet form. In rabbits, slight positive responses were observed in intracutaneous studies of Nylon-11 in HAE, but negative results were observed in normal saline, cottonseed oil, and 30% ethanol.

While there were no data available on the nylon polymers, data were available on the monomer caprolactam. These data largely indicate that caprolactam is not genotoxic, with negative results in a bacterial cell assay up to 50 mg/plate and in Chinese hamster ovary cell assay up to 11.25 mg/ml. However, dose-dependent increases were observed in recombination frequency in a yeast cell assay when tested with caprolactam up to 40,000 µg/ml. Caprolactam also produced weakly positive results in a newt larvae micronucleus test. In a previous CIR safety assessment of dicarboxylic acids, adipic acid was not genotoxic in bacterial assays at concentrations up to 10,000 mg/plate, with or without metabolic activation, or in a yeast gene assay up at concentrations up to 200 mg/L. In mammalian cells, adipic acid was not genotoxic at concentrations up to 200 mg/L in human embryonic lung fibroblast cells.

Caprolactam was not carcinogenic in a 103 week feed study in rats and mice. In a similar study, the monomer of Nylon-11, 11-aminoundecanoic acid, neoplastic nodules of the liver and transitional-cell carcinomas of the urinary bladder were observed in male rats, but not in female rats or female mice. The results were equivocal for male mice. As previously reported by CIR, adipic acid was not carcinogenic in a 2-year study in rats fed diets containing up to 5% adipic acid.

In human irritation and sensitization studies, Nylon-12 was not an ocular irritant nor was it a dermal sensitizer in products that contained the ingredient at concentrations up to 6%. Nylon 6/12 was not a dermal sensitizer in a face powder at a concentration of 1.4%.

DISCUSSION

The CIR Expert Panel discussed the issue of incidental inhalation exposure from fragrance preparations. There were no inhalation toxicity data available. The Panel considered pertinent data indicating that incidental inhalation exposures to Nylon-12 in such cosmetic products would not cause adverse health effects, including data characterizing the potential for Nylon-12 to cause dermal irritation or sensitization, and other effects. The Panel noted that 95% – 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. The potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. In principle, inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects depending on their chemical and other properties. However, coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

The Panel noted that the size of the polymers would appear to preclude significant dermal penetration, but expressed concern that residual monomer data were not available. The Panel reviewed human repeat patch test data on nylon-12 at its maximum use concentration of 35%. No sensitization or irritation was observed in this study. From these data, the Panel determined that whatever residual monomers may be present in nylon-12, were not present at a sufficient level to cause any biological reactions in test subjects at the maximum use concentration.

CONCLUSION

The CIR Expert Panel concluded that Nylon-6, Nylon-11, Nylon-12, Nylon 6/12, Nylon-66, Nylon-611, Nylon-10/10 and Nylon-12/6/66 Copolymer are safe in the present practices of use and concentration in cosmetics.

TABLES AND FIGURES

Table 1. Definitions, functions, and structures of nylon ingredients in this safety assessment.[13] (Italicized text and bracketed numbers have been provided by CIR staff.)

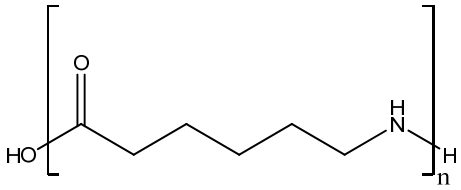
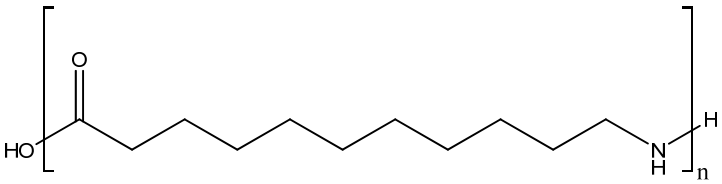
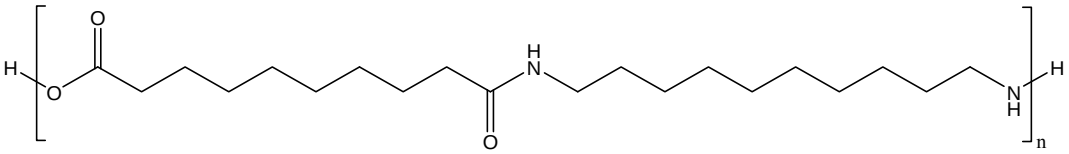
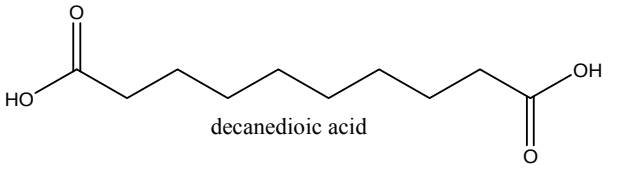
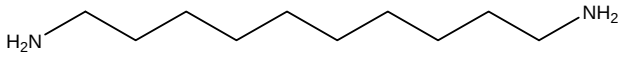
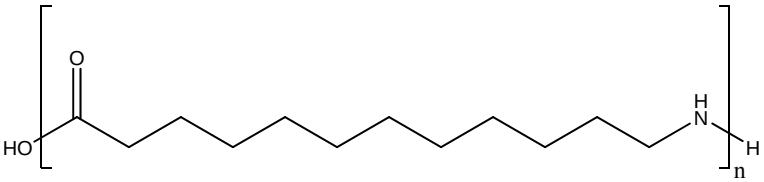
Ingredient CAS No.	Definition	Formula/structure
Nylon-6 25038-54-4	Nylon-6 is the polyamide that conforms to the formula *as shown. Nylon-6 is the linear polyamide obtained from caprolactam.*	
Nylon-11 25035-04-5	Nylon-11 is the polyamide that conforms to the formula *as shown. Nylon-11 is the polyamide polymerized from 11-aminoundecanoic acid.*	
Nylon-10/10 [28774-87-0]	*Nylon-10/10 is a polyamide formed by the reaction decanedioic acid with decylenediamine. It conforms generally to the formula as shown.* Functions like:  But the actual starting materials are:  decanedioic acid  decylenediamine	
Nylon-12 25038-74-8	Nylon-12 is a polyamide derived from 12-aminododecanoic acid. It conforms generally to the formula *as shown.*	
Nylon 6/12 [25191-04-2]	Nylon 6/12 is a polyamide coploymer formed by the reaction of caprolactam and dodecanolactam	

Table 1. Definitions, functions, and structures of nylon ingredients in this safety assessment.[13] (Italicized text and bracketed numbers have been provided by CIR staff.)

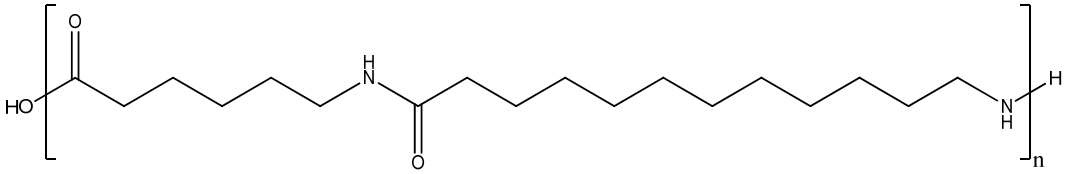
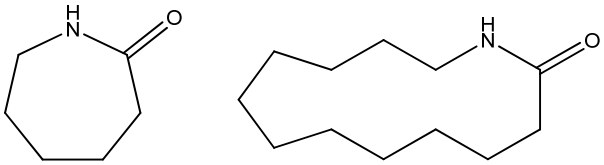
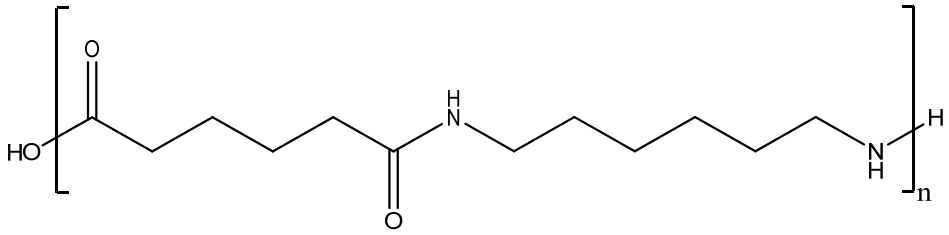
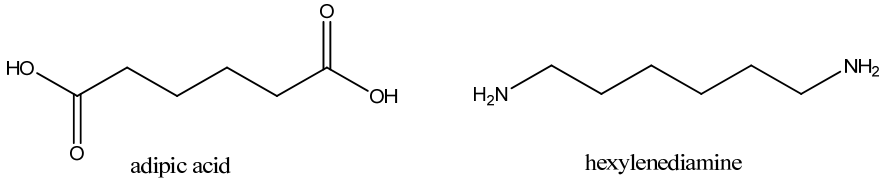
Ingredient CAS No.	Definition	Formula/structure
		Functions like:  But the actual starting materials are:  caprolactam dodecanolactam
Nylon-66 32131-17-2	Nylon-66 is a polyamide formed by the reaction of adipic acid with hexylenediamine. It conforms generally to the formula as *shown.*	Functions like:  But the actual starting materials are:  adipic acid hexylenediamine
Nylon-611 [50733-20-5]	Nylon-611 is a polyamide formed by the reaction undecanedioic acid with hexylenediamine. It conforms generally to the formula *as shown.*	

Table 1. Definitions, functions, and structures of nylon ingredients in this safety assessment.[13] (Italicized text and bracketed numbers have been provided by CIR staff.)

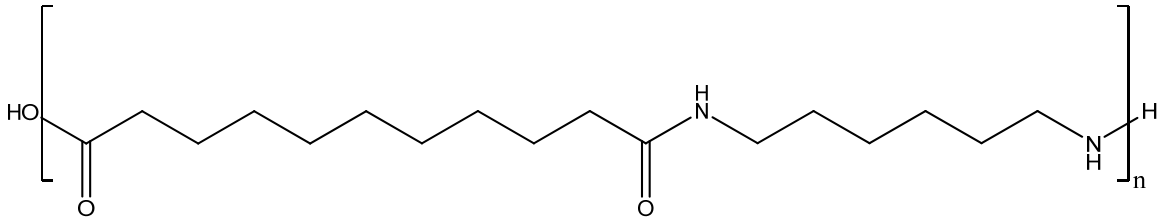
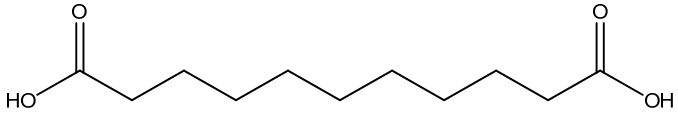
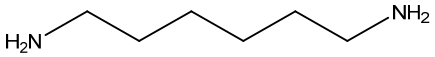
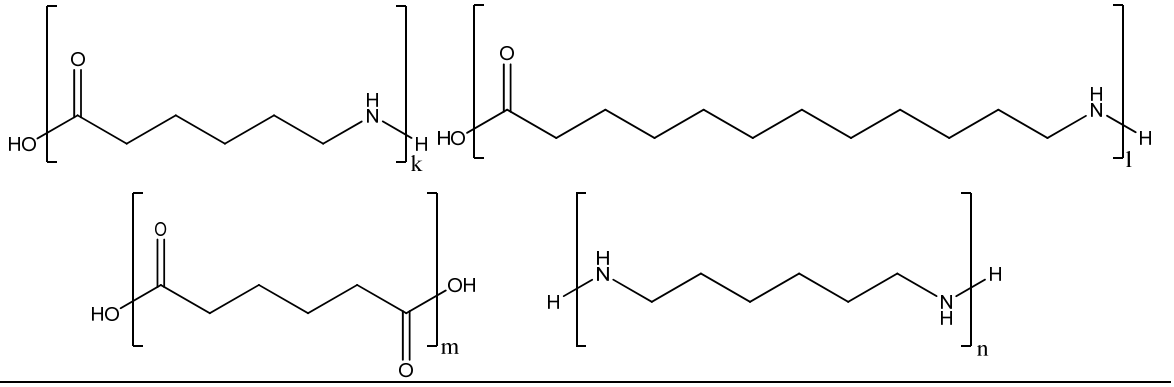
Ingredient CAS No.	Definition	Formula/structure
		Functions like:  But the actual starting materials are:  undecanedioic acid  hexylenediamine
Nylon-12/6/66 Copolymer [26777-62-8]	Nylon-12/6/66 Copolymer is a copolymer formed from the monomers used in the manufacture of Nylon-12, Nylon-6 and Nylon-66.	

Table 2. Physical and chemical properties.

Property	Value	Reference
Nylon-6		
Density/Specific Gravity	1.09-1.62	[37]
Melting Point °C	215-223	[3,20]
Glass Transition Temperature °C	25	[3]
Nylon-11		
Density/Specific Gravity	1.02-1.09	[3,37,38]
Melting Point °C	183-188	[3,38]
Glass Transition Temperature °C	115	[3]
Nylon-12		
Physical Form	Fine powder	[6]
Color	White	[6]
Odor	None	[6]
Molecular Weight g/mol	3.0×10^5	[6]
Density/Specific Gravity	0.960-1.21	[37]
Melting Point °C	165-175	[6]
pH (suspension in water)	6.0-8.0	[6]
Particle Size μm (avg.)	6-9	[6]
Particle Size μm (max.)	20	[6]
Nylon6/12		
Density/Specific Gravity	1.02-1.35	[3,37]
Melting Point °C	206	[3]
Glass Transition Temperature °C	72	[3]
Nylon-66		
Density/Specific Gravity	1.07-1.22	[37]
Melting Point °C	260	[3]
Glass Transition Temperature °C	47	[3]
Nylon-611		
Molecular Weight g/mol	1.3×10^4	[39]
Melting Point °C	212	[39]
Glass Transition Temperature °C	45.7	[39]

Table 3. Frequency and maximum concentration of use according to duration and type of exposure[14,40]

	Nylon-6		Nylon-11		Nylon-12	
	# of Uses	*Max Concs of Use (%)*	*# of Uses*	*Max. Concs of Use (%)*	*# of Uses*	*Max. Concs of Use (%)*
Totals*	**76**	**0.01-20**	**6**	**4**	**1185**	**0.001-35**
Duration of Use						
Leave-On	*74*	*0.01-20*	*2*	*NR*	*1179*	*0.001-35*
Rinse Off	*2*	*NR*	*4*	*4*	*6*	*0.5-1*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	50	0.1-20	NR	NR	369	0.2-25
Incidental Ingestion	1	5	NR	NR	28	0.05-13
Incidental Inhalation-Sprays	NR	NR	NR	NR	39	0.5-8
Incidental Inhalation-Powders	9	5-12	NR	NR	210	0.9-35
Dermal Contact	32	0.01-20	6	4	1113	0.05-35
Deodorant (underarm)	NR	NR	NR	NR	10	2-3[a]
Hair - Non-Coloring	1	NR	NR	NR	2	0.01
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	1	1	NR	NR	11	0.001-3
Mucous Membrane	2	5	1	NR	29	0.05-13
Baby Products	NR	NR	NR	NR	NR	NR

	Nylon 6/12		Nylon-66		Nylon†
	# of Uses	*Max. Concs of Use (%)*	*# of Uses*	*Max. Concs of Use (%)*	*# of Uses*
Totals*	**8**	**1**	**38**	**0.2-8**	**3**
Duration of Use					
Leave-On	*8*	*1*	*38*	*0.2-8*	*2*
Rinse Off	*NR*	*NR*	*NR*	*NR*	*1*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type					
Eye Area	NR	NR	13	0.3-6	NR
Incidental Ingestion	NR	NR	2	6	NR
Incidental Inhalation-Sprays	NR	NR	NR	NR	NR
Incidental Inhalation-Powders	4	1	2	NR	1
Dermal Contact	8	1	30	0.2-8	3
Deodorant (underarm)	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR
Nail	NR	NR	1	0.2-2	NR
Mucous Membrane	NR	NR	2	6	NR
Baby Products	NR	NR	NR	NR	

* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

†A generic description of a nylon ingredient was reported to the VCRP. Exact polymer is not known. This generic term was not included in the use survey.

NR = none reported

[a]Deodorant products are not spray products in the results of this survey of Nylon-12.

Table 4. Genotoxicity of Nylon Monomers

Concentration/Dose	Method	Results	Reference
In Vitro			
Caprolactam			
5-9 (-log; mg/ml)	Initiator tRNA acceptance assay	No activity	[41]
Up to 50 mg/plate with and without metabolic activation	Ames test in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, TA 1538	Negative	[42]
0-40,000 µg/ml with and without metabolic activation	*Saccharomyces cerevisiae* DEL recombination assay	6-fold increase in deletion recombination frequency, but no effect observed in interchromosomal recombination	[43]
Up to 11.25 mg/ml	Chinese hamster ovary cell mutagenicity assay (induction of 6-thioguanine mutants	Negative	[42]
2222-11250 µg/ml	Chinese hamster ovary cell/hypoxanthine guanine phosphoribosyl transferase assay	Negative	[44]
Up to 10.0 mg/ml	Enhancement of SA7 virus transformation of primary hamster embryo cells (HEC) before and after virus	Active at toxic doses in post-virus treatment	[42]
Up to 10.0 mg/ml	Chemical transformation of secondary HEC	No transformation of secondary HEC	[42]
Dodecanolactam			
Up to 5,000 µg/plate with and without metabolic activation	Ames test in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, TA 1538	No increase in mutant frequency	[45]
8-80 mg/l with and without metabolic activation	HPRT test with Chinese hamster ovary cells	Did not increase the mutant frequency in treated cells. Cytotoxicity was not observed at any of the concentrations tested	[45]
30-350 mg/l with and without metabolic activation	Cytogenetic assay in human lymphocytes	No significant increase in chromosomal aberrations, even at cytotoxic concentrations	[45]
In Vivo			
Caprolactam			
10.0, 20.0, or 30.0 mM	Rapid somatic genotoxicity assay in *Drosophila melanogaster* using multiple mutant mutagen-sensitive (*mus*) strains	Not genotoxic	[46]
0, 441.8, 883.7, or 927.9 µM (0, 50, 100, 105 ppm)	Micronucleus test using newt larvae (*Pleurodeles waltl*)	Weakly positive for 883.7 and 927.9 µM (100 and 105 ppm)	[47]
0, 400, or 500 mg/kg via i.p. injection	Spot test in mouse embryos (C57B1 x T) F_1	A higher frequency of mitotic recombination was observed when compared to the mutagen ethylnitrosourea	[48]
750 mg/kg via gavage	Induction of DNA-strand breaks (SB) and unscheduled DNA synthesis (UDS) in F-344 rat hepatocytes	No induction of SB or UDS was observed in hepatocytes	[49]
222, 333, 500, 750, or 1125 mg/kg via gavage	Abnormal spermhead assay in B6C3F1 mice	Negative	[50]

REFERENCES

1. Odian G. Principles of Polymerization. 3 *ed*. New York: John Wiley and Sons Inc, 1991.

2. Fiume MM, Heldreth B, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler D, Marks JG, Shank RC, Slaga TJ, Snyder PW, and Andersen FA. Final Report of the Cosmetic Ingredient Review Expert Panel on the Safety Assessment of Dicarboxylic Acids, Salts, and Esters. *IJT*. 2012;31(Suppl 1):5-76.

3. Mukhopadhyay SK. Manufacturing, properties and tensile failure of nylon fibres. Chapter: 8. In: *Handbook of Tensile Properties of Textile and Technical Fibres*. 91 ed. Woodhead Publishing in Textiles; 2009:197-222.

4. Evonik Industries. Route to Polyamide powders [pamphlet]. 2012.

5. Goldblatt MW, Farquharson ME, Bennett G, and Askew BM. å-Caprolactam . *Br.J.Industr.Med*. 1954;11:1-10.

6. Presperse. 2009. Technical Data/Specification Sheet Anybes (INCI: Nylon-12). Unpublished data submitted by the Personal Care Products Council on May 9, 2011.

7. SH Energy & Chemical Co., Ltd. 2011. Certificate of Analysis Anybes (INCI: Nylon-12). Unpublished data submitted by the Personal Care Products Council on May 9, 2011.

8. Korea Testing & Research Institute. 2005. Heavy metals, PBBs and PBDEs analysis of Anybes (Nylon-12). Unpublished data submitted by the Personal Care Products Council on May 9, 2011.

9. SH Chemical Co., Ltd. 2008. Residual solvent Anybes (INCI: Nylon-12). Unpublished data submitted by the Personal Care Products Council on May 9, 2011.

10. Consumer Product Testing Co. 2010. Analysis report Anybes (INCI: Nylon-12). Unpublished data submitted by the Personal Care Products Council on May 9, 2011.

11. SH Chemical Co., Ltd. 2007. Residual monomer, initiators and catalyst ranges Nylon 12. Unpublished data submitted by the Personal Care Products Council on May 9, 2011.

12. Lin F. Use of Nylon 6/12 Copolymers as component of articles intended for non-food contact use. 5-8-1997. Received in response to a FOIA request FOIA2011-5647-R sent on July 14, 2011.

13. Gottschalck TE and Breslawec HP. International Cosmetic Ingredient Dictionary and Handbook. 14 *ed*. Washington, DC: Personal Care Products Council, 2012.

14. Food and Drug Administration (FDA). Frequency of use of cosmetic ingredients. *FDA Database.* 2012. Washington, DC: FDA.Data received May 16, 2012 in response to a Freedom of Information Act request.

15. Rothe H, Fautz R, Gerber E, Neumann L, Rettinger K, Schuh W, and Gronewold C. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 2011;205(2):97-104.

16. Rothe H. Special Aspects of Cosmetic Spray Evalulation. 9-26-2011. Unpublished data presented at the 26 September CIR Expert Panel meeting. Washington, D.C.

17. Bremmer HJ, Prud'homme de Lodder LCH, and Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. 2006. Report No. RIVM 320104001/2006. pp. 1-77.

18. Johnsen MA. The influence of particle size. *Spray Technology and Marketing*. 2004;November:24-27.

19. European Union. 1976, Council Directive 1976/768/EEC of 27 July 1976 on the Approximation of the Laws of the Member States Relating to Cosmetic Products, as amended through Commission Directive 2008/42/EC. 2008. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1976L0768:20080424:en:PDF . Internet site accessed March 24, 2010.

20. The Merck Index. Nylon 6. http://themerckindex.cambridgesoft.com/TheMerckIndex/index.asp. Date Accessed 7-12-0011.

21. Kerschner Kirk L, Lewis BA, Ross DA, and Morrison MA. Identification of ninhydrin-positive caprolactam metabolites in the rat. *Fd Chem Toxic*. 1987;25(3):233-239.

22. Miller E. Proposal to amend additive regulation Sec 121.2502 to provide for safe use of [...] Nylon-12 as food packaging material for non-edible sausage casing, boilable bags, and as component of laminates composed of aluminum and Nylon-12 film to be used in the canned food industry. 8-11-1975. Received in response to a FOIA request FOIA2011-5647-R sent on July 14, 2011.

23. Guess WL and Autian J. Toxicity evaluation of Lexan, Kynar, and Rilsan - short term studies. *J Oral Therapeut Pharmacol*. 1966;3(2):116-123.

24. Gad SC, Robinson K, Serota DG, and Colpean BR. Developmental toxicity studies of caprolactam in the rat and rabbit. *J Appl Toxicol*. 1987;7(5):317-326.

25. Serota DG, Hoberman AM, Friedman MA, and Gad SC. Three-generation reproduction study with caprolactam in rats. *J Appl Toxicol*. 1988;8(4):285-293.

26. National Toxicology Program. NTP technical report on the carcinogenesis bioassay of caprolactam (CAS NO. 105-60-2) in F344 rats and B6C3F1 mice (feed study). US Department of Health and Human Services, Public Health Service, National Institutes of Health. 1982. Report No. NTP-80-26. NIH publication no. 81-1770.

27. International Agency for Research on Cancer (IARC). Caprolactam. 1999. (71): pp.383-400. http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-16.pdfDate Accessed 4-12-2012

28. National Toxicology Program. NTP technical report on the carcinogenesis bioassay of 11-aminoundecanoic acid (CAS No. 2432-99-7) in F344 rats and B6C3F1 mice (feed study). 1982. Report No. NTP-80-34. NIH publication no. 82-1772.

29. International Agency for Research on Cancer (IARC). 11-Aminoundecanoic Acid. 1998. (39): pp.239 http://monographs.iarc.fr/ENG/Monographs/vol39/volume39.pdfDate Accessed 10-29-2012

30. Consumer Product Testing Co. 2012. Ophthamological in use safety evaluation -- 50% sensitive eyes of an eye shadow containing Nylon-12. Experiment Reference Number: C12-2128.01. Unpublished data submitted by Personal Care Products Council.

31. Dermatest. 2000. Report on a human patch test of a lip product containing 3% Nylon-12. Unpublished data submitted by Personal Care Products Council. 5 pages.

32. Consumer Product Testing Co. 2012. Repeated insult patch test of an eye shadow containing 5% Nylon-12. Experiment Reference Number: C12-0364.01. Unpublished data submitted by Personal Care Products Council.

33. Consumer Product Testing Co. 2006. Repeated insult patch test of a concealer containing 6% Nylon-12 Experiment Reference Number: C05-1197.02. Unpublished data submitted by Personal Care Products Council.

34. Clinical Research Laboratories Inc. 2012. Repeated insult patch test of a solid perfume containing 5.24% Nylon-12. CRL Study Number: CRL93010-4. Unpublished data submitted by Personal Care Products Council.

35. Consumer Product Testing Co. 2001. Summary of repeated insult patch test of a face powder containing 35% Nylon 12. Experiment Reference Number C01-0553-11. Unpublished data submitted by Personal Care Products Council. 6 pages.

36. Consumer Product Testing Co. 2008. Repeated insult patch test of a face powder containing 1.4% Nylon 6/12. Experiment Reference Number: C08-0878.01. Unpublished data submitted by Personal Care Products Council. 13 pages.

37. IDES. Polyamide (Nylon) Typical Properties. http://www.ides.com/generics/Nylon/Nylon_typical_properties.htm. Date Accessed 11-16-2011.

38. Mehra RH and Mehra AR. Nylon-11 - Polyamide. *Colourage*. 1994;41(3):56.

39. Cui X, Liu Z, and Yan D. Synthesis and characterization of novel even-odd nylons based on undecanedioic acid. *European Polymer Journal*. 2004;40:1111-1118.

40. Personal Care Products Council. 10-25-2011. Concentration of Use by FDA Product Category: Nylon Ingredients. Unpublished data submitted by the Personal Care Products Council.

41. Hradec J, Spiegelhalder B, and Preussmann R. The initiator tRNA acceptance assay as a short-term test for carcinogens. 2. Results with ten compounds selected by the International Programme on Chemical Safety for the evaluation of short-term tests for carcinogens. *Carcinogenesis*. 1988;9(5):843-846.

42. Greene EJ, Friedman MA, and Sherrod JA. In vitro mutagenicity and cell transformation screening of caprolactam. *Environmental Mutagenesis*. 1979;1:399-407.

43. Carls N and Schiestl RH. Evaluation of the yeast DEL assay with 10 compounds selected by the International Program on Chemical Safety for the evaluation of short-term tests for carcinogens. *Mutation Research*. 1994;320:293-303.

44. Li AP, Gupta RS, Heflich RH, and Wassom JS. A review and analysis of the Chinese hamster ovary/hypoxanthine guanine phosphoribosyl transferase assay to determine the mutagenicity of chemical agents. A report of Phase III of the U.S. Environmental Protection Agency Gene-TOx Program. *Mutation Research*. 1988;196:17-36.

45. OECD SIDS. Dodecane-12-lactam. Arona, Italy, 2003. http://www.inchem.org/documents/sids/sids/947046.pdf.

46. Henderson DS and Grigliatti TA. A rapid somatic genotoxicity assay in *Drosophila melanogaster* using multiple mutant mutagen-sensitive (*mus*) strains. *Mutagenesis*. 1992;7(6):399-405.

47. Fernandez M, Gautheir L, and Jaylet A. Use of newt larvae for in vivo genotoxicity testing of water: Results on 19 compounds evaluated by the micronucleus test. *Mutagenesis*. 1989;4(1):17-26.

48. Fahrig R. Possible recombinogenic efect of caprolactam in the mammalian spot test. *Mutation Research*. 1989;224:373-375.

49. Bermudez E, Smith-Oliver T, and Delehanty LL. The induction of DNA-strand breaks and unscheduled DNA synthesis in F-344 rat hepatocytes following in vivo administration of caprolactam or benzoin. *Mutation Research*. 1989;224:361-364.

50. Salamone MF. Abnormal sperm assay tests on benzoin and caprolactam. *Mutation Research*. 1989;224:385-389.