Cosmetic ingredients with insufficient data to support safety (119 total, through December, 2006)

Ingredient	Data needs
Acacia Catechu Gum, Acacia Concinna Fruit Extract, Acacia Dealbata Leaf Extract, Acacia Dealbata Leaf Wax, Acacia Decurrens Extract, Acacia Farnesiana Extract, Acacia Farnesiana Flower Wax, Acacia Farnesiana Gum, Acacia Senegal Extract	concentration of use; while there are data on gum arabic, it is not known how the components of these ingredients compare to gum arabic, so the chemical composition needs to be identified; if different from gum arabic: UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; sensitization and irritation data (except for Acacia Farnesiana Extract and Acacia Concinna Fruit Extract); genotoxicity in two mammalian systems, if positive, a dermal carcinogenesis study using NTP methods; dermal absorption, if significant absorption, dermal reproductive and developmental toxicity
Adipic Acid Dihydrazide	metabolism (stability of compound *in vivo*, with respect to hydrolysis to hydrazine); impurities (especially hydrazine); and concentration of use in cosmetic formulations; depending on the results of stability and impurities studies, the following data may be needed: chemistry (including pH, method of manufacture, and UV absorption); ocular irritation; dermal irritation and sensitization
Alcohol Denat. denatured with Quassin, Brucine, and Brucine Sulfate	for Alcohol Denat. denatured with Quassin: genotoxicity data; dermal absorption of the denaturant, and if the denaturant is absorbed at significant level, dermal reproductive and developmental toxicity data; and dermal sensitization and irritation. for Alcohol Denat. denatured with Brucine or Brucine Sulfate: mammalian genotoxicity data, and dermal absorption of the denaturant, and if the denaturant is absorbed at a significant level, dermal reproductive and developmental toxicity data.
Aldioxa	chemistry (method of manufacture, impurities, and UV absorption); 28-day dermal toxicity; ocular irritation (non-animal studies will be considered); at least two genotoxicity tests; photosensitization (only if significant UV absorption); and carcinogenicty, if the genotoxicity tests are positive
Aloe Andongensis Extract, Aloe Andongensis Leaf Juice, Aloe Arborescens Leaf Extract, Aloe Arborescens Leaf Juice, Aloe Arborescens Leaf Protoplasts, Aloe Ferox Leaf Extract, Aloe Ferox Leaf Juice, Aloe Ferox Leaf Juice Extract	28-day dermal toxicity studies; such data may be developed on one ingredient from each species if it can be demonstrated that the tested material is representative of the group. In any Aloe-derived ingredient used in cosmetics, regardless of species, anthraquinone levels should not exceed 50 ppm.
6-Amino-o-Cresol	safe for use in oxidative hair dyes, but insufficient for use in non-oxidative (semi-permanent) hair dyes — physical and chemical properties, including the octanol/water partition coefficient; impurities data, especially m-Cresol, other organic molecules, and heavy metals; metabolism data, if the metabolism is not similar to that of 4-Amino-2-Hydroxytoluene and/or p-, m-, and o-Aminocresol, the following may be needed: (a) 28-day dermal toxicity with histopathology, (b) dermal reproductive toxicity, and (c) in vitro genotoxicity, if positive, a 2-year dermal carcinogenicity study using NTP methods
4-Amino-2-Nitrophenol	concern over potential carcinogenicity and absence of reproductive/developmental toxicity; need impurities data and percutaneous absorption under use conditions; if there is significant dermal absorption, dermal reproductive/developmental toxicity may be needed
Ammonium Cocoyl Sarcosinate, Ammonium Lauroyl Sarcosinate, Sodium Cocoyl Sarcosinate, Sodium Lauroyl Sarcosinate, and Sodium Myristoyl Sarcosinate	safe as used in rinse-off products; but ≤5% for leave-on products; should not be used in products where N-nitroso compounds may be formed — data are insufficient to determine safety for use in products where inhalation is likely
Arachidonic Acid	dermal absorption is the key, if absorbed there is a concern about immune suppression in the skin
Arnica Montana and Arnica Montana Extract	current concentration of use; function in cosmetics; UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; gross pathology and histopathology in skin and other major organ systems associated with repeated dermal exposures (commonly called 28-day dermal toxicity); dermal reproductive and developmental toxicity data; inhalation toxicity data, especially addressing the concentration, amount delivered, and particle size; genotoxicity testing in a mammalian system, if positive, a 2-year dermal carcinogenesis assay using NTP methods

Ingredient	Data needs
Azulene [1]	methods of manufacture and impurities, especially naphthalenes; concentration of use; skin penetration, if there is significant skin penetration, then both a 28-day dermal toxicity study to assess general skin and systemic toxicity and a reproductive and developmental toxicity study; one genotoxicity study in a mammalian system, if positive, then a 2-year dermal carcinogenesis study using NTP methods; phototoxicity and photosensitization; skin irritation and sensitization in animals or humans; and ocular toxicity
Benzoxiquine	chemical characterization (impurities/purity data); UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; 28-day dermal toxicity; skin irritation and sensitization; ocular irritation (if available); genotoxicity in two mammalian systems, if positive, a dermal carcinogenesis study using NTP methods; and dermal reproductive and developmental toxicity
Benzyl Alcohol, Benzoic Acid, and Sodium Benzoate [2]	inhalation toxicity
Brucine, and Brucine Sulfate	mammalian genotoxicity data, and dermal absorption, and if absorbed at a significant level, dermal reproductive and developmental toxicity data.
Calendula Officinalis and Calendula Officinalis Extract	current use concentration; function in cosmetics; UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; gross pathology and histopathology in skin and other major organ systems associated with repeated dermal exposures (commonly called 28-day dermal toxicity); dermal reproductive and developmental toxicity; inhalation toxicity, especially addressing the concentration, amount delivered, and particle size; and genotoxicity testing in a mammalian system, if positive, a 2-year dermal carcinogenesis assay using NTP methods
Captan	18-month skin carcinogenicity assay — note: safety concern re genotoxicity and possible CA
Cetethyl Morpholinium Ethosulfate	morpholine moiety is the safety concern (see morpholine)
4-Chloro-2-Aminophenol	safe for use in oxidative hair dyes, but insufficient for use in non-oxidative (semi-permanent) hair dyes — physical and chemical properties, including the octanol/water partition coefficient; impurities data, especially m-Cresol, other organic molecules, and heavy metals; metabolism data, if the metabolism is not similar to that of 4-Amino-2-Hydroxytoluene and/or p-, m-, and o-Aminocresol, the following may be needed: (a) 28-day dermal toxicity with histopathology, (b) dermal reproductive toxicity, and (c) one genotoxicity study in a mammalian system, if positive, a 2-year dermal carcinogenicity study using NTP methods
Chlorophene and Dichlorophene	method of manufacture and impurities (especially the trimer in Dichlorophene); photosensitization and photocarcinogenesis for Dichlorophene; dermal reproductive and developmental toxicity for Dichlorophene (as a function of dose); and ocular irritation at concentration of use, if available — note: Japan banned Dichlorophene because of photosensitization concern
Coal Tar	product types in which used (other than as an OTC drug ingredient); use concentrations; and the maximum concentration that does not induce a biological effect
Cocamidopropylamine Oxide	safe for rinse-off uses — extent of dermal penetration is needed to support the safety of leave-on uses; if there is significant dermal absorption, dermal reproductive and developmental toxicity data may be needed
Cocoyl Sarcosine, Lauroyl Sarcosine, Myristoyl Sarcosine, Oleoyl Sarcosine, and Stearoyl Sarcosine	safe as used in rinse-off products; but ≤5% for leave-on products; should not be used in products where N-nitroso compounds may be formed — data are insufficient to determine safety for use in products where inhalation is likely
p-Cresol	study needed to demonstrate absence of chemical leukoderma at use concentration in formulation

Ingredient	Data needs
Di-*t*-Butylhydroquinone	concentration of use; chemical characterization (purity/impurity); UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; skin penetration, if significantly absorbed, dermal reproductive and developmental toxicity; and two genotoxicity studies, one in a mammalian system, if positive a 2-year dermal carcinogenesis assay using NTP methods
Dimethyl Lauramine	chemistry (pH, impurities, UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed); 28-day dermal toxicity; ocular irritation; human dermal irritation and sensitization; two genotoxicity studies, one in a mammalian system, if positive a 2-year dermal carcinogenesis assay using NTP methods
Dimethyl Stearamine	concentration of use; impurities; inhalation toxicity or information on particle size; ocular irritation; dermal irritation and sensitization; 28-day dermal toxicity, and depending on the results, dermal absorption, distribution, and metabolism; and if significantly absorbed, dermal reproductive and developmental toxicity and two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods
Disperse Blue 7	methods of manufacture, including clarification of the relationship between Disperse Blue 7 and Disperse Turquoise ALF and Disperse Turquoise LF2G mixed with Reux 83A, Tamol SW, and Twitchell Oil; analytical methods by which Disperse Blue 7 is measured; impurities; concentration of use as a function of product type; confirmation that this is a direct hair dye; and clarification of genotoxicity study results. (e.g., Disperse Turquoise ALF and Disperse Turquoise LF2G were genotoxic in bacteria - what is the specific relation to Disperse Blue 7? Disperse Blue 7 at 60% purity was genotoxic in bacteria - is the other 40% the inert Reax 83A, Tamol SW, and Twitchell Oil?).
Disperse Yellow 3	dermal absorption — note: if absorbed, there is a carcinogenicity concern
Glyceryl Arachidonate	dermal absorption is the key, if absorbed there is a concern about immune suppression in the skin
Glucose Glutamate [3]	concentration of use; chemistry, including method of manufacture and impurities; UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; dermal absorption, if dermally absorbed, 28-day dermal toxicity and dermal developmental toxicity; skin irritation and sensitization; and two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods
Hazel (Corylus Avellana) Extract, Hazel (Corylus Americana) Extract, Hazel (Corylus Rostrata) Extract, Hazel (Corylus Avellana) Nut Extract, Hazel (Corylus Americana) Nut Extract, and Hazel (Corylus Rostrata) Nut Extract	current concentration of use; method of extraction/manufacture and quality control (e.g., chemical analysis); contaminants and methods of extraction (especially pesticides and heavy metals); dermal irritation and sensitization; UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; 28-day dermal toxicity; and two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods
Hazel (Corylus Avellana) Nut Oil, and Hazel (Corylus Americana) Nut Oil	have data on fatty acids in the oil, but don't know how representative the data is; if these could be confirmed and information on contaminants provided this could be resolved
Human Placental Enzymes,Lipids, and Protein; Human Umbilical Extract; and Hydrolyzed Human Placental Protein	skin sensitization at concentration of use; gross pathology and histopathology in skin and other major organ systems associated with repeated exposures; dermal reproductive and developmental toxicity; photosensitization; one genotoxicity study in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods may be needed; and ocular toxicity, if available
Hypericum Perforatum Extract and Oil	current concentration of use; function in cosmetics; photosensitization and phototoxicity using visible light (550-610 nm, 5 - 10 J); gross pathology and histopathology in skin and other major organ systems with repeated dermal exposures; dermal reproductive and developmental toxicity; skin irritation and sensitization in humans with the oil; and ocular irritation, if available
Isopropyl Linoleate	human skin irritation and sensitization and genotoxicity data

Ingredient	Data needs
Juniperus Communis Extract, Juniperus Oxycedrus Extract, Juniperus Phoenicea Extract, Juniperus Virginiana Extract, and Juniperus Oxycedrus Tar	current concentration of use; function in cosmetics; methods of manufacture and impurities, especially presence of pesticide residues; UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; developmental and reproductive toxicity to include determination of the no-effect level on implantation; two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; a dermal carcinogenicity study on the tar; and skin irritation and sensitization
Lauramine	impurities (especially nitrosamines); two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; human repeated insult patch test
Lecithin and Hydrogenated Lecithin[6]	inhalation toxicity
Melamine/Formaldehyde Resin	chemical characterization (pH, % free formaldehyde at pH of use in aqueous or alcohol vehicles); impurities; physical form used in cosmetics; concentration of use; UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; 28-day dermal toxicity; and human irritation and sensitization
Mixed Cresols	study needed to demonstrate absence of chemical leukoderma at use concentration in formulation
Morpholine	quantitative data regarding the formation of N-nitrosomorpholine under conditions of use
2,3-Naphthalenediol	animal dermal irritation and photosensitization; 90-day subchronic dermal toxicity; chemical description; and impurities
4-Nitro-m-Phenylenediamine	methods of production; impurities; UV absorption; animal skin irritation and sensitization; and 28-day dermal toxicity
Oxyquinoline and Oxyquinoline Sulfate [4]	impurities and UV absorption data needed
Peanut (Arachis Hypogaea) Flour	aflatoxin residue levels and possible plant protein residues that may sensitize
PEG-2, -3, -5, -10, -15, and -20 Cocamine	physical and chemical properties; impurities, especially nitrosamines; genotoxicity in a mammalian system; 28-day dermal toxicity using PEG-2 Cocamine; and dermal sensitization using PEG-2 Cocamine
Pentaerythrityl Rosinate	two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; dermal absorption, if significantly absorbed, both a 28-day dermal toxicity and a dermal reproductive and developmental toxicity study may be needed; chemical properties, including structure and impurities
Phloroglucinol	purity/impurities; human dermal irritation; two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods (since there is some positive genotoxicity data, going directly to a carcinogenesis assay would not be inappropriate); types of products in which used, with concentration of use; and 28-day dermal toxicity, depending on the results, dermal absorption, metabolism, and distribution may be needed and if significantly absorbed, dermal reproductive and developmental toxicity will be needed
Placental Enzymes, Lipids, Protein; Umbilical Extract; and Hydrolyzed Placental Protein	skin sensitization at concentration of use; gross pathology and histopathology in skin and other major organ systems associated with repeated exposures; dermal reproductive and developmental toxicity; photosensitization; one genotoxicity study in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods may be needed; and ocular toxicity, if available
Potassium Chlorate	purpose in cosmetics; use concentration; 28-day dermal toxicity; if used in products used on or near the eye, ocular irritation; two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; human skin irritation dose-response and sensitization

Ingredient	Data needs
PPG-9, -25, and -40 Diethylmonium Chloride	current concentration of use; dermal absorption using PPG-9 Diethylmonium Chloride, if significantly absorbed, then a 28-day dermal toxicity study; two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; dermal sensitization and irritation in humans at concentration of use; and impurities, especially nitrosamines
Pyrocatechol [5]	if absorbed in skin from hair dyes, carcinogenicity concern
Quassin	genotoxicity data; dermal absorption, and if absorbed at significant level, dermal reproductive and developmental toxicity data; and dermal sensitization and irritation
SD Alcohol 39	genotoxicity data; dermal absorption of the denaturant Quassin, and if the denaturant is absorbed at significant level, dermal reproductive and developmental toxicity data; and dermal sensitization and irritation.
SD Alcohol 40	mammalian genotoxicity data, and dermal absorption of the denaturant Brucine or Brucine Sulfate, and if the denaturant is absorbed at a significant level, dermal reproductive and developmental toxicity data.
Sodium Iodate	purpose in cosmetics; use concentration; 28-day dermal toxicity; and animal dermal irritation dose-response
Sodium Lauraminopropionate and Sodium Lauriminodipropionate	concentration of use; impurities/purity; chemical and physical properties of Sodium Lauraminopropionate; method of manufacture; 28-day dermal toxicity; dermal reproductive and developmental toxicity; ocular irritation at use concentration, if available; dermal irritation and sensitization at use concentration; and two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods
Sodium-m- Nitrobenzenesulfonate	impurities/purity; 28-day dermal toxicity, if positive, dermal absorption and distribution in animals; if significantly absorbed, two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; and ocular toxicity, if available
Stearamide DIBA Stearate	method of manufacture; chemical characterization, including impurities; dermal absorption, if significantly absorbed, 28-day dermal toxicity and dermal reproductive and developmental toxicity studies may be needed; two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; and UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed
Stearamine	impurities (especially nitrosamines); two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; human repeated insult patch test
Stearic Hydrazide	genotoxicity; human skin irritation and sensitization; method of synthesis; impurities, especially free hydrazine; and UV absorption
Urocanic Acid	human photoimmunosuppression data; modulation of previous photocarcinogenicity studies using 20 or more animals per group and 3 Urocanic Acic dose levels with procedures and UV exposure as in published study; and DNA adduct study *in vivo* and *in vitro*
Yarrow (Achillea Millefolium) Extract	UV absorption, if absorption occurs in the UVA or UVB range, photosensitization may be needed; gross pathology and histopathology in skin and other major organ systems with repeated exposures (28-day dermal toxicity); reproductive and developmental toxicity data; two genotoxicity studies, one in a mammalian system, if genotoxicty studies are positive, a 2-year dermal carcinogenesis assay using NTP methods; and clinical sensitization testing (repeated insult patch test with 150 subjects) at maximum use concentration

[1] this ingredient may not be in use; confusion with guiazulene

[2] all 3 are safe for use in cosmetic formulations up to 5%, except that the data are insufficient to support the safety in cosmetic products in which the primary route of exposure is inhalation (i.e., aerosols). Benzyl Alcohol is safe for use in hair dye formulations up to 10%.

[3] this ingredient is currently called Deoxyglutamyl Fructose
[4] safe as used as stabilizers for hydrogen peroxide in rinse-off hair care products, but insufficient data for leave-on products
[5] unsafe for leave-on products; insufficient data for hair dyes
[6] safe as used in rinse-off products, safe for use in leave-on products at concentrations ≤15%, but insufficient data for use in products likely to be inhaled. These ingredients should not be used in cosmetic products in which N-nitroso compounds may be formed.