Safety Assessment of Modified Terephthalate Polymers 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date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A Hill, 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 Lillian C. Becker, Scientific Analyst/Writer.

1101 17th Street, NW, Suite 412 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢ cirinfo@cir-safety.org

TABLE OF CONTENTS

ABSTRACT

This is a safety assessment of six modified terephthalate polymers as used in cosmetics. These ingredients mostly function as exfoliants, bulking agents, hair fixatives, and viscosity increasing agents-nonaqueous. The Cosmetic Ingredient Review (CIR) Expert Panel determined that it was likely that the polyethylene terephthalate (PET) used in cosmetics is chemically equivalent to that used in medical devices. As a result, the Food and Drug Administration's (FDA) determination of safety of PET use in several medical devices, which included human and animal safety data, can be used as the basis of safety of PET and related polymers in cosmetics. The Panel concluded that modified terephthalate polymers were safe as cosmetic ingredients in the practices of use and concentration in this safety assessment.

INTRODUCTION

This is a tentative safety assessment of modified terephthalate polymers as used in cosmetics. The six ingredients reviewed in this safety assessment mostly function as exfoliants, bulking agents, hair fixatives, and viscosity increasing agents-nonaqueous (Table 1). These ingredients are:

- Adipic acid/1,4-butanediol/terephthalate copolymer,
- Polybutylene terephthalate,
- Polyethylene isoterephthalate,
- Polyethylene terephthalate (PET),
- Polypentaerythrityl terephthalate,
- Polypropylene terephthalate.

The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) believes that the modified terephthalate polymers produced for cosmetics are analogous to the polymers used in surgical sutures and other commercial medical devices made of terephthalate polymers. The safety information for those medical devices has been provided to the Food and Drug Administration (FDA) in medical device applications. The FDA found those data to be adequate and determined that terephthalate polymers are safe for use in devices when used in soft tissue approximation and/or ligation, including cardiovascular, ophthalmic, and neurological tissue. Systemic exposures of terephthalate polymers from devices used in these settings far exceed that expected for modified terephthalate polymer use in cosmetics.

The Panel considers that the assessment of modified terephthalate polymer safety as used in medical devices by the FDA provides the basis to establish the safety of these polymers in cosmetics because the polyethylene terephthalate is substantially the same as that used in approved medical devices and is used in a manner that presents less exposure risk. The Panel also contends that given the chemical similarity of the modified terephthalate polymer used in cosmetics to the same ingredient used in medical devices, data previously submitted to the FDA on that ingredient could be extrapolated to support the safety of adipic acid/ 1,4-butanediol/ terephthalate copolymer, polybutylene terephthalate, polyethylene isoterephthalate, polyethylene terephthalate, polypentaerythrityl terephthalate, and polypropylene terephthalate.

The literature does contain information on impurities and possible estrogenic activity related to liquids and foods stored in terephthalate polymer containers. This data was reviewed by the Panel for this safety assessment.

One issue has been raised that appears unique to cosmetic uses of these polymers. There is a concern that glitter made of modified terephthalate polymers may cause eye damage. The glitter is created by the chopping of sheets of the polymers in a manner that leaves jagged edges that will adhere to skin and hair better. If these become imbedded in the eye, irritation and other injuries may occur, necessitating removal of the jagged-edge material by a doctor to avoid further injury. Relevant data were reviewed by the Panel.

CHEMISTRY

Overview of Chemistry and Manufacture

The modified terephthalate polymer ingredients are related to polyesters, wherein terephthalic acid (or an ester thereof) is a primary monomeric repeat unit. Terephthalic acid is an aromatic, p-dicarboxylic acid, which does not readily form a homopolymer, but easily copolymerizes with polyols (i.e., multifunctional alcohols). The ingredients in this review are formed from diols (i.e., two alcohol functional groups per molecule), with the exception of polypentaerythrityl terephthalate which is prepared from a tetrol (i.e., four alcohol moieties per molecule; pentaerythritol). Accordingly, with the exception of polypentaerythrityl terephthalate, these polymers are essentially linear. The polymerization reaction proceeds first through the esterification of terephthalic acid (or transesterification of a simple terephthtalate ester, such as dimethyl terephthalate), with a diol (Figure 1).[1,2] This results in a new, di-functional monomeric unit with alcohols at the both ends (e.g., bis(hydroxyethyl)terephthalate). The exception, again, is polypentaerythrityl terephthalate, wherein the synthesis results in a mixture of tetrafunctional monomers. These new monomers then undergo polycondensation to produce the modified terephthalate polymer ingredients. Idealized structures of the modified terephthalate polymer ingredients in this safety assessment are provided in Figure 2.

When terephthalic acid is used as the starting material, water is released from the initial condensation reactions.[1,2] When a simple terephthalate ester is used (e.g., dimethyl terephthalate), the corresponding alcohol (e.g., methanol) is the byproduct. Early manufacturing methods of modified terephthalate polymers proceeded primarily from terephthalate esters, because the ester was easier to purify; however, since the mid-1960's, when significant progress was made in high-yielding, high-purity acid syntheses, terephthalic acid has become the primary starting material for these polymers, because of the lack of alcohol (e.g., methanol) produced.

The polycondensation step, however, is essentially independent of whether an acid or ester has been used to synthesize the ester intermediate.[1,2] The polycondensation step proceeds via a metaloid oxide (e.g., antimony(III) glycolate) catalyzed transesterification and results in the release of some of the starting material alcohol, and dimers thereof (some of which may be incorporated into the backbone of the polymer).

Depending on processing methodologies (e.g., product cooling rates), most of these ingredients can range from an amorphous glass to having a high degree of crystallinity.[3]

It is common for manufacturers to market copolymers for purposes previously filled by homopolymer PET. Copolymer blends, such as polybutylene terephthalate/PET, have certain advantages over homopolymer PET with regard to mechanical properties and resistance to degradation.[4,5] In the United States, clear plastic bottles made with copolymers may still be legally marketed as PET (21CFR177.1630).

The size and shape of PET particles are defined by precision cutting PET sheets and there is not a typical size distribution. One reported particle size is 0.004" (0.1016 mm).[6] The shapes of these particles may be hexagonal or square.

Physical and Chemical Properties

Limited physical and chemical properties for PET were discovered in the literature (Table 2). There were no corresponding data discovered for the rest of the ingredients in this safety assessment.

Impurities

It has been noted that not all PET materials are of the same chemical quality.[7] Therefore, it is important that the PET-related ingredients in this safety assessment are analogous to those used in medical devices and that there are no concerns about impurities and estrogenic activity.

An analysis of the impurities of a sample of PET glitter showed the following results: arsenic, < 0.05; antimony, 169.0; lead, 2.0; cadmium, <0.5; mercury, <0.1; nickel, <1; and chromium, <1 mg/kg.[8] The analysis of the migration of heavy metals showed that arsenic, antimony, lead, cadmium, mercury, chromium, barium, and selenium were below the levels of detection. Any possible free formaldehyde was below the limits of detection.

Diisononylphthalate, diethethylhexylphthalate, dibutylphthalate (DBP), diisodecylphthalate, di-*n*-octylphthalate, butylbenzylphthalate (BBP), diisobutylphthalate (DiisoBP), dimethylphthalate (DMP), diethylphthalate (DEP), dibutylsebacate, di(2-ethylhexyl)adipate, and tributylacetylcitrate were below the levels of detection for this sample.[8] The same was found for nonylphenols, organotin compounds, organic solvents, primary aromatic amines, polycyclic aromatic hydrocarbons, and monomeric plasticizers. The color was fast in the presence of perspiration and saliva.

The available data on impurities of PET are from studies using bottles and food containers made of PET and PET copolymers. A representative sample is provided in Table 3. Under different experimental conditions, ethylene glycol and other monomers/processing aids have been detected. In most cases, the amounts of impurities detected were greatest shortly after manufacture, with levels decreasing over time. Whether the impurities broke down or were resorbed was not addressed. Heat increases the amount of antimony (catalyst) that leaches into the contents of bottles and food packages. In all cases, detected amounts were small.[9-23]

Estrogenic activity was demonstrated in substances stored in these containers.[7,24] Representative studies are presented in Table 4. However, Enneking stated that "It is important to note that modified terephthalate copolymers do not contain phthalates nor leach them with use. PET is not considered an orthophthalate, nor does PET require the use of phthalates or other softening additives."[25]

USE

Cosmetic

Data on ingredient usage are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP; Table 5).[26] A survey has been conducted by the Personal Care Products Council (Council) of the maximum use concentrations for ingredients in this group. This survey also included the physical forms (i.e., flake, powder) of the ingredients being used.

Polyethylene terephthalate was reported to be used in 394 leave-on products (173 lipsticks and 98 used in the eye area), 1 rinse-off product, and 1 diluted for bath. It is used in leave-on products up to 100% and in rinse-off products up to 2%. There were no concentrations of use reported for products used in the bath. Products used around the eye were reported to be used in flake form up to 46.3% (eye shadow), in powders (form not reported) up to 2%, and in make-up preparations up to 100% (face powders up to 99.6% and other makeup preparations up to 100%). Polyethylene terephthalate is used in body and hand sprays up to 0.3%. Polyethylene terephthalate is reported to be used in fiber form in mascara up to 0.05%. It is

reported to be used as a gel in nail extenders up to 0.6% and in powder form up to 14%. It is also used in powder form in body and hand creams, lotions, and powders up to 0.005%. It was not reported what form polyethylene terephthalate is used in powders (dusting and talcum); other fragrance preparations; bath soaps and detergents; other personal cleanliness products; and body and hand sprays.

Polybutylene terephthalate was reported to be used in 21 leave-on products up to 12% and 2 rinse-off products up to 0.2%. It was reported to be used in flake form in eye liner up to 12%, blushers up to 4%, and nail polish and enamel up to 9%. It was used in powder form in nail extenders up to 6%. The form of polybutylene terephthalate is used in lipstick; other personal cleanliness products; and body and hand creams, lotions, and powders was not reported.

Polyethylene isoterephthalate was reported to be used in two lipsticks. The Council reported that it was used in flake form in eye shadow (up to 0.5%); tonics, dressings and other hair grooming aids (up to 0.04%); lipstick (up to 0.12%); and nail polish and enamel (up to 0.35%).

Polypropylene terephthalate was reported to be used in 13 leave-on products and 10 rinse-off products (7 in bath soaps and detergents). There were no concentrations of use reported by the Council.

There were no reported uses or concentrations of use for: adipic acid/1,4-butanediol/terephthalate copolymer and polypentaerythrityl terephthalate.

Polyethylene terephthatae was reported to be used in body and hand sprays, powders, and fragrance preparations, and could possibly be inhaled. These ingredients are reportedly used at concentrations up to 99.6%. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater fraction of droplets/particles below 10 μm compared with pump sprays. 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.[27-32]

Non-Cosmetic

PET is used for high-impact resistant containers.[33] It is used for packaging of soda, mouthwash, pourable dressings, edible oils, and peanut butter. It is used for cereal box liners, soda bottles, boil-in-the-bag pouches and microwave food trays. Modified PETs can be heated in a microwave or in a conventional oven at 180°C for 30 minutes.

Regulation

Regulations regarding the ingredients in this safety assessment are provided in Table 6. These regulations allow for contact with food substances.

With regard to phthalate contamination in water, the US Environmental Protection Agency set the maximum contaminant level goal of di(2-ethylhexyl) phthalate to be zero.[34] The acceptable maximum contaminant level is 0.006 mg/L.

PET IN MEDICAL DEVICES

The FDA considered the safety of polyethylene terephthalate when approving the following medical devices that include this material:

- Surgical sutures (i.e., PremiCron® Nonabsorbable PET Surgical Suture, TRUBOND® Nonabsorbable Surgical Suture, U.S.P[35,36]),
- Esophageal dilators (i.e., Bard® ELIMINATOR® PET Balloon Dialator[37]), and
- Surgical mesh (i.e., Peri-Strips® Staple Line Reinforcement[38]).

The use of polyethylene terephthalate to make surgical sutures was approved by the FDA as a Class II (special controls) medical device that requires premarket notification and adherence to standards (21CFR878.5000). Required testing includes acute and long-term (>30 day) biocompatibility testing for cytotoxicity, irritation or intracutaneous reactivity, sensitization, systemic toxicity, implantation effects, and hemocompatibility.[39] The sutures may be provided uncoated, coated, undyed, or dyed with appropriate approved colors. The FDA found the data on the safety of PET to be adequate and determined that medical devices containing PETs are safe and effective when used for soft tissue approximation and/or ligation, including cardiovascular, ophthalmic, and neurological tissue.[40]

Esophageal and gastrointestinal dialators are Class II medical devices (21CFR876.5365) that must adhere to the same standards listed above for the surgical sutures. An esophageal dilator, used to dilate a stricture of the esophagus, may consist of a hollow cylindrical instrument (bougie), a weighted bougie with a mercury or metal olive-shaped weight that slides on a guide, such as a string or wire, or may consist of a bougie with a deflated ballon attached to a guidewire. The balloon is made of polyethylene terephthalate.

Patches, pledgets, and intracardiac devices (surgical mesh) are made of polypropylene, polyethylene terephthalate, or polytetrafluoroethylene. They are fabric devices placed in the heart to repair septal defects, for patch grafting, to repair tissue, and to buttress sutures (21CFR870.3470). These devices are also Class II devices and adhere to the same standards listed above for the surgical sutures.

IRRITATION AND SENSITIZATION

Ocular Irritation

In several use tests of eye shadows, gels, liners, and mascara containing PET (up to 46.272%), there were little or no reports of adverse effects (Table 8).

In a use test of three mascaras containing PET (4.2%) and polybutylene terephthalate (4.8%), they were found to not have the potential to be irritating or sensitizing.[41] The subjects (n = 29) applied the test material at least once/day for 4 weeks. The terephthalate polymers were described as solid particles cut from sheets of these materials.

Sensitization

In a human repeated insult patch test (HRIPT) of an eyeliner containing PET (1.5%), there were no signs of irritation nor sensitization.[42] The test material (0.2 g) was administered to the backs of subjects (n = 107) under occlusion three times/week for three weeks. After a 2-week rest, the test material was applied to a naïve site.

An HRIPT (n = 30) of an eye shadow pencil containing polyethylene terephthalate (12%; square flakes) administered undiluted to healthy skin was negative for primary irritation and allergic hypersensitivity reactions at 24, 48 and 72 h.[43]

GENOTOXICITY

In Vitro

POLYETHYLENE TEREPHTHALATE LEACHATE

In several tests of water stored in PET for up to 6 months, the water was not mutagenic to *Salmonella* (strains TA98, and TA100) with or without metabolic activation except for one test where the water was mutagenic after storage for 1 month but not at 3 and 6 months (Table 7).[10,16]

CLINICAL USE

POLYETHYLENE TEREPHTHALATE

PET sutures were used in two studies of penetrating keratoplasty surgery (n = 20 and 45) comparing PET and nylon sutures and style of suture using these materials.[44] All complications were mechanical or technique related and not toxicological.

PET sutures were used in penetrating keratoplasty for keratoconus surgery (n = 14).[45] The subjects were followed for 22 – 48 months. There was no vascularization of the stitches, cheese-wiring, or graft rejections. There were four cases of stitch removal, three for mechanical reasons and one for an ulceration (which resolved when the stitch was removed). The author concluded that the problems had to do with technique and not toxicity.

In an evaluation of the use of a mesh made of PET for use in brow suspension ptosis surgery, a survey of five case reports and other cases in the literature were reviewed.[46] There were reported cases of extrusion and granuloma formation one month to one year after implantation characterized as foreign body reactions. There were also cases followed for up to 45 months with no complications. The authors concluded that technique (for example, knot size) and placement were the reasons for the problems and not toxicity.

POLYETHYLENE TEREPHTHALATE AS GLITTER

It has been suggested that glitter made of PET may cause injury if it gets into the eye.[47] The glitter is cut from sheets in such a way as to have jagged edges so that it would adhere to the skin and hair.

Blinking should clear the particles from the eye but could also push the glitter onto or into the cornea. Hairsprays with glitter were problematic, not because of spraying in the face but due to moving through the cloud after spraying. It was recommended that the glitter only be removed by a physician so to avoid further injury. [personal communication: DR. Stephen Glasser, ophthalmologist, interview October 27, 2012]

However, a literature search revealed no case reports or published studies on this issue. A search of the internet found several eye makeup products that contain glitter as well as products that are containers of loose glitter that are meant to be used on the eye lids as well as elsewhere on the body. It should be noted that there is a difference between cosmetic grade glitter and craft glitter.

In 1985, the FDA initiated a Class II recall of a glitter makeup product because the product was injurious under normal conditions of use and the product did not contain a warning statement that would preclude its use in the area of the eye.[48] The product was sold as a costume accessory, which may or may not have been intended to be used on or around the face. The company withdrew the glitter product. There were no records of any other action taken by the FDA with regard to cosmetic glitter.

SUMMARY

This is a draft report of modified terephthalate polymers as used in cosmetics. The six ingredients in this safety assessment mostly function as exfoliants, bulking agents, hair fixatives, and viscosity increasing agents-nonaqueous.

CIR believes that the modified terephthalate polymers produced for cosmetics is analogous to the polymers in surgical sutures and other commercial medical devices made of terephthalate polymers. The safety information for those medical devices was provided to the FDA in medical device applications including: acute and long-term biocompatibility testing for cytotoxicity, irritation or intracutaneous reactivity, sensitization, systemic toxicity, implantation effects, and hemocompatibility. The FDA found those data to be adequate and determined that PETs were safe and effective for use in surgical sutures, esophageal dilators and surgical mesh.

An analysis of the impurities of a sample of PET glitter showed the following: arsenic, < 0.05; antimony, 169.0; lead, 2.0; cadmium, <0.5; mercury, <0.1; nickel, <1; and chromium, <1 mg/kg. The analysis of the migration of heavy metals showed that arsenic, antimony, lead, cadmium, mercury, chromium, barium, and selenium were below the levels of detection. Free formaldehyde was below the limits of detection. Diisononylphthalate, diethethylhexylphthalate, DBP, diisodecylphthalate, di-*n*-octylphthalate, BBP, DiisoBP, DMP, DEP, dibutylsebacate, di(2-ethylthexyl)adipate, and tributylacetaylcitrate were below the levels of detection.

The available data on impurities of PET are from studies using bottles and food containers made up of PET and PET copolymers. Under different experimental conditions, ethylene glycol and other monomers/processing aids have been detected. In most cases, the amount of impurities detected was greatest in short time exposures and decreased with time, but at all times were low. In some studies, phthalates were also detected in PET containers as well as estrogenic activity demonstrated in substances stored in these containers.

Polyethylene terephthalate was reported to be used in 396 cosmetic products up to 100%, polybutylene terephthalate in 23 products up to 12%, polyethylene isoterephthalate in 2 products, and polypropylene terephthalate in 23 products up to 0.5%. Many of these uses were reported to be in flake, powder, and fiber form. There were no reported uses for: adipic acid/1,4-butanediol/terephthalate copolymer, polypentaerythrityl terephthalate, and polypropylene terephthalate.

PET is safe for use in food packaging that may be stored, heated, or microwaved.

In use tests of several different eye products containing PET up to 46.272%, the products were found to be non-irritating and non-sensitizing.

An eyeliner containing PET (1.5%) was not irritating or sensitizing in a repeated insult patch test.

In several tests of water stored in PET, the water was not mutagenic to *Salmonella* except for one test where the water was mutagenic after storage for 1 month but not at 3 and 6 months.

Complications from the use of PET sutures were attributed to mechanical or technique issues and not toxicological issues.

One issue has been raised that appears unique to cosmetics uses of these polymers. Glitter made of modified terephthalate polymers is used in eye cosmetics and may cause eye irritation, etc. because of the jagged edges of the glitter material. There are no case reports or studies in the literature and there has not been an FDA recall of a glitter makeup product since 1985.

DISCUSSION

The Panel concluded that if the polyethylene terephthalate polymers used in cosmetics is chemically equivalent to PET used in medical devices (i.e., surgical sutures, esophageal dilators, surgical mesh), then the Panel was comfortable using the safety review by the FDA as a basis for the assessment of the safety of polyethylene terephthalate polymers in cosmetics.

Although there are data gaps, the similar chemical structures, expected physicochemical properties, functions, and concentrations in cosmetics allow grouping these ingredients together and interpolating the available toxicological data to support the safety of the entire group. All of these ingredients are large polymers and would have no surface activity. The consensus of the Panel was that because dermal penetration of long chain polymers is likely to be low.

The Panel discussed the issue of incidental inhalation exposure from body and hand sprays, powders, and fragrance preparations. There were no inhalation toxicity data available. The Expert Panel believes that the sizes of a substantial majority of the particles of these ingredients, as manufactured, are larger than the respirable range. These ingredients are reportedly used at concentrations up to 8% in cosmetic products that may be aerosolized and up to 99.6% in face powders that may become airborne.

The Panel noted that 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of this ingredient. 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. Since polyethylene terephthalate polymers is used in implanted medical devices approved by the FDA, the Panel was satisfied that the modified terephthalate polymers in this safety assessment are chemically inert under physiological conditions and conditions of use, which supports the view that they are unlikely to be absorbed or cause local effects in the respiratory tract. 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 concluded that there is no concern with regard to ocular injury by glitter products composed of these ingredients. The use studies of eye products showed that the glitter did not enter the eye under normal conditions. Also, the

lack of case reports, studies on this issue, and lack of FDA actions on this subject with regard to glitter supported this conclusion.

CONCLUSION

The CIR Expert Panel concluded that the following ingredients are safe in the present practices of use and concentration described in this safety assessment:

- Adipic acid/1,4-butanediol/terephthalate copolymer*
- Polybutylene terephthalate
- Polyethylene isoterephthalate
- Polyethylene terephthalate (PET)
- Polypentaerythrityl terephthalate*
- Polypropylene terephthalate

*Not in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

TABLES AND FIGURES

Table 1. Definitions and functions of the ingredients in this safety assessment.[49]
(The italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
Adipic Acid/ 1,4-Butanediol/ Terephthalate Copolymer 55231-08-8	Adipic Acid/1,4-Butanediol/Terephthalate Copolymer is a copolymer of Adipic Acid, 1,4-Butanediol and dimethyl terephthalate monomers.	Exfoliant
Polybutylene Terephthalate 24968-12-5 26062-94-2	Polybutylene Terephthalate is the polymer that *is as shown in the structure in Figure 2. Polybutylene Terephthalate is a copolymer of 1,4-butanediol and dimethyl terephthalate or terephthalic acid.*	Film former; hair fixative; viscosity increasing agent-nonaqueous
Polyethylene Isoterephthalate	Polyethylene Isoterephthalate is the polymer that *is as represented in the structure in Figure 2. Polyethylene Terephthalate is a copolymer of ethylene glycol and one or more dimethyl terephthalates or terephthalic acids (i.e. not exclusive to 1,4-dicarboxylic acid monomers, but may include 1,2- and/or 1,3-dicarboxylic acid monomers).*	Bulking agent
Polyethylene Terephthalate 25038-59-9	Polyethylene Terephthalate is the organic compound that *is as represented in the structure in Figure 2. Polyethylene Terephthalate is a copolymer of propylene glycol and dimethyl terephthalate or terephthalic acid.*	Adhesive; film former; hair fixative; viscosity increasing agent-nonaqueous
Polypentaerythrityl Terephthalate	Polypentaerythrityl Terephthalate is the polyester of Pentaerythritol and Terephthalic Acid.	Film former; hair fixative
Polypropylene Terephthalate	Polypropylene Terephthalate is the homopolymer that *is as shown in the structure in Figure 2. Polypropylene Terephthalate is a copolymer of propylene glycol and dimethyl terephthalate or terephthalic acid.*	Emulsion stabilizer; skin-conditioning agent-miscellaneous

Table 2. Chemical and physical properties of modified terephthalate polymers.

Property	Value	Reference
Polyethylene terephthalate		
Density/Specific Gravity @ ºC	1332	33
Melting Point ºC	270 255-265	3 33
Water Solubility g/L @ ºC & pH	Insoluble	33

Table 3. Studies on chemicals leaching from PET.

<table>
<tr><th>Study</th><th>Results</th><th>References</th></tr>
<tr><td>Potential migrants were isolated from commercial amber PET bottles by Soxhlet extraction using absolute ethanol, concentrated by distillation and nitrogen flushing, and analyzed.</td><td>A total of 19 migrants identified. Most were intermediate reaction products or residual monomers of their dehydration and transesterification products. Processing aids (i.e., fatty acids, plasticizers) also identified. The 7 most common compounds were: ethylene glycol (14.4 µg/g), terephthalic acid (19.7 µg/g), bis-2-ethylhexyl) phthalate (820 µg/g), bis-(2-ethylhexyl) adipate (560 µg/g), dibutyl phthalate (220 µg/g) diethyl phthalate (120 µg/g), pyrogallol (0.6 µg/g).</td><td>14</td></tr>
<tr><td>PET packaging materials (laminates, bottles, and roasting bags) were tested for volatile content after exposure to high temperatures (120, 150, or 230°C) for 50 min, according to sample type.</td><td>Few volatiles were found for samples composed only of PET. Volatiles from laminates varied according to the sample structure, but the main substances identified were not related to PET (probably from printing inks and adhesives). The authors concluded that the migration potential of PET in high temperature applications is very low.</td><td>12</td></tr>
<tr><td>Migration of ethylene glycol from PET bottles into a food simulate that was 3% acetic acid was measured. The bottles were stored at 32°C for up to 6 months.</td><td>1 month - trace ethylene glycol in food simulant; 6 months - ~100 ppb (~ 94 µg/bottle).</td><td>13</td></tr>
<tr><td>3 PET bottles were crush to < 0.7 mm particles and exhaustively extracted with methylene chloride for 3 d</td><td>Ethylene glycol was extracted at ~ 15 ppm.</td><td>13</td></tr>
<tr><td>The migration of benzene, butyric acid, dodecane, octadecane, tetracosane, diazinon, lindane, and copper (II) ethyl hexonate from PET sheets into the food simulants, 8% ethanol/water, and n-heptane. The contaminated PET sheets were extruded from PET chips that had been previously contaminated but were washed, dried, and remelted.</td><td>Contaminants levels ranged from benzene at 0.6 mg/kg - copper salt at 24 mg/kg. Migration of the residual contaminants from the extruded PET sheets resulted in concentrations < 10 µg/kg in the food simulants.. The crystallinity of PET sheets in this study ranged from 5% to 15%, which is lower than that of most commercial PET (30%). The authors concluded that the samples represent the most severe conditions for conservative exposure evaluations.</td><td>15</td></tr>
<tr><td>Two food contact grade PET samples (in pellet form) were analyzed for content of elements. Fresh samples were exposed to food simulants (olive oil of a suitable grade for overall migration testing, acetic acid, or ethanol) for 10 d @ 40°C or 2 h @ 100°C according to European Economic Community directives.[50]</td><td>
<table>
<tr><th rowspan="2">Sample content (mg/kg)</th><th colspan="2">Content in 3% acetic acid (µg/kg)</th><th>Content in 15% ethanol (µg/kg)</th><th colspan="2">Content in olive oil (mg/kg)</th></tr>
<tr><th>40°C/10 d</th><th>100°C/ 2 h</th><th>40°C/10 d</th><th>40°C/10 d</th><th>100°C/ 2 h</th></tr>
<tr><td colspan="6">Mg</td></tr>
<tr><td>< 1</td><td>0.51</td><td><0.1</td><td>< 210</td><td>< 13</td><td>< 10</td></tr>
<tr><td>5.9</td><td>2.8</td><td><0.1</td><td><220</td><td><0.9</td><td><8</td></tr>
<tr><td colspan="6">Al</td></tr>
<tr><td>0.66</td><td>0.78</td><td><0.1</td><td><160</td><td><200</td><td><140</td></tr>
<tr><td>620</td><td>0.75</td><td><0.1</td><td><170</td><td><1</td><td><220</td></tr>
<tr><td colspan="6">Co</td></tr>
<tr><td>58</td><td>0.08</td><td>0.05</td><td>0.13</td><td><0.01</td><td><0.01</td></tr>
<tr><td>33</td><td>0.24</td><td>0.15</td><td>0.24</td><td><0.01</td><td><0.01</td></tr>
<tr><td colspan="6">Ge</td></tr>
<tr><td>0.95</td><td><0.07</td><td><0.05</td><td><0.2</td><td><0.1</td><td><0.09</td></tr>
<tr><td>14</td><td>0.25</td><td><0.05</td><td><0.2</td><td><0.1</td><td><0.07</td></tr>
<tr><td colspan="6">Sb</td></tr>
<tr><td>160</td><td>2.7</td><td>3.9</td><td>23</td><td><0.01</td><td><0.01</td></tr>
<tr><td>230</td><td>1.2</td><td>2.6</td><td>1.1</td><td><0.01</td><td><0.01</td></tr>
</table>
</td><td>11</td></tr>
<tr><td>1.5 liter green PET bottles of naturally carbonated mineral water were stored up to 6 months.</td><td>The total organic content of the mineral water was similar to that stored in glass bottles except for week 2 of storage. Acetaldehyde, dimethyl terephthalate, and terephthalic acid were detected.</td><td>16</td></tr>
<tr><td>1.5 liter green PET bottles tested according to EEC and FDA tests with and without the modification of freeze-drying the distilled water.</td><td>EEC standard and modified: 16 ± 1.2 and 121 ± 4.0 ppm total migrants (60 ppm limit).
FDA standard and modified: 38 ± 1.4 and 171 ± 2.5 ppm total migrants (50 ppm limit).</td><td>16</td></tr>
<tr><td>Distilled water was stored in PET bottles for 10 d at 40°C and 2 h at 120°. The water was tested for total organic carbon content.</td><td>Total organic carbon content was 1.5 ppm.</td><td>10</td></tr>
<tr><td>Distilled water was stored in PET bottles in the dark and sun light. The water was tested for total organic carbon content every 15 d for 6 months.</td><td>There was more organic carbon content detected in the light- than the dark-stored bottles. The peaks were approximately at 1, 3, and 5 months (in daylight: ~1, ~1, and ~3.5 mg/L; in dark ~1, ~0.6, and ~1.5 mg/L, respectively).</td><td>10</td></tr>
<tr><td>7 Brands of PET bottles were washed with Milli-Q water or used as received. Ultrapure water (20 ml) was poured into the bottles at room temperature or boiling. The original caps were used when the temperature reached room temperature. The bottles were stored in the dark for 24 h.</td><td>Boiling water increased the amount of antimony (2.077 vs 8.145 ppb) for all 7 brands of PET bottles. The authors concluded that this was a minor effect on leaching. There was more antimony in unwashed bottles than in washed bottles. No significant leaching was detected for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Ag, Cd, Sb, Ba, Tl, or Pb.</td><td>9</td></tr>
</table>

Table 3. Studies on chemicals leaching from PET.

Study	Results	References
The above experiment was repeated with room temperature and ice-cold water	There was no difference in the amount of leaching of antimony from the PET bottles between the temperatures. There was more antimony in unwashed bottles than in washed bottles. No significant leaching was detected for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Ag, Cd, Sb, Ba, Tl, or Pb.	9
The above experiment was repeated with room temperature water and placement in a microwave oven (1200 W) for 3 min in cook mode.	Microwaving the water in the bottles increased antimony content (0.381 - 10.51 µg/L) relative to controls. The authors concluded that this was a minor effect on leaching. There was more antimony in unwashed bottles than in washed bottles. No significant leaching was detected for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Ag, Cd, Sb, Ba, Tl, or Pb.	9
The above experiment was repeated with 20 ml acidic water (pH = 4.0). These bottles were stored for 7 days.	Acidic water increased the antimony content (0.459 – 4.611 µg/L) relative to controls. The authors concluded that this was a minor effect on leaching. There was more antimony in unwashed bottles than in washed bottles. No significant leaching was detected for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Ag, Cd, Sb, Ba, Tl, or Pb.	9
The above experiment was repeated with the bottles left directly in natural sunlight for 7 days with or without a foil cover.	Direct sunlight increased the antimony content (0.049 – 2.428 µg/L) relative to controls. The authors concluded that this was a minor effect on leaching. There was more antimony in unwashed bottles than in washed bottles. No significant leaching was detected for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Ag, Cd, Sb, Ba, Tl, or Pb.	9
The above experiment was repeated with the bottles left in an unairconditioned car, window closed and parked in an open parking lot during the day for 7 days.	Environmental conditions in a car (20°C - 45°C) increased the antimony content (0.482 – 3.08 µg/L) relative to controls. The authors concluded that this was a minor effect on leaching. There was more antimony in unwashed bottles than in washed bottles. No significant leaching was detected for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Ag, Cd, Sb, Ba, Tl, or Pb.	9
Commercially packaged carbonated mineral water and lemon/orange/citrus drinks were analyzed for acetaldehyde.	Acetaldehyde was detected in 2/4 mineral waters at 30 and 31 ng/ml. The amount of acetaldehyde in the bottles ranged from 1.7 – 3.8 µg/g and did not correlate with the results in the mineral waters. In the citrus drinks, the amount of acetaldehyde ranged from 11 – 7447 ng/ml. The amount of acetaldehyde in the bottles ranged from 1.1 – 3.8 µg/g and did not correlate with the results in the citrus drinks.	17
71 commercial brands of bottled water, available both in glass and PET, were analyzed for: PhA, DEHP, DMP, DEP, DiisoBP, and DBP[1].	The concentration of all phthalates combined was > 20x higher in PET (3.52 µg/l) than in glass (0.19 µg/l) bottled water in all brands. The concentration of phthalates in water from glass bottles was below the limits of detection in most cases. The most abundant phthalates observed in PET-bottled water were DBP, DiisoBP, and DEP. There were slightly higher concentrations of phthalates observed for the PET bottled still water samples than for sparkling water samples. There was no correlation between the phthalate concentrations and other physicochemical properties of the different water samples. The concentration of phthalates was always below 0.1% of the limit set by the EPA in 2006.	22
Water from PET and glass bottles were analyzed at purchase and after 10 weeks of storage for DMP, DEP, di-n-butylphthalate, butylbenzylphthalate, DEHP, and bisphenol A diglycyleter. Source waters from aquifers were also analyzed.	At purchase, the concentration of phthalates was at or below detection limits in almost every case. At 10 weeks the concentration of phthalates in glass-bottled water was similar. 3/5 brands with PET bottles showed measurable levels of DEHP after 10 weeks (ave 0.134 µg/L). All 5 brands had measurable levels of DEP at 10 weeks (ave 0.214 µg/L). Total phthalate were up to 1.7 µg/ L. Water from aquifers measured 0.005 – 0.331 µg/L.	20
PET bottles filled with water were incubated in direct sunlight. for 17 hr	The maximum concentration of DEHP was 0.71 µg/L, respectively, similar to those reported in studies on commercial bottled water. Only food flavor constituents of previous bottle contents identified above a detection limit of 1 µg/L. The country of origin was the only consistent variable.	23
Mineral water (still and carbonated) collected from a bottling plant was used to fill PET and glass bottles. All bottles were stored at room temperature. Each month, for 12 months, samples of water were lyophilized, the powders then shaken with acetone, and the acetone extracts analyzed using GC/MS.	No phthalates were observed for the first 8 months in any sample. Beginning at month 9 for PET-bottled noncarbonated water, and month 10 for PET-bottled carbonated water, the phthalate content increased from 0.4 to > 3.0 mg/L. DEHP was detected.	18
The interaction of incubation time with storage temperature on the leaching of DEHP from PET bottles was studied by using a solution of 3% acetic acid as a food simulant. Bottles were incubated up to 120 days, at 25°C or 45°C.	On day 0, DEHP in PET bottles was below detection limits. On day 25, the amount of DEHP at 25°C was 1.2 mg/L; at 45°C was 2.1 mg/L. On day 66, the amount of DEHP at 25°C peaked at 1.4 mg/L; 45°C at 2.5 mg/L.	21
45 samples of products packed in PET containers were incubated for 30 days. Group 1 (n = 9), soft drinks preserved with orthophosphoric acid; group 2 (n = 14), soft drinks preserved with Na-benzoate; group 3 (n = 5), soft drinks preserved with K-sorbate; group 4 (n = 8), soft drinks preserved with a combination of Na-benzoate and K-sorbate; and group 5 (n = 9), mineral water without preservatives. The amounts of DMP, DBP, DOP, DEP, BBP, and DEHP were measured.	Group 1- mean pool phthalate levels were 91.67 µg/L at a pH of 2.82 ± 0.30; Group 2 - 116.93 µg/L at 2.75 ± 0.32; Group 3 - 819.40 µg/L at 2.88 ± 0.15; Group 4 - 542.63 µg/L at 2.82 ± 0.54; Group 5 - 20.22 µg/L at 5.82 ± 1.26. There were large variations in the concentrations of phthalates both across beverages and across manufacturers (i.e., no DMP in any brand of mineral water after 30 days was detected, whereas DMP was the most abundant phthalate detected in the soft drinks). Among soft drinks preserved with both sodium benzoate and potassium sorbate incubated for 30 days, the concentration of DMP ranged from 18 - 2,666 µg/L, mean 501 µg/L. DMP in mineral water was below detection limits. DEHP (unlike DMP) did not differ between soda beverages and mineral water (ave < 100 µg/L in all their specimens, with no difference between soda and mineral water. The authors suggested that the lower pH of the soft drinks might account for differences.	19

[1] BBP – benzylbutyl phthalate; DBP - dibutyl phthalate; DEHP - bis(2-ethylhexyl) phthalate; DEP - diethyl phthalate; DiisoBP - diisobutyl phthalate; DMP - dimethyl phthalate; DOP – dioctyl phthalate; EEC – Commission of the European Communities ; FDA – Food and Drug Administration; PhA - phthalic acid.

Table 4. Estrogenic activity of PET containers.

Study	Results	Reference
20 brands of mineral water, 9 of which are available both in glass and in PET bottles were tested with a yeast estrogen screen, employing a strain transfected with the human estrogen receptor α. Negative control- borosilicate Erlenmeyer flasks with culturing water.	3/9 brands in glass and 7/9 brands from PET bottles demonstrated estrogenic activity in this bioassay. Estrogenic contamination was detected in 60% of all samples with a maximum activity equivalent to 75.2 ng/L of the natural sex hormone 17β-estradiol. It is not certain that the estrogenic substance or substances leached from the bottles; the contamination may have been prior to bottling.	[24]
PET water bottles and glass bottles (same as above) were emptied of water and filled with a defined culture medium (pH 8.0 ± 0.5) and incubated New Zealand mudsnails, *Potamopyrgus antipodarum*, for 56 days.	Production of embryos increased among snails incubated in PET bottles compared with snails incubated in glass bottles across all brands ($p < 0.001$). For example, production of embryos incubated in PET bottles of brand D was roughly double the production of embryos incubated in glass bottles of brand D. However, in the yeast estrogen screen, this same brand showed no difference in estrogenic activity between PET bottle and glass bottle. The authors suggest that the *in vivo* snail bioassay might be more sensitive than the *in vitro* yeast estrogen screen. The authors concluded that the PET material were potent enough to trigger estrogenic effects *in vivo* similar to 25 ng/L 17α ethinylestradiol . The maximum estrogen activity detected in any brand of water was equivalent to 75 ng/L of ethinylestradiol.	[24]
30 samples of commercial brands (n = 9) of Italian mineral water packaged PET were analyzed for estrogenic activity using the Yeast Estrogen Screen (S. cerevisiae RMY326 (His3 Leu2-3,112trp1-1ura3-52/hER-TRP1-2 μ [pG/ER(G)], ERE-CYC-LacZ-URA3-2 μ [pUCΔSS-ERE],HIS-3CEN/ ARS[pRS423]) containing the human estrogen receptor a (hERa) and an estrogen-responsive element (ERE) bound to the reporter gene lacZ encoding for the enzyme β-galactosidase.	90% of samples exhibited estrogenic activity lower than 10% of the activity induced by 10nM 17β-estradiol (E2). The highest estrogenic activity measured was 11.32% of E2, corresponding to 23.1 ng/L estradiol equivalents.	[7]

[1] BBP – benzylbutyl phthalate; DBP - dibutyl phthalate; DEHP - bis(2-ethylhexyl) phthalate; DEP - diethyl phthalate; DiisoBP - diisobutyl phthalate; DMP - dimethyl phthalate; DOP – dioctyl phthalate; PhA - phthalic acid.

Table 5. Frequency of use according to duration and exposure of modified terephthalate polymers.[26,51]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Polyethylene terephthalate		Polybutylene Terephthalate		Polyethylene Isoterephthalate		Polypropylene Terephthalate	
Total/range	**396**	**0.005-100**	**23**	**0.006-12**	**2**	**0.04-0.5**	**23**	NR
Duration of use								
Leave-on	394	0.005-100	21	0.006-12	2	0.04-0.5	13	NR
Rinse-off	1	0.05-2	2	0.2			10	NR
Diluted for (bath) use	1	NR	NR	NR	NR	NR	NR	NR
Exposure type								
Eye area	98	0.007-46.3	3	2-12	NR	0.5	NR	NR
Incidental ingestion	173	1-10	1	2	2	0.12	NR	NR
Incidental Inhalation-sprays	16	0.09-8	2	NR	NR	NR	NR	NR
Incidental inhalation-powders	7	2-99.6	NR	NR	NR	NR	NR	NR
Dermal contact	167	0.005-100	10	0.02-12	NR	0.5	23	NR
Deodorant (underarm)	NR		NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	2-100	NR	NR	NR	0.04	NR	NR
Hair-coloring	1	2	NR	NR	NR		NR	NR
Nail	47	0.6-100	12	0.006-9	NR	0.35	NR	NR
Mucous Membrane	175	0.05-10	1	0.2-2	2	0.12	8	NR
Baby	NR	NR	NR	NR	NR	NR	NR	NR

NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

Table 6. Code of Federal Regulations regarding the polybutylene terephthalate and PET.

Ingredient	Rule	Reference
Polybutylene terephthalate	Approved as a substance that may come in contact with food in packaging. Poly (tetramethylene terephthalate) is the reaction product of dimethyl terephthalate with 1,4-butanediol to which may have been added certain optional substances to impart desired technological properties to the polymer. Poly(tetramethylene terephthalate) may contain optional adjuvant substances. The quantity of any optional adjuvant substance employed in the production of the polymer does not exceed the amount reasonably required to accomplish the intended technical or physical effect. Such adjuvants may include substances generally recognized as safe in food, substances used in accordance with prior sanction, and substances permitted under applicable regulations in this part.	21CFR177.1660
Polyethylene terephthalate (PET)	May be safely used as, or components of plastics (films, articles, or fabric) intended for use in contact with food. Polyethylene phthalate films consist of a base sheet of ethylene terephthalate polymer, ethylene terephthalate-isophthalate copolymer, or ethylene-1,4-cyclohexylene dimethylene terephthalate copolyesters, to which have been added optional substances, either as constituents of the base sheet or as constituents of coatings applied to the base sheet. Polyethylene phthalate articles consist of a base polymer of ethylene terephthalate polymer, or ethylene-1,4-cyclohexylene dimethylene terephthalate copolyesters to which have been added optional substances, either as constituents of the base polymer or as constituents of coatings applied to the base polymer. Polyethylene phthalate spunbonded nonwoven fabric consist of continuous filaments of ethylene terephthalate polymer and ethylene terephthalate-isophthalate copolymer to which may have been added optional adjuvant substances required in their preparation and finishing. The ethylene terephthalateisophthalate copolymer component of the fabric shall not exceed 25 percent by weight. The filaments may be blended with other fibers regulated for the specific use and the spunbonded fabric may be further bonded by application of heat and/or pressure.	21CFR177.1630
	May be safely used as articles or components of articles, intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting or holding food.	21CFR177.1850
	May be safely used in producing, manufacturing, processing, and preparing food.	21CFR177.2260
	May safely be used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.	21CFR177.2800
	Hydrogen peroxide solution identified in and complying with the specifications in this section may be used by itself or in combination with other processes to treat food-contact surfaces to attain commercial sterility at least equivalent to that attainable by thermal processing for metal containers as provided for in part 113 of this chapter. The packaging materials identified in paragraph (e)(1) of this section may be used for packaging all commercially sterile foods.	21CFR178.1008
	May be safely subjected to irradiation incidental to the radiation treatment and processing of prepackaged foods.	21CFR179.45
	Cardiovascular Prosthetic Devices Intracardiac patch or pledget made of polypropylene, polyethylene terephthalate, or polytetrafluoroethylene. Identification: An intracardiac patch or pledget made of polypropylene, polyethylene terephthalate, or polytetrafluoroethylene is a fabric device placed in the heart that is used to repair septal defects, for patch grafting, to repair tissue, and to buttress sutures.	21CFR870.3470
	Nonabsorbable poly(ethylene terephthalate) surgical suture. Identification: Nonabsorbable poly(ethylene terephthalate) surgical suture is a multifilament, nonabsorbable, sterile, flexible thread prepared from fibers of high molecular weight, long-chain, linear polyesters having recurrent aromatic rings as an integral component and is indicated for use in soft tissue approximation. The poly(ethylene terephthalate) surgical suture meets U.S.P. requirements as described in the U.S.P. Monograph for Nonabsorbable Surgical Sutures; it may be provided uncoated or coated; and it may be undyed or dyed with an appropriate FDA listed color additive. Also, the suture may be provided with or without a standard needle attached.	21CFR878.5000
	Esophageal dilator. Identification:. An esophageal dilator is a device that consists of a cylindrical instrument that may be hollow and weighted with mercury or a metal olive-shaped weight that slides on a guide, such as a string or wire and is used to dilate a stricture of the esophagus. This generic type of device includes esophageal or gastrointestinal bougies and the esophageal dilator (metal olive)	21CFR876.5365

Table 7. Genotoxicity tests of contents of PET bottles after storage.

Study	Results	Reference
Ames test performed on water stored in PET bottles (500 – 4000 ml/plate) for up to 6 months	Not mutagenic to *Salmonella* (strains TA98, TA100) with or without metabolic activation.	[16]
Ames test performed on concentrated mineral water after storage in shaken PET bottles for 24 or 48 h at 40°C.	Not mutagenic to *Salmonella* (strains TA98, TA100) with or without metabolic activation. The 48-h sample was toxic to the bacteria.	[10]
Ames test performed on mineral water stored in PET bottles[1] in the dark and in sunlight for 1, 3, or 6 months. Glass bottles served as controls.	The samples stored for 1 month (both dark and day light) were mutagenic to *Salmonella* (strain TA98) with metabolic activation. At 3 and 6 months, the samples were not mutagenic.	[10]
Salmonella (strains TA98, TA100) were incubated in PET bottles containing mineral water. *Salmonella* (strains TA98, TA100) were incubated in glass flasks containing mineral water that was stored in PET bottles for up to 6 months.	Not mutagenic to *Salmonella* (strains TA98, TA100) with or without metabolic activation.	[10]
Salmonella (strains TA98, TA100) was inoculated into sterilized PET bottles. Glass flasks served as + controls; flasks with known mutagens added served as - controls	Not mutagenic to *Salmonella* (strains TA98, TA100) with or without metabolic activation.	[10]
Distilled water (100%, 95%, 90%, 75%, 50%) stored in PET bottles at 10 d at 40°C and for 1 month at room temperature in sunlight was used as the water phase for preparation of Vogel-Bonner stock. Stock was placed in glass flasks and inoculated with *Salmonella*. Flasks were shaken for 24 h at 37°C. The bacteria were then tested for reversion.	Not mutagenic to *Salmonella* (strains TA98, TA100) with or without metabolic activation.	[10]

[1] PET made from the polycondensation of dimethyl terephthate and ethyleneglycol.

Table 8. Use tests of cosmetic products containing polyethylene terephthalates.

Product (n)	Concentration; form; use	Results	Reference
Eye gel (10; 5 with contact lenses)	9%; square flakes (0.006 x 0.006"; ~150 x 150 µm); once daily for 4 weeks.	The use of the product was assessed by the subjects as very positive. Ophthalmological examination: no subject had subjective or objective eye irritation in form of tears or pain. Eyelid irritation has not observed after the use of the product for four weeks. Slit-lamp microscope examination of the eye showed that no irritant contact conjunctivitis with chemosis could be observed after the use of the product. No incompatibility (redness. itching) was observed.	52
Eye gel (10; 7 with contact lenses)	9%; square flakes (size not provided); once daily for 4 weeks.	The use of the product was assessed by the subjects as very positive. Ophthalmological examination: no subject had subjective or objective eye irritation in form of tears or pain. Eyelid irritation has not observed after the use of the product for four weeks. Slit-lamp microscope examination of the eye showed that no irritant contact conjunctivitis with chemosis could be observed after the use of the product. No incompatibility (redness. itching) was observed.	53
Eyeliner (10; 6 with contact lenses)	10%; square flakes (size not provided); once daily for 4 weeks.	The use of the product was assessed by the subjects as very positive. Ophthalmological examination: no subject had subjective or objective eye irritation in form of tears or pain. Eyelid irritation has not observed after the use of the product for four weeks. Slit-lamp microscope examination of the eye showed that no irritant contact conjunctivitis with chemosis could be observed after the use of the product. No incompatibility (redness. itching) was observed.	54
Eyeliner (10; 5 with contact lenses)	8%; hexagonal flakes (size not provided); once daily for 4 weeks.	The use of the product was assessed by the subjects as very positive. Ophthalmological examination: no subject had subjective or objective eye irritation in form of tears or pain. Eyelid irritation has not observed after the use of the product for four weeks. Slit-lamp microscope examination of the eye showed that no irritant contact conjunctivitis with chemosis could be observed after the use of the product. No incompatibility (redness. itching) was observed.	55
Eyeshadow (10; 6 with contact lenses)	12%; square flakes (0.006 x 0.006"; ~150 x 150 µm); Once daily for 4 weeks.	The use of the product was assessed by the subjects as very positive. Ophthalmological examination: no subject had subjective or objective eye irritation in form of tears or pain. Eyelid irritation has not observed after the use of the product for four weeks. Slit-lamp microscope examination of the eye showed that no irritant contact conjunctivitis with chemosis could be observed after the use of the product. No incompatibility (redness. itching) was observed.	56
Eye gel (10; 5 with contact lenses)	9%; square flakes (0.006 x 0.006"; ~150 x 150 µm); once daily for 4 weeks.	The use of the product was assessed by the subjects as very positive. Ophthalmological examination: no subject had subjective or objective eye irritation in form of tears or pain. Eyelid irritation has not observed after the use of the product for four weeks. Slit-lamp microscope examination of the eye showed that no irritant contact conjunctivitis with chemosis could be observed after the use of the product. No incompatibility (redness. itching) was observed.	57
Eye shadow (15; considered to have sensitive eyes)	46.272%; cut into flakes; applied to the upper eye lid once or twice daily for 8 days	The subjects were examined before and after the test period and at 10 min after the first and last application. There was one reported adverse event of palpebral stinging/burning of short duration (6 min). The authors stated that there is a very slight ocular irritant potential, which is normal for this type of product. The test material was found to be nonirritating.	58

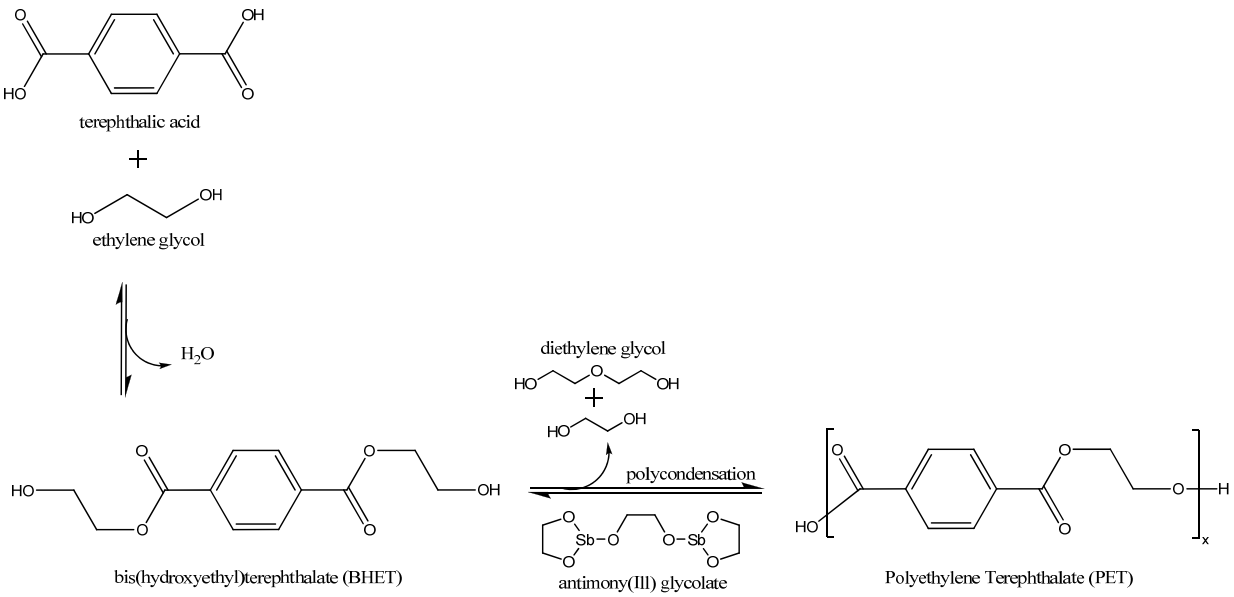
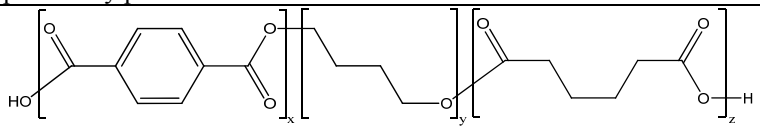
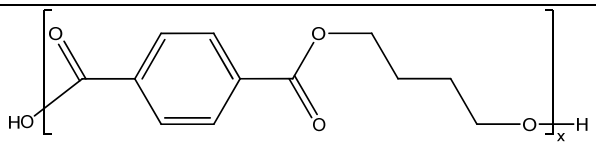
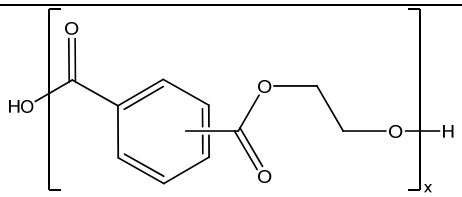
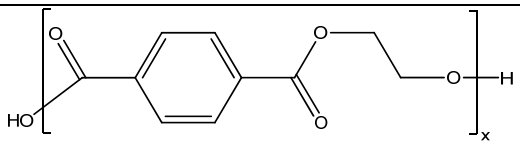
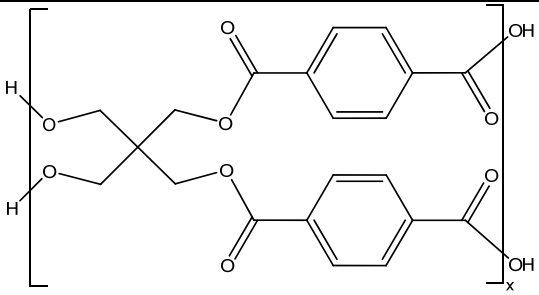
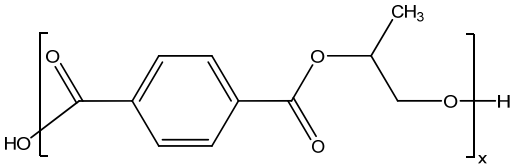


Figure 1. Most common manufacturing method for PET.

Figure 2. Idealized structures of the modified terephthalate polymer ingredients in this safety assessment. These idealized structures are merely generalized, two-dimensional estimations of the true three-dimensional frameworks that comprise theses polymers. Though monomer units are in some instances drawn sequentially, by necessity, this by no means implies that these are block-type polymers. Instead, these structures are meant to represent only one example of the multitude of potentially produced connectivities found within these macromolecules.

Adipic Acid/1,4-Butanediol/ Terephthalate Copolymer	
Polybutylene Terephthalate	
Polyethylene Isoterephthalate	
Polyethylene Terephthalate	
Polypentaerythrityl Terephthalate	
Polypropylene Terephthalate	

REFERENCES

1. Ravindranath K and Mashelkar RA. Polyethylene terephthalate - I. chemistry, thermodynamics and transport properties. *Chemical Engineering Science*. 1986;41(9):2197-2214.

2. Schiraldi DA. Synthesis of dimethyl terephthalate/terephthatlic acid and poly(ethylene terphthalate). In: *Applied homogenous catalysis with organic compounds*. 2 ed. Veinheim Germany: Verlag; 2002:

3. Sharples A. The relation between structure and properties in plastics used in packaging. *Journal of the Society of Cosmetic Chemists*. 1966;17:415-427.

4. Grossetete T, Rivaton A, Gardette JL, Hoyle CE, Ziemer M, Fagerburg DR, and Clauberg H. Photochemical degradation of poly(ethylene terephthalate)-modified copolymer. *Polymer*. 2000;41(10):3541-3554.

5. Guerrica-Echevarría G and Eguiazábal JI. Structure and mechanical properties of impact modified poly(butylene terephthalate)/poly(ethylene terephthalate) blends. *Polymer Engineering & Science*. 2009;49(5):1013-1021.

6. Personal Care Products Council. 8-31-2012. Information Regarding Polyethylene Terephthalate. Unpublished data submitted by Personal Care Products Council. Memo pages.

7. Pinto B and Reali D. Screening of estrogen-like activity of mineral water stored in PET bottles. *International Journal of Hygiene and Environmental Health*. 2009;212(2):228-232.

8. SGS Institut Fresenius. 2011. Analytical report for polyester glitter (Polyethylene Terephthalate). Test Report No. 2052901-01. Unpublished data submitted by Personal Care Products Council. 8 pages.

9. Cheng X, Shi H, Adams CD, and Ma Y. Assessment of metal contaminations leaching out from recycling plastic bottles upon treatments. *Environmental Science and Pollution Research*. 2010;17:1326-1330.

10. De Fusco R, Monarca S, Biscardi D, Pasquini R, and Fatigoni C. Leaching of mutagens into mineral water from polyethyleneterephthalate bottles. *US Department of Health and Human Services*. 1990;90:241-248.

11. Fordham PJ, Gramshaw JW, Crews HM, and Castle L. Element residues in food contact plastics and their migration into food simulants, measured by inductively-coupled plasma-mass spectrometry. *Food Additives and Contaminants*. 1995;12(5):651-669.

12. Freire MT, Castle L, Reyes FG, and Damant AP. Thermal stability of polyethylene terephthalate food contact materials: formation of volatiles from retain samples and implications for recycling. *Food Additives and Contaminants*. 1998;15(4):473-480.

13. Kastock M and Breder CV. Migration of ethylene glycol from polyethylene terephthalate bottles into 3% acetic acid. *Journal of the Association of Analhytical Chemists*. 1980;63(2):168-172.

14. Kim H, Gilbert SG, and Johnson JB. Determination of potential migrants from commercial amber polyethylene terephthalate bottle wall. *Pharmaceutical Research*. 1990;7(2):176-179.

15. Kimolprasert V, Lawson AR, and Begley TH. Migration of residual contaminants from secondary recycled poly(ethylene terephthalate) into food-simulating solvents, aqueous ethanol and heptane. *Food Additives and Contaminants*. 1997;14(5):491-498.

16. Monarca S, De Fusco R, Biscardi D, De Feo V, Pasquini R, Fatigoni C, Moretti M, and Zanardini A. Studies of migration of potentially genotoxic compounds into water stored in PET bottles. *Food and Chemical Toxicology*. 1994;32(9):783-788.

17. Linssen J, Reitsma H, and Cozijnsen J. Static headspace gas chromatography of acetaldehyde in aqueous foods and polythene terephthalate. *Zeitxchrift für Lebensmittel-Untersuchung und-Forschung*. 1995;201:253-255.

18. Biscardi D, Monarca S, De Fusco R, Senatore F, Poli P, Buschini A, Rossi C, and Zani C. The evaluation of the migration of mutagens/carcinogens from PET bottles into mineral water by Tradescantia/micronulei test, Comet assay on leukocytes and GC/MS. *The Science of the Total Environment*. 2003;302(1-3):101-108.

19. Bošnir J, Puntaric D, Galic A, Škes I, Dijanic T, Klaric M, Grgic M, Curkovic M, and Šmit Z. Migration of phthalates from plastic containers into soft drinks and mineral water. *Food Technology and Biotechnology*. 2007;45(1):91-95.

20. Casajuana N and Lacorte S. Presence and release of phthalic esters and other endocrine compounds in drinking water. *Chromatographia*. 2003;57(9-10):649-655.

21. Farhodi M, Emam-Djomeh Z, Ehsani MR, and Oromiehie A. Effect of environmental conditions on the migration of di(2-ethylhexyl)phthalate from PET bottles into yogurt drinks: influence of time, temperature, and food simulant. *Arabian Journal of Science and Engineering*. 2008;33(2):279-287.

22. Montuori P, Jover E, Morgantini M, Bayona JM, and Triassi. Assessing human exposure to phthalic acid and phthalate esters from mineral water stored in polyethylene terephthalate and glass bottles. *Food Additives & Contaminants.Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment*. 2008;25(4):511-518.

23. Schmid P, Kohler M, Meierhofer R, Luzi S, and Wegelin M. Does the reuse of PET bottles during solar water disinfection pose a health risk due to the migration of plasticisers and other chemicals into the water? *Water Research*. 2008;42(20):5054-5060.

24. Wagner M and Oehlmann J. Endocrine disrutors in bottled mineral water: Total estrogenic burden and migration from platic bottles. *Environmental Science and Pollution Research International*. 2009;16(3):278-286.

25. Enneking PA. Phthalates not in plastic food pachaging. *Environmental Health Perspective*. 2005;113(10):A664-A668.

26. US Food and Drug Administration (FDA). Frequency of use of cosmetic ingredients. *FDA Database*. 2012. Washington, DC: FDA.

27. 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*. 8-28-2011;205(2):97-104.

28. Bremmer HJ, Prud'homme de Lodder LCH, and van Engelen JGM. General Fact Sheet: Limiting conditions and reliability, ventilation, room size, body surface area; Updated version for ConsExpo 4. 2006. http://www.rivm.nl/bibliotheek/rapporten/320104002.pdf. Date Accessed 8-24-2011. Report No. RIVM 320104002/2006. pp. 1-31.

29. Bremmer HJ, Prud'homme de Lodder LCH, and van Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. 2006. http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. Date Accessed 8-24-2011. Report No. RIVM 320104001/2006. pp. 1-77.

30. Johnsen MA. The Influence of Particle Size. *Spray Technology and Marketing*. 2004;24-27.

31. Rothe H. Special aspects of cosmetic spray safety evaluation. 2011. Unpublished information presented to the 26 September CIR Expert Panel. Washington D.C.

32. Rothe H. Special aspects of powders in decorative cosmetics. 2011. Unpublished information presented at the 26 September 2011 CIR Expert Panel Meeting. Washington, DC.

33. Sheftel VO. Indirect Food Additives and Polymers: Migration and Toxicology. 1 *ed*. Boca Raton, FL: Lewis Publishers, 2000.

34. US Environmental Protection Agency (EPA). Drinking water contaminants: National primary drinking water regulations. *EPA*. 3-6-2012. Date accessed: 05/30/2012. http://water.epa.gov/drink/contaminants/index.cfm#Organic

35. US Food and Drug Administration. AESCULAP®, Inc. 510(k) Premarket Notification: *PremiCron*® Nonabsorbable PET Surgical Suture. Washington, DC, 9-19-2001. http://www.accessdata.fda.gov/cdrh_docs/pdf/K012201.pdf. Report No. K012201. pp. 1-6.

36. US Food and Drug Administration. Sutures India PVT, LTD; Submission of premarket notification (510K) for nonabsorbable polyester surgical suture. Washington, DC, 6-2-2005. Report No. K041512. pp. 1-7.

37. US Food and Drug Administration. Bard Endoscopic Technologies; 510(k) Summary Safety and Effectivenss Information. 2012. 2004. Report No. K033936. pp. 1-5.

38. US Food and Drug Administration. Synovis Surgical Innovations: Peri-Strips® Staple Line Reinforcement; 510(k) Summary. 4-14-2004. Report No. K040415.

39. US Food and Drug Administration. Medical Devices: Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing' (Replaces #G87-1 #8294) (blue book memo). *US Department of Health and Human Services*. 5-1-1995. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080735.htmDate Accessed 5-18-2012

40. US Food and Drug Administration. Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Surgical Sutures. *US Department of Health and Human Services*. 6-3-2003. file:///N:/CIR/LCB/WPDOCS/CURRENT%20REPORTS/Modified%20Terephthalate%20Polymers/FDA%20Med%20Device%20Docs/FDA%20Guidance%20Surg%20Sutures.htmDate Accessed 5-15-2012

41. Consumer Product Testing Co. 2007. Ophthalmological in-use safety evaluation of mascara containing 4.8% Polyethylene Terephthalate and 4.2% Polybutylene Terephthalate. Experiment Reference Number: C06-1021.01-.03. Unpublished data submitted by Personal Care Products Council.

42. Consumer Product Testing Co. 2011. Repeated insult patch test of an eyeliner containing 1.5% Polyethylene Terephthalate. Experiment Reference Number: C11-2066.03. Unpublished data submitted by Personal Care Products Council.

43. Dermatest. 1999. Human patch test of an eye shadow pencil containing 12% Polyethylene Terephthalate precision cut flakes square shape. Unpublished data submitted by Personal Care Products Council.

44. Bertram BA, Drews-Botsch C, Gemmill M, Guell J, Murad M, and Raringg III GO. Complications of Mersilene sutures in penetrating keratoplasty. *Refractive & Corneal Surgery*. 1992;8(4):296-305.

45. Frucht-Pery J. Mersilene sutures for corneal surgery. *Ophthalmic Surgery*. 1995;26(2):117-120.

46. Mutlu FM, Tuncer K, and Can C. Extrusion and granuloma formation with Mersilene mesh brow suspension. *Clincal Science*. 1999;30(1):47-51.

47. Steinberg D. davidpreserve@comcast.net. CIR-PET. *Steinberg & Associates, Inc.* 8-24-2012. Date Accessed 8-24-2012

48. Gerstenberg GJ. Recall No. F-575-5. 6-3-1985.

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

50. European Community Coucil. European Community Council Directive No. 85/572/EEC Council Directive of 19 December 1985 laying down the list of simulants to be used for testing migration of constituents of plastic materials intended to come into contact with foodstuffs. *Official Journal of the European Communities*. 1982;23(10):0026-0030.

51. Personal Care Products Council. 11-20-2012. Concentration of Use by FDA Product Category: Terephthalate Polymers. Unpublished data submitted by Personal Care Products Council. 4 pages.

52. Derma Consult GmbH. 2008. Controlled user test of the product eye gel texture ANB with glitter (9% Polyethylene Terephthalate precision cut flakes- square shape). Unpublished data submitted by Personal Care Products Council.

53. Derma Consult GmbH. 2007. Controlled user test of the product eyeshadow with glitter (12% Polyethylene Terephthalate precision cut flakes- square shape). Unpublished data submitted by Personal Care Products Council.

54. Derma Consult GmbH. 2008. Controlled user test of the product eyeliner MLOV with glitter (8% Polyethylene Terephthalate precision cut flakes - hexagonal shape). Unpublished data submitted by Personal Care Products Council.

55. Derma Consult GmbH. 2008. Controlled user test of the product eyeliner texture MAA with glitter (10% Polyethylene Terephthalate precision cut flakes - square shape). Unpublished data submitted by Personal Care Products Council.

56. Derma Consult GmbH. 2008. Controlled user test of the product eye gel texture AEB +glitter (9% Polyethylene Terephthalate precision cut flakes - square shape). Unpublished data submitted by Personal Care Products Council.

57. Derma Consult GmbH. 2008. Controlled user test of the product eye gel texture ANG with glitter (9% Polyethylene Terephthalate precision cut flakes- square shape). Unpublished data submitted by Personal Care Products Council.

58. Peritesco. 2009. Ocular acceptability study of two eye shadows during 8 days under ophthalmological supervision (product 701102 contains 46.272% Polyethylene Terephthalate as precision cut flakes). Unpublished data submitted by Personal Care Products Council. 25 pages.