tert-Butylacrylamide

107-58-4

OVERVIEW

Prepared for the National Cancer Institute (NCI) for consideration by the Chemical Selection Working Group (CSWG) by Technical Resources International, Inc. under contract no. N02-07007.

tert-Butylacrylamide came to the attention of the National Cancer Institute (NCI) Division of Cancer Biology as the result of a review of high production chemicals in commerce that do not meet the criteria for inclusion in the United States (U.S.) Environmental Protection Agency (EPA) HPV Challenge Program.

tert-Butylacrylamide is a monomer used for the production of many polymers and is an intermediate in organic chemical synthesis. Human exposure to tert-butylacrylamide can occur in the workplace and from leaching out of consumer products prepared from tert-butylacrylamide polymers. The monomer is approved as an indirect food additive (adhesive constituent) by the U.S. Food and Drug Administration (FDA). The cumulative effective daily intake of tert-butylacrylamide was estimated to be 0.00035 mg/kg bw/day, a default value when no experimental data are available.

The available information on tert-butylacrylamide is insufficient to profile the toxicological effects of this chemical. tert-Butylacrylamide was described as negative in the Ames assay and did not produce the neurotoxic effects characteristic of acrylamide in animal studies.

NOMINATION OF tert-BUTYLACRYLAMIDE TO THE NTP

Based on a review of the available literature and the recommendations of the Chemical Selection Working Group (CSWG) on December 15, 2004, NCI nominates this chemical for testing by the National Toxicology Program (NTP) and forwards the following information:

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- The attached Summary of Data for Chemical Selection
- Copies of references cited in the Summary of Data for Chemical Selection
- CSWG recommendations to:

(1) Characterize the toxicity of tert-butylacrylamide in a 90-day study

(2) Conduct metabolic and disposition studies to determine if acrylamide is formed.

(3) Conduct standard assays to characterize genotoxicity, including tests for chromosomal aberrations and the mouse lymphoma assay.

PRIORITY

The CSWG suggested that the recommended testing be conducted with moderate to high priority.

COMMENTS

Testing of this compound is justified based on the high potential for human exposure, particularly in the workplace, and concerns raised about the carcinogenic potential of acrylamides in general.

An evaluation of the levels of tert-butylacrylamide in foods and the environment and ecotoxicity tests, depending on the results of environmental testing, may be warranted by other groups.

Acrylamide (CAS No. 79-06-1) has received much recent attention after it was determined that it could be produced in foods during processing. Acrylamide was nominated to NTP by the Food and Drug Administration (FDA) and is on test at the National Center for Toxicological Research (NCTR) for toxicological characterization, toxicokinetics, mechanistic (hemoglobin adducts), carcinogenicity, and bioavailability (FDA, 2003). The studies selected for tert-butylacrylamide should be designed in conjunction with ongoing and anticipated tests of acrylamide.

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SUMMARY OF DATA FOR CHEMICAL SELECTION

CHEMICAL IDENTIFICATION

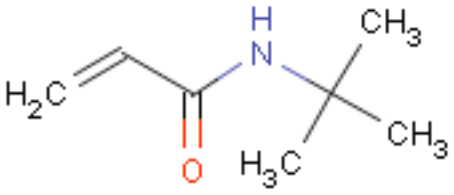
CAS Registry No: 107-58-4

Chemical Abstracts Service Name: 2-Propenamide, N-(1,1-dimethylethyl)- (9CI)

Synonyms and Trade Names: tert-Butylacrylamide; EINECS 203-505-6; N-tert-butylacrylamide (ChemIDplus, 2004)

Structural Class: Acrylamide

Structure, Molecular Formula, and Molecular Weight:



$C_7H_{13}NO$ Mol. wt.: 127.18

Chemical and Physical Properties:

Description: White crystalline solid (Lewis, 2001)

Melting Point: 128 ºC (Lide, 2005)

Solubility: Slightly soluble in water; soluble in alcohol, chloroform, and acetone; insoluble in petroleum ether (Lewis, 2001; Lide 2005)

Density/Specific Gravity: 1.015 at 30 ºC (Lewis, 2001)

Reactivity: Hazardous polymerization may occur; incompatible with strong oxidizing agents and strong bases (Sigma Aldrich MSDS, 2004)

Technical Products and Impurities:

tert-Butylacrylamide, at 97% purity, is available from Sigma Aldrich and from Fisher Scientific, purity not specified (Fisher Scientific, 2004; Sigma Aldrich, 2004).

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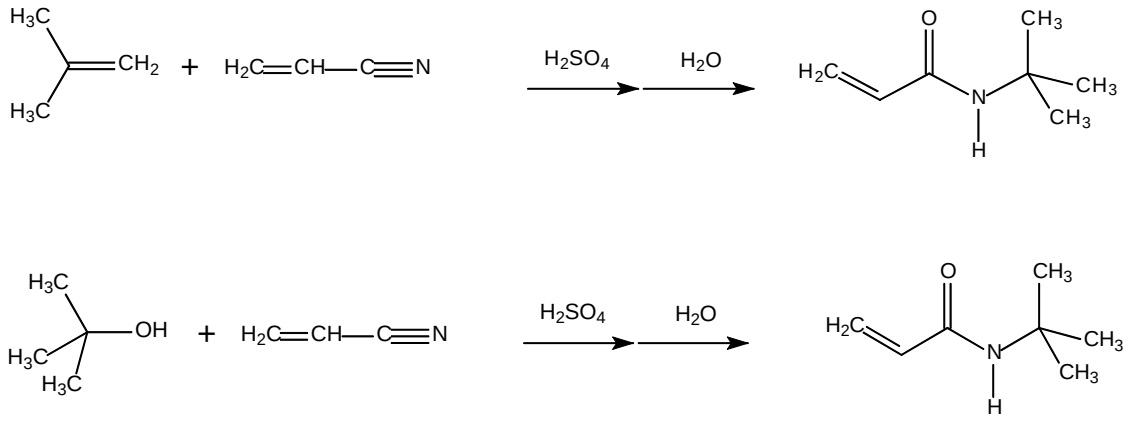
EXPOSURE INFORMATION

Production and Producers:

Manufacturing Process.

The preferred method to manufacture tert-butylacrylamide is the Ritter reaction (Habermann, 1991). In this process, tert-butylacrylamide is produced by the acid-catalyzed reaction of acrylonitrile with isobutylene followed by hydrolysis. tert-Butyl alcohol can be used in place of isobutylene in this reaction (Organic-chemistry.org, 2004). A schematic representation of these reactions is shown in Figure 1.

Figure 1. Commercial Synthesis Routes for tert-Butylacrylamide using the Ritter Reaction



Producers and Importers.

Nine U.S. producers or distributors of tert-butylacrylamide are listed by Chemical Sources International (2004). According to recent issues of chemical directories, tert-butylacrylamide is manufactured and/or distributed by Acros - USA; Alfa Aesar; Fluka; Frinton Laboratories, Inc.; ICN; JLM Marketing, Inc.; Lancaster; Monomer-Polymer & Dajac Labs, Inc; MP Biomedicals; San Esters Corp.; TCI (ChemACX, 2004; ChemBuyersGuide.com, Inc., 2004; Chemical Information Services, Inc., 2004; Chemical Week Associates, 2003; Tilton, 2004).

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Production/Import Level. The EPA's Inventory Update Rule reports nonconfidential production ranges of chemicals every four years. The production levels of tert-butylacrylamide during the years 1986-2002 are listed in Table 1.

Table 1. Production Levels of tert-Butylacrylamide

Year	Production Range (lbs.)
1986	No Reports
1990	> 500,000 - 1,000,000
1994	10,000 - 500,000
1998	> 1,000,000 - 10,000,000
2002	> 1,000,000 - 10,000,000

Source: EPA (2004)

tert-Butylacrylamide is an LPV chemical in Europe, meaning that 10-1,000 metric tons were produced or imported in the European Union between 1990-1994 (ESIS, 2004). tert-Butylacrylamide is listed in the EPA Toxic Substances Control Act (TSCA) Inventory (ChemIDplus, 2004).

For the 9-month period from April 2003 to December 2003, the Port Import/Export Reporting Service (PIERS) database reported tert-butylacrylamide imports with a cargo weight of 41,612 pounds (Dialog Information Services, 2004).

Use Pattern:

tert-Butylacrylamide monomer has reported uses as an organic intermediate (Lewis, 2001).

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Homopolymers and copolymers of tert-butylacrylamide are FDA-approved indirect food additives used in adhesives that are components of articles intended for use in packaging, transporting, or holding food (FDA, 2004a).

Copolymers derived from tert-butylacrylamide, ethyl acrylate, and acrylic acid have applications as film-forming agents in hair sprays (BASF Aktiengesellschaft, 1997; Lang, 2002).

New developments in thermosensitive poly(acrylamide)-based hydrogels have created a niche market for tert-butylacrylamide in the pharmaceutical industry. tert-Butylacrylamide monomer is used in synthesis of thermosensitive hydrogels to modify the lower critical solution temperature (LCST), which has enabled these hydrogels to be used as drug delivery systems. Studies in the literature indicate that these hydrogels are being investigated for their ability to deliver pharmaceuticals to vascular smooth muscle cells and the colon (Brondsted & Kopecek, 1991; Cai & Gupta, 2002; ChemFinder, 2004; Doorty *et al*., 2003).

N-tert-Butylacrylamide and t-butylacrylamide are cited in 393 and 374 U.S. patents, respectively, from 1976 to the present. The patents described suggest that tert-butylacrylamide also has applications in the photographic, dye, and printing industries (United States Patent and Trademark Office, 2004).

Human Exposure:

Occupational Exposure. Workers could be exposed to tert-butylacrylamide during the production, transport, or use of the monomer, e.g., to produce homopolymers and copolymers.

No listing was found for tert-butylacrylamide in the National Occupational Exposure Survey (NOES), which was conducted by the National Institute for Occupational Safety and

Health (NIOSH) between 1981 and 1983. This information does not reflect the recent dramatic increase in the use of tert-butylacrylamide in the United States.

Environmental Exposure. Human exposure to tert-butylacrylamide in the environment may occur from waste streams produced from the manufacturing, use, and disposal of tert-butylacrylamide and products made from tert-butylacrylamide. Since small amounts of tert-butylacrylamide may be present in hair spray products and leached from food packaging, additional environmental exposure may occur in the air and water and in refuse disposal sites.

Consumer Exposure. The general population may be exposed to tert-butylacrylamide leached into foods because of the presence of small amounts of the monomer in packaging that comes into contact with foods. The FDA has developed a cumulative estimated daily intake (CEDI) database for food contact substances such as adhesives. In the absence of appropriate studies to determine migration, the Office of Food Additive Safety assumes a default CEDI of 7 ppb or a cumulative intake of 0.00035 mg/kg bw per day. tert-Butylacrylamide has been assigned a CEDI of 7 ppb (FDA, 2004b).

Because tert-butylacrylamide is listed among substances suspected to have carcinogenic properties, the European Commission has declared that tert-butylacrylamide should not be present in detectable amounts in foods (European Commission, 2003).

Other sources of consumer exposure to tert-butylacrylamide may be from its leaching from polymers used in cosmetics, photography, and printing. Another exposure pathway for tert-butylacrylamide that may become significant in the future would involve the approval of hydrogels prepared from tert-butylacrylamide as a means to deliver pharmaceutical agents in patients.

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Environmental Occurrence:

tert-Butylacrylamide does not occur naturally. No information was found in the available literature identifying tert-butylacrylamide in environmental media. It would be expected that tert-butylacrylamide could be released into various waste streams during its manufacture and use.

Regulatory Status:

No standards or guidelines have been set by NIOSH or OSHA for occupational exposure to or workplace allowable levels of tert-butylacrylamide. tert-Butylacrylamide was not on the American Conference of Governmental Industrial Hygienists (ACGIH) list of compounds for which recommendations for a Threshold Limit Value (TLV) or Biological Exposure Index (BEI) are made.

tert-Butylacrylamide is not regulated under SARA Section 302 (Extremely Hazardous Substances) and is not reportable under Section 313. This chemical is also not listed as a hazardous air pollutant under the Clean Air Act and is not listed as a hazardous substance under the Clean Water Act (Fisher Scientific MSDS, 2003).

TOXICOLOGICAL INFORMATION

Human Data:

No epidemiological studies or case reports investigating the association of exposure to tert-butylacrylamide and cancer risks in humans were identified in the available literature.

The sensitization potential of tert-butylacrylamide was assessed in 22 individuals by patch testing with 1% tert-butylacrylamide in petrolatum. None of the patients experienced sensitization to tert-butylacrylamide although one patient showed slight to moderate irritation from this compound (Kanerva *et al.*, 1988).

Animal Data:

Acute Studies. The oral LD_{50} for male mice of the ddY strain was reported to be 941 mg/kg (Biblioline, 2004; Hashimoto *et al*., 1981).

Prechronic/Subchronic Studies. Subchronic studies on tert-butylacrylamide have focused on neurotoxicity and reproductive toxicity as endpoints and are discussed in the *Other Biological Effects* section.

Chronic/Carcinogenicity Studies. No 2-year carcinogenicity studies of tert-butylacrylamide in animals were identified in the available literature.

Short-term Tests:

tert-Butylacrylamide, dissolved in 0.1 ml DMSO, was not mutagenic in the standard Ames assay or in the Ames assay using the preincubation method when concentrations between 0.5 to 5,000 μg/plate were tested in *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, and TA1538 with or without metabolic activation with Aroclor 1254-induced rat liver S-9 (Hashimoto & Tanii, 1985).

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Metabolism:

The metabolism of tert-butylacrylamide was studied *in vitro* using the livers of male mice. For studies involving metabolic activation, animals received intraperitoneal injections of sodium phenobarbital at 50 mg/kg for five successive days up until one day before they were killed. tert-Butylacrylamide was metabolized in the mouse hepatic microsomal enzymes with a NADPH generating system and by hepatic glutathione-S-transferase. However, the metabolic products were not identified in these experiments. Both reactions were enhanced by phenobarbital (Tanii & Hashimoto, 1981).

Other Biological Effects:

Neurotoxicity. Several studies have documented the ability of acrylamide to produce peripheral neuropathy in experimental animals and humans. These studies have led to the evaluation of the neurotoxic properties of several acrylamide derivatives, including tert-butylacrylamide.

The neurotoxicity of tert-butylacrylamide was evaluated in rats based on its effects on rotarod performance, morphology of nerves, and neurotubulin. Four male Wistar rats that were dosed with 15 mM tert-butylacrylamide in drinking water for a period of 90 days experienced significant depressions of body weight gain. No deficits of rotarod performance or morphological changes in nerve tissues were observed in treated animals. tert-Butylacrylamide, using the above protocol, except for a duration of 60 days, did not affect neurotubulin integrity assessed by the binding of [^{3}H]colchicine (Tanii & Hashimoto, 1983).

Effects on Glycolytic Enzymes. One of the proposed mechanisms of acrylamide-induced neuropathy involves the inhibition of glycolytic enzymes in nerve tissues. This inhibition interferes with axonal transport, which is dependent on energy from oxidative metabolism. The ability of tert-butylacrylamide to inhibit glycolytic enzymes in mice and rats was investigated in *in vitro* studies. tert-Butylacrylamide inhibited glyceraldehyde-3-phosphate

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dehydrogenase (GAPDH) and enolase in the brains of mice and rats. Phosphofructokinase (PFK) was unaffected by this compound in the mouse brain. In contrast, tert-butylacrylamide failed to inhibit GAPDH and enolase in rat sciatic nerve in *in vivo* studies. Because there is evidence that glycolytic enzymes are inhibited by neurotoxic chemicals like acrylamide and nonneurotoxic chemicals like tert-butylacrylamide, neuropathy induced by acrylamide and its analogues may occur through a different pathway (Sakamoto & Hashimoto, 1985a,b; Tanii & Hashimoto, 1984).

Effects on Reproductive Organs. Six male mice were orally administered 318 mg/kg tert-butylacrylamide twice weekly for 10 weeks. Body weight and relative testicular weights were similar between control and treated animals. There was no evidence of testicular atrophy or histopathogical changes in the testis in treated animals (Hashimoto *et al*., 1981).

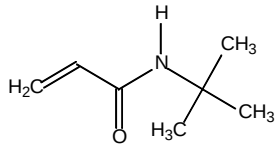
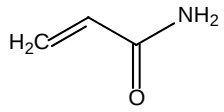
Dermal Effects Following Implantation. Copolymers of N-(2-hydroxypropyl)meth-acrylamide or N,NN-diethylacrylamide with tert-butylacrylamide are polymeric hydrophilic gels that are implanted into organisms for medical purposes. To study the biological tolerance of hydrophilic gels, these copolymers were implanted subcutaneously on the backs of 60 Wistar rats and observations were taken 10, 30, 60, 90, 180, and 360 days after implantation. Macroscopic and microscopic evaluation of the implantation sites demonstrated that no adverse reactions occurred following the implantation of these copolymers into living organisms (Sprincl & Ulbrich, 1979).

Structure/Activity Relationships:

A key feature raising concerns about the possible carcinogenicity of tert-butylacrylamide is the presence of the acrylamide moiety. Acrylamide (CAS No. 79-06-1), classified as a probable human carcinogen, can be leached into foods during contact with food packaging materials containing acrylamide, and it can be formed in food during heating or baking. The possibility that tert-butylacrylamide may be present in foods via similar mechanisms should be considered.

Two additional compounds considered in the structure-activity analysis are N-isopropylacrylamide (CAS No. 2210-25-5) and N-methyl-acrylamide (CAS No.1187-59-3). Studies of the mutagenicity and carcinogenicity of tert-butylacrylamide and the three related acrylamides are summarized Table 2.

Table 2. Summary of Information on tert-Butylacrylamide and Related Compounds

Chemical Name	Mutagenicity Studies	Carcinogenicity Studies
tert-Butylacrylamide  (CAS No. 107-58-4)	Negative in *S. typhimurium* TA98, TA100, TA1535, TA1537, and TA1538 with and without S-9 (Hashimoto & Tanii, 1985)	No data found in available literature
Acrylamide (CAS No. 79-06-1) 	Negative in *S. typhimurium* TA97, TA98, TA100, TA102, TA1535, TA1537, and TA1538 with and without S-9 (Zeiger *et al*., 1987 and Knaap *et al*., 1988 as cited in CCRIS, 2004; Hashimoto & Tanii, 1985) Positive in the mouse lymphoma assay with and without S-9 (Knaap *et al*., 1988 as cited in CCRIS, 2004) Negative for unscheduled DNA synthesis (UDS) in rat hepatocytes (Butterworth *et al*., 1992 as cited in CCRIS, 2004) Positive for UDS in rat spermatocytes and human mammary epithelial cells (Butterworth *et al*., 1992 as cited in CCRIS, 2004) Positive for clastogenicity, *in vitro* cell transformation, and amplification of SV40 DNA inserts of SV40-transformed Chinese hamster cells (IRIS, 1993)	Increased incidences of tumors of the testis and thyroid in male rats and of tumors of the thyroid, mammary gland, glial, oral cavity, uterus, and clitoral gland in female rats (IARC, 1997) Increased incidence of lung adenomas in strain A mice (IARC, 1997) Increased incidence of skin tumors in mice following promotion by 12-*O*-tetradecanoylphorbol 13-acetate (IARC, 1997)

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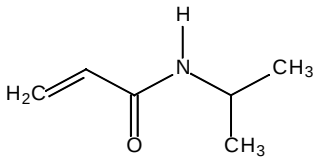
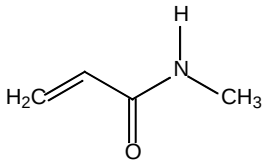
N-Isopropylacrylamide (CAS No. 2210-25-5) 	Negative in *S. typhimurium* TA98, TA100, TA1535, TA1537, and TA1538 w/wo S-9 (Hashimoto & Tanii, 1985)	No data found in available literature
N-Methyl acrylamide (CAS No. 1187-59-3) 	Negative in *S. typhimurium* TA98, TA100, TA1535, TA1537, and TA1538 w/wo S-9 (Hashimoto & Tanii, 1985)	No data found in available literature

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References

BASF Aktiengesellschaft (1997) Ultrahold® Strong. *Technical Information.* [http://www.basf-korea.co.kr/02_products/04_finechemicals/document/cosmetic/tech/hairpolymer/down.asp?file=ultraholdstrong.pdf] Searched November 5, 2004

Biblioline (2004) Acrylamide, N-tert-butyl-. *RTECS (Registry of Toxic Effects of Chemical Substances)*, Accessed through "107-58-4" at [http://biblioline.nisc.com/scripts/login.dll?BiblioLine] Searched July 28, 2004

Brondsted, H. & Kopecek, J. (1991) Hydrogels for site-specific oral drug delivery: synthesis and characterization. *Biomaterials*, **12**(6), 584-92 [abstract]

Cai, W. & Gupta, R.B. (2002) *Hydrogels*. 3. Properties and preparation. [http://www.mrw.interscience.wiley.com/kirk/articles/hydrgupt.a01/sect4-fs.html] Searched November 4, 2004

CCRIS (2004) Acrylamide. *Chemical Carcinogenesis Research Information System*. Record no. 7. National Library of Medicine, Bethesda. MD. Accessed through [http://toxnet.nih.gov] Searched November 2004

ChemACX (2004) tert-Butylacrylamide [107-58-4]. *Search results*. [http://chemacx.cambridgesoft.com/ChemACX/index.asp] Searched July 28, 2004

ChemBuyersGuide.com (2004) tert-Butylacrylamide [107-58-4]. *Search results*. [http://www.chembuyersguide.com/index.htm] Searched November 5, 2004

ChemFinder.com (2004) *tert-Butylacrylamide [107-58-4]*. Cambridge Software Corporation. [http://chemfinder.cambridgesoft.com/] Searched October 13, 2004

Chemical Information Services, Inc. (2004) Global Info Centre for N-tert-butylacrylamide [107-58-4]. *DWCP*. [http://chemicalinfo.com/products/dwcp/dwcp_overview.htm] Searched November 16, 2004

Chemical Sources International (2004) ALL chemical suppliers for N-tert-butylacrylamide. *Chem Sources - Chemical Search*. [http://db.chemsources.com/cgi-bin/foxweb.exe/validate_user@csi/ login] Searched November 5, 2004

Chemical Week Associates (2003) N-tert.butylacrylamide. *2004 Chemical Week Buyers' Guide*, New York, p 94

ChemIDplus (2004) *Chemical Identification plus*. [Record no. 000107584]. National Library of Medicine, Bethesda, MD. [http://chem.sis.nlm.nih.gov/chemidplus] Searched November 4, 2004

Dialog Information Services (2004) *Search for N-tert-butylacrylamide and tert-butylacrylamide*. PIERS Imports (US Ports) (File 573), Palo Alto, CA, [Record nos. 0037153165, 0033198677, 0032467719] Searched November 11, 2004

Doorty, K.B., Golubeva, T.A., Gorelov, A.V., Rochev, Y.A., Allen, L.T., Dawson, K.A., Gallagher, W.M. & Keenan, A.K. (2003) Poly(N-isopropylacrylamide) co-polymer films as potential vehicles for delivery of an antimitotic agent to vascular smooth muscle cells. *Cardiovasc. Pathol.*, **12**(2), 105-10 [abstract]

EPA (2004) 2-Propenamide, N-(1,1-dimethylethyl)- [107-58-4]. *2002 Inventory Update Rule Search Result Page*. [http://www.epa.gov/oppt/iur/iur02/search03.htm] Searched July 30, 2004

ESIS (2004) N-tert-butylacrylamide [107-58-4]. *European Chemical Substances Information System*. [http://ecb.jrc.it/esis] Searched November 4, 2004

European Commission (2003) Provisional list of monomers and additives notified to European Commission as substances which may be used in the manufacture of plastics intended to come into contact with foodstuffs. *Synoptic Document*. [http://europa.eu.int/comm/food/food/ chemicalsafety/ foodcontact/synoptic_doc_en.pdf] Searched November 9, 2004

FDA (2003) FDA Draft Action Plan for Acrylamide in Food- February 24, 2003 Update. *U.S. Department of Health and Human Services*. [http://www.cfsan.fda.gov/~dms/acrypla2.html] Searched November 23, 2004

FDA (2004a) Title 21 - Food and Drugs. Subchapter B - Food for human consumption (continued). Part 175 Indirect food additives: adhesives and components of coatings. *Code of Fed. Regulat.*. 21CFR175 [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/ cfcfr/CFRSearch.cfm? CFRPart=175&showFR=1&subpartNode=21:3.0.1.1.6.2] Searched November 9, 2004

FDA (2004b) Food contact substance notification program's cumulative estimated daily intake/acceptable daily intake database. *CFSAN/Office of Food Additive Safety*. [http://www. cfsan.fda.gov/~dms/opa-edi.html] Searched November 5, 2004

Fisher Scientific (2004) N-tert-butylacrylamide. *Product Detail*. Accessed through [https://www1.fishersci.com/] Searched November 4, 2004

Fisher Scientific MSDS (2003) N-tert-butylacrylamide. *Material Safety Data Sheet*. [https:// fscimage.fishersci.com/msds/72233.htm] Searched November 4, 2004

Habermann, C.E. (1991) Acrylamide. In: Kroschwitz, J.I. & Howe-Grant, M., eds., *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed., Vol. 1, New York, John Wiley & Sons, Inc., p 259

Hashimoto, K., Sakamoto, J. & Tanii, H. (1981) Neurotoxicity of acrylamide and related compounds and their effects on male gonads in mice. *Arch. Toxicol.*, **47**, 179-189

Hashimoto, K. & Tanii, H. (1985) Mutagenicity of acrylamide and its analogues in *Salmonella typhimurium*. *Mut. Res.*, **158**, 129-133

IARC (1997) Acrylamide (Group 2A) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.* [http://www-cie.iarc.fr/htdocs/monographs/vol60/m60-11.htm] Searched November 15, 2004

IRIS (1993) II.A. Evidence of human carcinogenicity. Acrylamide. *Integrated Risk Information System*. National Library of Medicine, Bethesda. MD. Accessed through [http://toxnet.nih.gov] Searched November 2004

Kanerva, L., Estlander, T. & Jolanki R. (1988) Sensitization to patch test acrylates. *Contact Derm.*, **18**, 10-15

Lang, G. (2002) 4. Hairstyling preparations. *Hair Preparations*. [http://www.mrw.interscience. wiley.com/ueic/articles/a12_571/sect4-fs.html] Searched November 4, 2002

Lewis, R.J., ed. (2001) N-tert-butylacrylamide. *Hawley's Condensed Chemical Dictionary*, 14th ed., New York, John Wiley & Sons, Inc., p 173

Lide, D.R., ed. (2005) N-tert-butyl-2-propenamide. *CRC Handbook of Chemistry and Physics*, Version 2005, (On CD-ROM), Boca Raton, FL, CRC Press

Organic-chemistry.org (2004) *Ritter Reaction*. [http:// www.organic-chemistry.org/named reactions/ritter-reaction.shtm] Searched November 8, 2004

Sakamoto, J. & Hashimoto, K. (1985a) Effect of acrylamide and related compounds on glycolytic enzymes in rat sciatic nerve *in vivo*. *Arch. Toxicol.*, **57**, 282-284

Sakamoto, J. & Hashimoto, K. (1985b) Effect of acrylamide and related compounds on glycolytic enzymes in mouse brain *in vitro*. *Arch. Toxicol.*, **57**, 276-281

Sigma-Aldrich (2004) N-tert-butylacrylamide [107-58-4]. *Search results for 107-58-4*. [http:// www.sigmaaldrich.com/Area_of_Interest/The_Americas/United_States.html] Searched July 27, 2004

Sigma-Aldrich MSDS (2004) N-tert-butylacrylamide, 97% Material Safety Data Sheet. *Search Results for 107-58-4*. [http://www.sigmaaldrich.com/Area_of_Interest/The_Americas/United_States.html] Searched July 27, 2004

Sprincl, L. & Ulbrich, K. (1979) Biological tolerance of copolymers of N-substituted (meth)acrylamides in test organism. *Polym. Med.*, **9**(2), 69-73

Tanii, H. & Hashimoto, K. (1981) Studies on *in vitro* metabolism of acrylamide and related compounds. *Arch. Toxicol.*, **48**, 157-166

Tanii, H. & Hashimoto, K. (1983) Neurotoxicity of acrylamide and related compounds in rats. Effects on rotarod performance, morphology of nerves and neurotubulin. *Arch. Toxicol.*, **54**, 203-213

Tanii, H. & Hashimoto, K. (1984) Inhibition of brain enolases by acrylamide and its related compounds *in vitro*, and the structure-activity relationship. *Experientia*, **40**, 971-972

Tilton, H., ed. (2004) tert-Butyl acrylamide and N-tert-butylacrylamide. *OPD Chemical Buyers Directory 2005*, New York, Schnell Publishing Co., p 129

United States Patent and Trademark Office (2004) Results of search (all years) of database for "N-tert-butylacrylamide" and "t-butylacrylamide." *USPTO Patent Full-Text and Image Database*. [http://patft.uspto.gov/netahtml/search-bool.html] Searched November 4, 2004