Safety Assessment of Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin as Used in Cosmetics

Status:	Draft Amended Report for Panel Review
Release Date:	September 11, 2026
Panel Meeting Date:	October 5-6, 2026

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Temima Nguyen, M.S., Scientific Analyst/Writer, CIR, and Jinqiu Zhu, Ph.D., DABT, ERT, DCST, CIR Toxicologist.

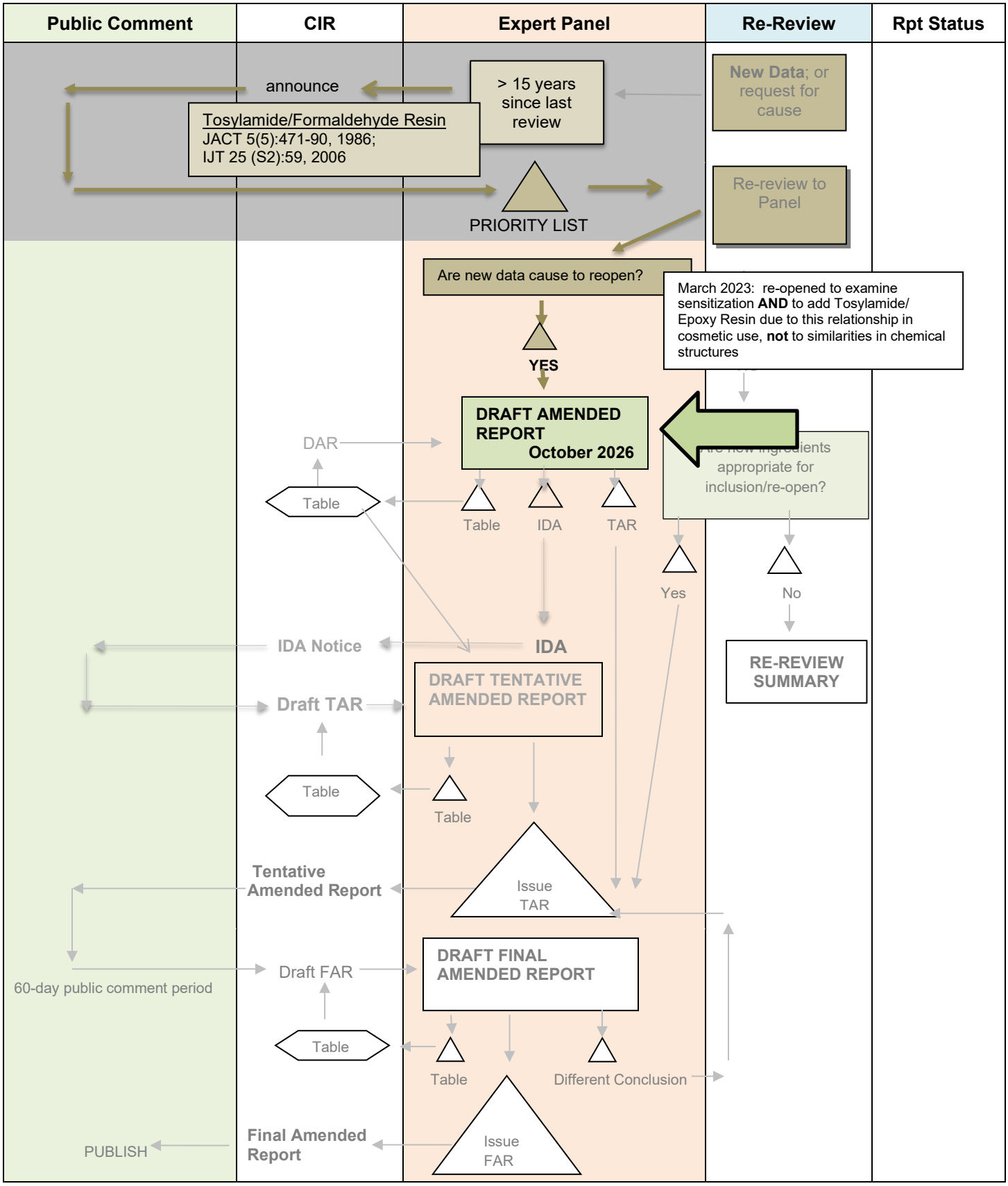
© Cosmetic Ingredient Review
555 13th Street, NW, Suite 300W, Washington, DC 20004
cirinfo@cir-safety.org

Distributed for Comment Only -- Do Not Cite or Quote

RE-REVIEW FLOW CHART

INGREDIENT/FAMILY Tosylamide Resins

MEETING October 2026



COSMETIC
INGREDIENT REVIEW
Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Temima Nguyen, M.S., Scientific Analyst/Writer, CIR
Date: September 11, 2026
Subject: Amended Safety Assessment of Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin as Used in Cosmetics

Enclosed is the Draft Amended Report on the Safety Assessment of Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin as Used in Cosmetics. (It is identified as *report_TosylamideResins_102026* in the report package.) The Expert Panel for Cosmetic Ingredient Safety (Panel) first published a review of the safety of Tosylamide/Formaldehyde Resin (known then as Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/Formaldehyde Resin-80) in 1986 (*originalreport1986_TosylamideResins_102026*). The Panel concluded that Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/Formaldehyde Resin-80 are safe as cosmetic ingredients in the present practices of use and concentration (as described in the report). Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/Formaldehyde Resin-80 are now both referred to as Tosylamide/Formaldehyde Resin and will be identified as such throughout the remainder of this document.

The Panel considered a re-review of these ingredients at the September 2004 meeting. At that meeting, the Panel determined not to re-open this safety assessment and reaffirmed the 1983 conclusion, as published in 2006 (*rereview2006_TosylamideResins_102026*). The data from the original report and from the re-review evaluated by the Panel at the September 2004 meeting (*RRdata2004_TosylamideResins_102026*) have been summarized in the Draft Amended Report, in *italicized text*.

During an annual priorities-setting discussion at the March 2023 meeting, the Panel noted a potential sensitization concern following exposure to Tosylamide/Epoxy Resin, as epoxides are often strong sensitizers. Also at that meeting, the Panel mentioned that Tosylamide/Epoxy Resin should be further prioritized due to its increasing use in nail polishes as a replacement for Tosylamide/Formaldehyde Resin. Due to this relationship in cosmetic use (and **not** to similarities in chemical structures), these two ingredients are presented together here in this amended report.

In 2025, RLD reported that Tosylamide/Epoxy Resin and Tosylamide/Formaldehyde Resin are used in 2173 formulations and 239 formulations, respectively. In 2003, the highest reported concentration of use for Tosylamide/Formaldehyde Resin was 13% in nail polishes and enamels. The results of the 2025 concentration of use survey conducted by the Council (*data_TosylamideResins_102026*) indicate that the maximum concentration of use for Tosylamide/Formaldehyde Resin in nail polishes and enamels increased slightly, to 13.9%. However, the 2025 results indicated that Tosylamide/Epoxy Resin had a maximum concentration of use of 6.3% in basecoats and undercoats. Please note, inn 2025 the RLD reported use in perfume sprays and in lipsticks and lip glosses (including children's make-up), but concentration of use data were not provided for these product types.

Supporting documents for this report package include a flow chart (*flow_TosylamideResins_102026*), report history (*history_ TosylamideResins_102026*), a search strategy (*search_TosylamideResins_102026*), a data profile (*dataprofile_TosylamideResins_102026*), minutes from the meetings at which the original reports were discussed (*originalminutes_TosylamideResins_102026*), and transcripts from the March 2023 meeting where the Panel discussed that there is a concern for possible sensitization for Tosylamide/Epoxy Resin as epoxies are strong sensitizers (*transcripts_TosylamideResins_102026*).

If no further data are needed, the Panel should formulate an updated Discussion and Conclusion, and issue a Tentative Amended Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an Insufficient Data Announcement.

Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin History

November 1985

1st Review / Draft Report:

- The Panel then unanimously accepted and approved the standard "safe" conclusion as recommended by the Bergfeld team.

1986

Final report was published.

On the basis of the available data, the CIR Expert Panel concludes that Toluenesulfonamide/Formaldehyde Resin (TSFR) and Toluenesulfonamide/Formaldehyde Resin-80% are safe as cosmetic ingredients in the present practices of use and concentration.

September 2004

2nd Review / Re-Review:

- Dr. Belsito noted that his Team had reviewed a meeting abstract at yesterday's Team meeting indicating that at least some preparations containing Tosylamide/Formaldehyde Resin release greater than 200 ppm free formaldehyde. He said that this should not be the case, given the CIR Expert Panel's prior restrictions on formaldehyde release.
- Thus, the following statement was recommended for inclusion in the Discussion section of the Annual Review: There is no need to reopen this safety assessment. However, manufacturers using Tosylamide/Formaldehyde Resin should be sure that it releases less than 200 ppm free formaldehyde.
- After reviewing data that have entered the published literature since the Final Report was issued, the Panel unanimously concluded that the Final Report on Toluenesulfonamide/Formaldehyde Resin should not be reopened.

2006

Re-review was published affirming conclusion from 1986.

March 2023

The Panel reviewed the 2024 Priorities list and discussed that there is a concern for possible sensitization for Tosylamide/Epoxy Resin as epoxies are strong sensitizers and that Tosylamide/Epoxy Resin should be further prioritized due to its increasing use in nail polishes as a replacement for Tosylamide/Formaldehyde Resin.

October 2026

The Panel reviews Draft Amended Report.

Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin Data Profile* – October 2026 – Writer, Temima Nguyen																															
	Use				**Toxico-kinetics**			**Acute Tox**			**Repeated Dose Tox**			**DART**		**Genotox**		**Carci**		**Dermal Irritation**			**Dermal Sensitization**				**Ocular Irritation**		**Clinical Studies**	
	New Rpt	**Old Rpt**	**Method of Mfg**	**Impurities**	**log P/log K$_{ow}$**	**Dermal Penetration**	**ADME**	**Dermal**	**Oral**	**Inhalation**	**Dermal**	**Oral**	**Inhalation**	**Dermal**	**Oral**	**In Vitro**	**In Vivo**	**Dermal**	**Oral**	**In Vitro**	**Animal**	**Human**	**In Vitro**	**Animal**	**Human**	**Photoxicity**	**In Vitro**	**Animal**	**Retrospective/ Multicenter**	**Case Reports**
Tosylamide/ Formaldehyde Resin	X	O	O	O				O	O			O			X	O					OX	O			O	O		O	OX	OX
Tosylamide/ Epoxy Resin	X						X		X						X						X								X	

* “X” indicates that new data were available in this category for the ingredient; “O” indicates that data from the original assessment were available

Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin

Ingredient	CAS #	PubMed	FDA	CompTox	ChemPort	NIOSH	NTIS	NTP	FEMA	EU	ECHA	SIDS	SCCS	AICIS	FAO	WHO	Web
Tosylamide/Formaldehyde Resin	25035-71-6	√	√	√	√	NR	NR	NR	NR	√*	√*	NR	NR	NR	NR	√*	√
Tosylamide/Epoxy Resin		NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	√	NR	NR	√

NR- not reported; √* - data is available, but is not new or relevant

Search Strategy (from 2001 onwards for Tosylamide/Formaldehyde Resin)

Pubmed

(Tosylamide Formaldehyde Resin) OR (25035-71-6) from 2001 - 3000/12/12 – 14 hits / 10 useful

Web

Tosylamide Formaldehyde Resin – 275,000 hits / 14 useful

Search Strategy (Tosylamide/Epoxy Resin)

Pubmed

(Tosylamide/Epoxy Resin) AND (toxicity) – 954 hits / 0 useful
(Tosylamide/Epoxy Resin) AND (irritation) – 133 hits / 0 useful

Web

Tosylamide/Epoxy Resin – 209,000 hits / 3 useful

LINKS

Search Engines

- Pubmed - https://pubmed.ncbi.nlm.nih.gov/
  - appropriate qualifiers are used as necessary
  - search results are reviewed to identify relevant documents
- CompTox: https://comptox.epa.gov/dashboard/chemical/pubmed-abstract-sifter ; https://www.epa.gov/comptox-tools/downloadable-computational-toxicology-data#LM
- eChemPortal: https://www.echemportal.org/echemportal/
- DeepDyve: https://www.deepdyve.com/
- Connected Papers - https://www.connectedpapers.com/

Pertinent Websites

- wINCI - https://incipedia.personalcarecouncil.org/winci/ingredient-custom-search/
- FDA Cosmetics page - https://www.fda.gov/cosmetics
- eCFR (Code of Federal Regulations) - https://www.ecfr.gov/
- FDA search databases: https://www.fda.gov/industry/fda-basics-industry/search-databases
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras
- SCOGS database: https://www.fda.gov/food/generally-recognized-safe-gras/gras-substances-scogs-database
- Inventory of Food Contact Substances Listed in 21 CFR: https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=IndirectAdditives
- Drug Approvals and Database: https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases
- FDA Orange Book: https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book
- OTC Monographs - https://www.accessdata.fda.gov/scripts/cder/omuf/
- Inactive Ingredients Approved For Drugs: https://www.accessdata.fda.gov/scripts/cder/iig/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) technical reports search page: https://ntrl.ntis.gov/NTRL/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- EUR-Lex - https://eur-lex.europa.eu/homepage.html
- Scientific Committees (SCCS, etc) opinions: https://health.ec.europa.eu/scientific-committees/scientific-committee-consumer-safety-sccs_en
  - Mandates: https://health.ec.europa.eu/scientific-committees/scientific-committee-consumer-safety-sccs/sccs-mandates_en
- ECHA (European Chemicals Agency – REACH dossiers) – https://chem.echa.europa.eu/
- CosIng - https://ec.europa.eu/growth/tools-databases/cosing/
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- EFSA (European Food Safety Authority) - https://www.efsa.europa.eu/en
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) IRIS library - https://apps.who.int/iris/
- a general Google and Google Scholar search should be performed for additional background information, to identify references that are available, and for other general information - www.google.com https://scholar.google.com/

MARCH 2023 PANEL MEETING

Belsito Team – March 6, 2023

DR. BELSITO: Okay. Priorities, PCPC had a lot of comments. Their comment list was longer than the priority list almost.

[…]

DR. HELDRETH: I mean, we should be able to get all of these reports going next year. It's just a matter of if there's ones that you really don't want to look at. Or we can certainly talk about in order of which ones are more important and we can start sooner than later.

DR. BELSITO: Yeah. I mean, I would like to see, personally, tosylamide epoxy resin and propolis moved up to the very top of that list so it's something that we start sooner rather than after phytosphingosine or polyacrylate crosspolymer-6 or a lot of the others -- or sodium hyaluronic cross-polymer. Just move them up a bit, simply because they're so different from what we reviewed before. My personal opinion.

DR. SNYDER: I think that's okay. I think we have the four cause ingredients that we're looking at. And then, based upon these but based on their frequency of use, we can prioritize them based upon cause. So I think that's okay. I think your proposal is fine with me.

DR. BELSITO: Okay. After that, I really don't care. But I would just like to see the tosylamide epoxy resin and the propolis moved up to the top of the list, even though they're not at the top with frequency of use.

DR. HELDRETH: Yeah.

DR. SNYDER: I think that gives Bart good justification -- or us good justification to the other group to see what they say.

Cohen Team – March 6, 2023

[Tosylamide Resins were not specifically addressed in the Cohen Team's discussion of Priorities]

Full Panel – March 7, 2023

DR. BERGFELD: We're going to move on, then, to the priorities list. And, Dr. Belsito, you have this one.

DR. BELSITO: […]

I would like to see tosylamide/epoxy resin brought up much higher despite the frequency of use, because it's really replaced tosylamide formaldehyde resin in nail polishes. So if (audio skip) an acrylic gel, you're probably using a nail polish with tosylamide/epoxy resin.

[…] And, again, just move up the tosylamide/epoxy resin and the proplis a little bit higher, despite their frequency of use. Otherwise, we're fine with the table.

DR. BERGFELD: Thank you. David, do you have any additions to make or comments?

DR. COHEN: No. We agree with Don's review

[…]

DR. COHEN: Don, did you think that we should move the tosylamide/epoxy resin up further?

DR. BELSITO: I'm testing with it, David. I'm not seeing a lot of reactions. Occasionally, I'll see a reaction to epoxy resin but not tosylamide/epoxy, and I don't know what to make with it. […]

DR. BELSITO: -- a huge bugaboo. I mean, to really understand what's going on with that material would be great.

DR. COHEN: Bart, is there a chance for it to appear this year?

DR. HELDRETH: So, we could always amend the 2023 priorities list. If we took it up right now at this moment and writer had time to be assigned to it, we would need at least four months leeway for industry survey to be done, get concentration of use information. So, the way I'm looking at it, if we tried to get it this year, probably the soonest we could get a draft report to you would be the December meeting anyway.

DR. BELSITO: Yeah, but it still would be ahead of the 2024.

DR. HELDRETH: Yeah. I mean, we can certainly do it.

DR. COHEN: Yeah. I agree with Don on, not the urgency, but the discussions that come around this at meetings and in the offices all the time.

DR. HELDRETH: Okay. Well, if it's the panels' consensus we can move it to the 2023 priority list right now.

DR. BELSITO: I would like to do that.

DR. BERGFELD: I don't think anyone would disagree.

DR. COHEN: Yeah, that was great.

DR. HELDRETH: All right. It's done.

DR. BELSITO: I think dermatologist needs -- I mean, hopefully we'll find out where this product is being used, the types of concentrations that are being used, that might answer questions why we're seeing so many positive patch test reactions.

DR. BERGFELD: Okay. Well, we're going to see another draft, you said in September, the final draft.

DR. HELDRETH: That's correct, yes.

DR. BERGFELD: And will we take a look also at the 2023, in the June meeting, maybe, just to make sure that we're up to date?

DR. HELDRETH: I can certainly bring it for review.

NOVEMBER 1985 MEETING – FIRST REVIEW/DRAFT REPORT

Dr. Bergfeld reported that her team had requested mutagenicity data on TSFR; this data had subsequently been supplied and the results were negative. Her team therefore was recommending a boiler plate "safe" conclusion.

She then read the tentative discussion:

"Although the clinical data were limited to studies with products, it is the Panel's opinion that the combined animal and clinical data were sufficient to assess the safety of TSFR and TSFR-80."

Dr. Bergfeld stated that her team had wanted to emphasize that they were distressed at the large amounts of clinical data all limited to products. She indicated that this was a problem they were starting to hone in on.

Dr. Hoffmann requested that the write-up of eye irritation data on products be substantially reduced in that the severe irritation noted was due to the whole product, but not necessarily the specific ingredient.

Dr. Schroeter noted he was concerned that this ingredient was possibly a sensitizer based on the number of case reports and suggested including this in the discussion. Dr. Bergfeld responded that previously, only those data substantiated by studies have been addressed in the discussion and that the case studies were specifically included in a paragraph in the summary. She pointed out that this sensitization did not come through in the clinical studies. Dr. Elder also noted that case reports have frequently been deleted.

Mr. Eiermann mentioned a published paper reporting 16 incidences of sensitivity to this ingredient in products. It was agreed that this paper should be included in the report. Dr. McEwen stressed that it should be noted this incidence occurred in a patient population.

Dr. Schroeter stated he still felt that the possibility of sensitization should be mentioned in the discussion, particularly as he feels this ingredient has not been widely tested.

The Panel then unanimously accepted and approved the standard "safe" conclusion as recommended by the Bergfeld team.

The Tentative Final Report will shortly be announced for a 90-day comment period.

SEPTEMBER 2004 MEETING – SECOND REVIEW/FIRST RE-REVIEW

A Final Report with the following conclusion was published in 1986. On the basis of the available data, the CIR Expert Panel concludes that Toluenesulfonamide/Formaldehyde Resin (TSFR) and Toluenesulfonamide/Formaldehyde Resin-80% are safe as cosmetic ingredients in the present practices of use and concentration.

Dr. Belsito noted that his Team had reviewed a meeting abstract at yesterday's Team meeting indicating that at least some preparations containing Tosylamide/Formaldehyde Resin release greater than 200 ppm free formaldehyde. He said that this should not be the case, given the CIR Expert Panel's prior restrictions on formaldehyde release.

Thus, the following statement was recommended for inclusion in the Discussion section of the Annual Review: There is no need to reopen this safety assessment. However, manufacturers using Tosylamide/Formaldehyde Resin should be sure that it releases less than 200 ppm free formaldehyde.

After reviewing data that have entered the published literature since the Final Report was issued, the Panel unanimously concluded that the Final Report on Toluenesulfonamide/Formaldehyde Resin should not be reopened.

Safety Assessment of Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin as Used in Cosmetics

Status: Draft Amended Report for Panel Review
Release Date: September 11, 2026
Panel Meeting Date: October 5-6, 2026

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Temima Nguyen, M.S., Scientific Analyst/Writer, CIR, and Jinqiu Zhu, Ph.D., DABT, ERT, DCST, CIR Toxicologist.

© Cosmetic Ingredient Review
555 13th Street, NW, Suite 300W, Washington, DC 20004
cirinfo@cir-safety.org

ABBREVIATIONS

ACD	allergic contact dermatitis
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
DGEBA	bisphenol A diglycidyl ether
Dictionary	*International Cosmetic Ingredient Dictionary*
EC	European Commission
EPA	US Environmental Protection Agency
FDA	US Food and Drug Administration
GPMT	guinea pig maximization test
HRIPT	human repeated-insult patch test
ICDRG	International Contact Dermatitis Research Group
LD_{50}	median lethal dose
LLNA	local lymph node assays
l.o.	leave-on
log K_{ow}	octanol-water partition coefficient
MED	minimal erythemal dose
MoCRA	Modernization of Cosmetics Regulation Act of 2022
MOE	margin of exposure
MOS	margin of safety
MW	molecular weight
NACDG	North American Contact Dermatitis Group
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NR	not reported
Panel	Expert Panel for Cosmetic Ingredient Safety
POD	point of departure
RIVM	Dutch National Institute for Public Health and the Environment
RLD	Registration and Listing Data
r.o.	rinse-off
SCCS	EC Scientific Committee on Consumer Safety
SED	systemic exposure dose
SPIN	significance-prevalence index number
US	United States
UV	ultraviolet
WoE	weight-of-evidence

INTRODUCTION

This assessment reviews the safety of Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin as used in cosmetic formulations. According to the *International Cosmetic Ingredient Dictionary* (*Dictionary*), Tosylamide/ Formaldehyde Resin and Tosylamide/Epoxy Resin are reported to function as dispersing agents, film formers, and plasticizers.[1]

The Expert Panel for Cosmetic Ingredient Safety (Panel) published a review of the safety of Tosylamide/Formaldehyde Resin (known then as Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/Formaldehyde Resin-80) in 1986. [2] Based on the available data presented in the report, the Panel concluded that Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/Formaldehyde Resin-80, are safe as cosmetic ingredients in the present practices of use and concentration (as described in the report). The Panel first considered a re-review of this report in September 2004[3] and reaffirmed the 1986 conclusion, as published in 2006.[4]

In accordance with its Procedures, the Panel evaluates the conclusions of previously issued reports approximately every 15 years, and it has been at least 15 years since the previous re-review on Tosylamide/Formaldehyde Resin was published. However, this is the first time the Panel has assessed the safety of Tosylamide/Epoxy Resin. During an annual priorities-setting discussion at the March 2023 meeting, the Panel noted a potential sensitization concern following exposure to Tosylamide/Epoxy Resin, as epoxides are often strong sensitizers. Also at that meeting, the Panel mentioned that Tosylamide/Epoxy Resin should be further prioritized due to its increasing use in nail polishes as a replacement for Tosylamide/Formaldehyde Resin. Due to this relationship in cosmetic use (and **not** to similarities in chemical structures), these two ingredients are presented together here in this amended report.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an extensive search of the world's literature; a search was last conducted in September 2026. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Much of the data included in this safety assessment was found on the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) website.[5-7] (Please note that the NICNAS website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when NICNAS is cited.)

Excerpts from the summaries of the original 1986 report and data considered in 2004 for re-review on Tosylamide/Formaldehyde Resin are disseminated throughout the text of this re-review document, as appropriate, and are identified by *italicized text*. (This information is not included in the tables or the Summary section.) In the original report, Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/ Formaldehyde Resin-80% were listed as separate ingredients. However, Toluenesulfonamide/Formaldehyde Resin-80% is no longer recognized as a separate ingredient and the ingredient nomenclature of "toluenesulfon-" has been shortened to "tosyl-". Accordingly, summaries referencing Toluenesulfonamide/Formaldehyde Resin-80% will refer to the ingredient as Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol).

CHEMISTRY

Definition and Structure

According to the *Dictionary*, Tosylamide/Formaldehyde Resin (CAS No. 25035-71-6) and Tosylamide/Epoxy Resin are synthetic polymers. Tosylamide/Formaldehyde Resin is the polymer derived from toluenesulfonamide and formaldehyde. Tosylamide/Epoxy Resin is the toluenesulfonamide of the condensation product of 4,4'-isopropylidenediphenol/epichloro-hydrin copolymer, also known as the epoxy resin. These ingredients have chemical structures as shown in Figures 1 and 2, respectively.[1]

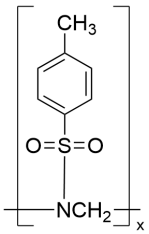


Figure 1. Tosylamide/Formaldehyde Resin (wherein the value of x is unknown)[CIR Staff]

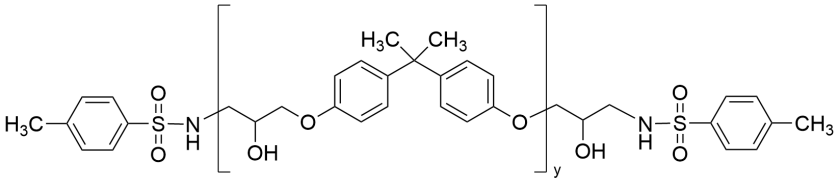


Figure 2. Tosylamide/ Epoxy Resin (wherein y may have a value ranging from ~ 1 to 6) [CIR Staff]

While the names of these two polymeric ingredients are quite similar, the structures thereof are significantly different. The backbone of Tosylamide/Formaldehyde Resin is a simple AB-repeat of nitrogen and carbon atoms, wherein each backbone-nitrogen atom is substituted with a tosyl group and each backbone-carbon atom with 2 hydrogen atoms. Presumably, this ingredient is also end-capped with tosylamides. The quantity of AB-repeats in a molecule of Tosylamide/Formaldehyde Resin is not supplied in the *Dictionary* monograph; however, with a reported number-average molecular weight (MW) of greater than 1000 Da, there presumably must be greater than 5 AB-repeats (including endcaps).

The backbone of Tosylamide/Epoxy Resin on the other hand is a less simple AB-repeat of propoxide and 4,4'-isopropylidenediphenol condensation residues (monomers), and comprises no tosylamides. Tosylamides are only present in this polymer as endcaps. According to the *Dictionary* monograph for Tosylamide/Epoxy Resin, this ingredient is oligomeric with between only 1 and 6 repeat units (and thus, an estimated MW range of 683 to 2105 Da).

Chemical Properties

Tosylamide/Formaldehyde Resin is available as a solid or as a tradename mixture (80% in a blend of butyl acetate and butyl alcohol), which is a soft, viscous liquid. [2]. *Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) is insoluble in water at 25°C but miscible with common organic solvents and thinners except for aliphatic petroleum hydrocarbons. Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) can form brittle compositions with cellulose acetate and nitrocellulose, which can be permanently flexible with the addition of a plasticizer. Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) is combustible but is not a primary oxidant, reducing agent or reactive with water or air under ambient conditions. At 25°C, Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) has a specific gravity of ~ 1.256, a vapor pressure of ~ 10 mmHg, and a viscosity ranging from 6000 - 11,000 cps. Tosylamide/Formaldehyde Resin and Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) are moderately stable to light.*

Tosylamide/Epoxy Resin is a white to pale yellow viscous liquid with a molecular weight of < 1000 Da and is considered as a low molecular weight polymer.[6] A tradename mixture containing ~74% Tosylamide/Epoxy Resin is a clear liquid with a strong, esteric odor.[8] Based on a an oligomer comprising between 1 and 6 repeats, the estimated log K_{ow} for Tosylamide/Formaldehyde Resin is ≥ 5.16.[8] Based on an oligomer of comprising 6 or more repeats, the estimated log K_{ow} for Tosylamide/Epoxy Resin is ≥ 4.98. Other chemical properties of Tosylamide/Formaldehyde Resin, Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol), a tradename mixture containing ~ 74% Tosylamide/Epoxy Resin, and Tosylamide/Epoxy Resin can be found in Table 1.[2,6,8-12]

Method of Manufacture

Tosylamide/Formaldehyde Resin is produced by the condensation of aryl sulfonamides with formaldehyde.[2] *It may be produced when formaldehyde and p-toluenesulfonamide are employed in equimolecular proportions before being condensed and heated to 110°C to form a hard, colorless resin.*

Additional methods of manufacture were not found in the published literature, and unpublished data were not submitted.

Impurities

Tosylamide/Formaldehyde Resin contains free formaldehyde.[2] *Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) has a formaldehyde content of < 0.2%.*

Tosylamide/Formaldehyde Resin does not release formaldehyde due to it being encased in the resin.[13] In nail polish, Tosylamide/Formaldehyde Resin is bound upon drying and the film forming function is completed.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin in cosmetics. Registration and Listing Data (RLD) obtained from the FDA report frequency of use, and responses to a survey conducted by the Personal Care Products Council (Council) indicate maximum reported concentrations of use; it is these values that define the present practices of use and concentration that are assessed by the Panel. Since 2024, as a result of the Modernization of Cosmetics Regulation Act of 2022 (MoCRA), manufacturers and processors are required to register facilities and list their products (and ingredients therein) with the FDA (i.e., RLD). An exception is made for small businesses (average gross annual sales in the US of cosmetic products for the previous 3-yr period is less than $1,000,000, adjusted for inflation), which are exempt from MoCRA reporting for most cosmetic product categories. Eye area products, injected products, internal use products, or products that alter appearance for more than 24 h, and the facilities that manufacture these products, are not included in this exemption.[14] Another change resulting from MoCRA is the addition of tattoo preparations (permanent tattoo inks, temporary tattoo inks, and other tattoo products) to the product categories for which companies need to list their products with FDA. However, evaluating the safety of ingredients as used in tattoo preparations is not within the purview of the Panel; accordingly, such use is not included as part of the present practices of use that are assessed by the Panel.

According to RLD obtained from the FDA in 2025, Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin are reported to be used in 239 and 2173 formulations, respectively (Table 2).[15,16] In response to the 2025 Council survey, the maximum concentration of use reported for Tosylamide/Epoxy Resin was 9% in nail polish and enamel formulations and for Tosylamide/Formaldehyde Resin was 13.9% in nail polish and enamel formulations.[17]

Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin are used in products that can be incidentally ingested and that result in mucous membrane exposure (e.g., lipsticks and lip glosses, including children's make-up preparations; concentration not reported). Additionally, Tosylamide/Epoxy Resin is used in sprays (perfumes; concentration not reported) and could therefore be incidentally inhaled. In practice, as stated in the Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.

Some products containing Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin may be marketed for use with airbrush delivery systems. With the advent of MoCRA and the current product categories outlined by the FDA, it is now mandatory that cosmetic products used in airbrush delivery systems be reported as such for some, but not all, product categories in the RLD. In other words, a reliable source of frequency of use data regarding the use of cosmetic ingredients in conjunction with airbrush delivery systems is now available, in some instances. Some of the reported product categories for these ingredients as listed in the RLD do require designation if airbrush application is used (e.g., leg and body paints), but no airbrush use was indicated. Additionally, the Council currently surveys the cosmetic industry for maximum reported use concentrations of ingredients in products which may be used in conjunction with an airbrush delivery system; thus, this type of data may also be available, when submitted. Please note that no concentration of use data were provided indicating airbrush application. Nevertheless, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety. Without information regarding the consumer habits and practices data or product particle size data (or other relevant particle data, e.g., diameter) related to this use technology, the data profile is incomplete, and the Panel is not able to determine safety for use in airbrush formulations. Accordingly, the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

Following the passage of MoCRA, the FDA created a number of new product categories including, "(17) Other preparations (i.e., those preparations that do not fit another category)" (Category 17). CIR and the Panel utilize these product categories to inform, in part, the weight-of-evidence (WoE) in exposure and risk analyses. However, citation of Category 17, alone, as the product use category is uninformative. When a product is co-categorized with both Category 17 and one or more common product use categories (e.g., eye makeup preparations), or other information in the RLD such as the product name are indicative of use type (e.g., "lip balm" is part of the product name), then those uses are accounted for and may be considered to be part of the "the present practices of use" for those products; as such, the Panel's safety conclusion may be inclusive thereon. Conversely, for instances wherein the use of an ingredient in a cosmetic product is only categorized as Category 17 and other information in the RLD is not indicative of use type, the present practices of use for these products remain unknown and the Panel's safety assessment conclusion, therefore, does not apply thereon.

Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin are not restricted from use in any way under the rules governing cosmetic products in the European Union.[18]

Non-Cosmetic

Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) can be used as a solvent for cellulose acetate and nitrocellulose in brushing, dipping, and spraying lacquers to make clear and odorless coatings. [2]

According to the Code of Federal Regulations (CFR), Tosylamide/Formaldehyde Resin has been regulated to be used in in paper and paperboard in contact with aqueous and fatty foods (21 CFR 176.170), in cellophane food packaging material up to 0.6% by weight of cellophane (21 CFR 177.1200), and as a side seam cement in articles intended for food contact (21 CFR 175.300). Tosylamide/Formaldehyde Resin can also be used as an optional adjuvant for acrylonitrile/styrene copolymers as used in the component of packaging materials up to a maximum of 0.15% (21 CFR 177.1040).

TOXICOKINETIC STUDIES

Toxicokinetics data were not found in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Dermal

Tosylamide/Formaldehyde Resin

Single doses of 2, 3.16, 5.01, or 7.94 g/kg of Tosylamide/Formaldehyde Resin (as a 40% solution/suspension in corn oil) were applied to New Zealand albino rabbits for 24 h.[2] One rabbit was tested at each of the three lowest doses while 2 were tested at the highest dose. No rabbits died during the 14-d observation period. One New Zealand albino rabbit received a dermal application of 5.01 g/kg and 2 rabbits received an application of 7.94 g/kg Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol). Deaths did not occur in the 14-d observation period, and lesions were not found at necropsy. A nail hardener with 8.26% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) was applied occlusively at 2 g/kg bw (wet product) to 2 groups of rabbits (n = 5) with either clipped or clipped and abraded skin. The sleeves were removed after 24 h, and no deaths were observed over the 2-wk observation period.

Oral

Tosylamide/Formaldehyde Resin

Tosylamide/Formaldehyde Resin was administered as a 70% solution in acetone in a single dose of 7.94 g/kg orally to 5 Sprague-Dawley albino rats.[2] Over the 14-d observation period, there were no deaths and the viscera appeared normal during the gross examination. In a similar study, 5 male Sprague-Dawley albino rats received a single oral dose of 5 g/kg of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) in a 50% solution in a 3A alcohol. All the animals survived, and gross examination after the 14-d observation period revealed normal viscera. Groups of 5 female albino rats were given 15.0 g/kg of one of three nail polish and enamel formulations containing ~12% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) via stomach tube. Within 2 d of dosing, two rats died from one formulation, while one rat died from another formulation. The median lethal dose (LD_{50}) was > 15 g/kg. A nail hardener with 8.26% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) was given at 5 g/kg in a single dose by oral intubation to 10 albino rats, and no deaths occurred over a 14-d observation period.

Tosylamide/Epoxy Resin

Two groups of Sprague Dawley rats (5/sex) received a single oral dose 2000 mg/kg bw of Tosylamide/Epoxy Resin in corn oil as a 23% w/w suspension.[7] After 24 h, there was instances of oily stains at the bases of tails of the test animals but no toxicity. The LD_{50} was > 2000 mg/kg.

A single 5000 mg/kg bw dose of Tosylamide/Epoxy Resin in corn oil was given orally to 10 Sprague Dawley rats (5/sex).[6] Clinical observations were made 1, 2.5, and 5 h after administration as well as twice daily for the 14 d that followed. Body weights were taken on days 0, 7, and 14, and the organs were examined macroscopically after the rats were killed on day 14. There were no signs of toxicity and the LD_{50} was > 5000 mg/kg bw.

Subchronic Toxicity Studies

Oral

Tosylamide/Formaldehyde Resin

Tosylamide/Formaldehyde Resin was fed to purebred beagle dogs (4/sex/dose) at 0, 1000, 3000, or 10,000 ppm for 90 d. [2] Compared to the untreated control group, behavior, blood chemistry parameters, food consumption, and results of urinalyses of the treated dogs were comparable. There were no treatment-related lesions found when gross and microscopic examination of the organs and tissues were completed. The study did not result in any deaths. At 10,000 ppm, slight decreases in body weight gain and hematological parameters as well as minimal increases in liver weight ratios were observed. These changes were considered minimal or remained within or near normal limits.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity data were not found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

In Vitro

In several Ames assays, Tosylamide/Formaldehyde Resin and Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) were tested in doses ranging from 20 – 1500 µg. [2] Both materials were not mutagenic to Salmonella strains in 2 separate Ames tests, with or without metabolic activation.

CARCINOGENICITY STUDIES

Carcinogenicity data were not found in the published literature, and unpublished data were not submitted.

OTHER RELEVANT STUDIES

Nail Polish Dermatitis

Approximately 80% of allergic contact dermatitis (ACD) reactions associated with nail polish occur on the eyelids, face, lips, and neck.[19] Tosylamide/Formaldehyde Resin may be considered a potent allergen due to its stable chemical structure that does not change between liquid and dried states.[20] Due to the presence of residual, unpolymerized methacrylate and acrylate monomers that can be found in dried nail polish, there is a possibility for other reactions to occur. In eight cases of ACD, patients who reacted to phthalic anhydride, trimellitic anhydride, or glycols copolymer had positive patch test reactions to their nail lacquers but negative patch test results to Tosylamide/Formaldehyde Resin, suggesting that water-soluble by-products of the hardened polymer were responsible for the ACD.[21] In a study of 25 nail polish brands marketed as allergen-free or hypoallergenic, 15 contained at least one component triggering ACD. [22] Out of the 25 brands, 44% contained Tosylamide/Formaldehyde Resin.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Animal

Tosylamide/Formaldehyde Resin was applied in powder form (0.5 g) with water under an occlusive patch to abraded clipped and intact skin of New Zealand albino rabbits (n=6). [2] The treatment sites were scored for edema and erythema after 24 h and skin reactions were monitored at 48, 72, and 168 h after the removal of the patches. There was no irritation observed. After a 24-h application of 0.5 ml of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) to the intact skin of 3 New Zealand albino rabbits, edema and skin erythema were evaluated at 4, 24, 48, 72, and 168 h. Irritation was not observed. A single insult occlusive patch test was performed on 27 female albino rabbits (9/product) in which each rabbit received 0.5 ml of one of three nail polish formulations containing ~12% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) for 24 h. The scoring of edema and erythema revealed that 4 rabbits had minimal skin erythema 2 h after removal and 1 rabbit that had minimal skin erythema at 24 h. Since the other rabbits treated did not have any irritation, the skin irritation potential for the 3 formulations was minimal. Six rabbits received an application of 0.5 ml of a nail hardener with 8.26% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) under occlusion to abraded and intact skin. After 24, 48, and 72 h, skin reactions (not specified) were evaluated, and the product was considered a nonirritant.

Human

Skin irritation effects were evaluated using a single insult occlusive patch procedure for 3 nail polish formulations containing ~12% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol).[2] Subjects (18/product) received a Blenderm patch each (unspecified amount) of one of the formulations to be placed on the forearm or upper arm area for 24 or 48 h. After the patch was removed, observations were made at 2 and 24 h. Two formulations did not produce any irritation, while one subject had minimal skin erythema when exposed to one of the formulations.

Sensitization

Human

An unspecified amount of 10% w/v solution of Tosylamide/Formaldehyde Resin in dimethyl phthalate was tested in a Shelanski human repeated-insult patch test (HRIPT) using 50 subjects. [2] The subjects underwent an induction phase of 15 serial applications before a challenge application 10 – 14 d later. The 10% w/v solution of Tosylamide/Formaldehyde Resin in dimethyl phthalate was not a fatiguing agent, irritant, or sensitizer. In a 4-wk controlled use study, 51 subjects used a nail hardener (unspecified amount) containing 8.26% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol). The fingernails, nail beds, nail folds, and surrounding skin were examined but there was no skin irritation after use. The skin irritation and sensitization potential of a nail polish (unspecified amount) containing 4.9% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) using a modified Shelanski and Shelanski repeat insult patch test in 53 subjects. The induction period consisted of 10 applications for 24 h for 3 times/wk. A 2 – 3 wk non treatment period followed before a challenge patch was applied for 48 h. There was no skin sensitization or irritation

recorded. A repeat insult patch test was performed to determine the skin sensitization and irritation of a nail strengthener containing 7.4% of Tosylamide/ Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol). The product (0.1 ml) was dispensed onto patches before being applied to 97 subjects. The induction period consisted of applications to the upper back for 24 h for 3 wk. The challenge patch was applied for 24 h of the 6th week of the study to an untreated area and assessments were made 24 and 48 h after patch removal. There was some evidence of mild erythema during the induction period, but no skin reactions were observed from the single challenge patch. The nail strengthener product did not induce allergic sensitization. Two nail product formulations (unspecified amount) containing 6.5 and 9.0% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) were evaluated for skin irritation and sensitization potential in 148 subjects and 203 subjects, respectively. In a Draize-Shelanski-Jordan repeat insult patch test, The subjects received 9 induction exposures on the upper back for 3 consecutive weeks before a 2 wk nontreatment period. Afterwards, each subject received two challenge patches adjacent to the original induction site for 48 h. The product with 6.5% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) did not produce significant reactions while for the 9.0% product, one subject had faint erythema. There was no sensitization in either product. Patients (n = 12) with a confirmed nail polish allergy were tested with 21 components of nail polish, including Tosylamide/ Formaldehyde Resin.[3] The positive reactions included 9 that reacted to an unspecified amount of 10% Tosylamide/ Formaldehyde Resin. The patients also reacted positively to 2 resin-derived fractions which contained a monomer and dimer that are created during the condensation of Tosylamide/ Formaldehyde Resin.

The dermal irritation and sensitization studies for Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin that are summarized below are described in Table 3.

Tosylamide/Epoxy Resin was slightly irritating to the skin of groups of 3 New Zealand albino rabbits at 0.5 g in a 0.9% saline solution and at a 60% (w/w) concentration.[6,7] In a local lymph node assay (LLNA) and guinea pig maximization test (GPMT), Tosylamide/Formaldehyde Resin was not a sensitizer (concentration not provided).[23] Tosylamide/Epoxy Resin was not a sensitizer in an LLNA study when tested at concentrations up to 50%. [6]

Photosensitization/Phototoxicity

A nail polish containing 4.9% Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) was tested in a 48-h modified Scwartz-Peck prophetic patch test in 100 subjects using open and closed patches.[2] The induction period lasted 10 d before the challenge patches were applied. In both the induction and challenge phase, the treated sites were exposed to ultraviolet (UV) irradiation (no other information provided on the methodology). The skin reactions were evaluated and besides one subject that had a weak, nonvesicular skin reaction to the closed induction patch, there was no irritation, photoreactions, or sensitization observed. In a single study, groups of 28 or 30 subjects were exposed to two nail color products with Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) and UV irradiation. The minimal erythemal dose (MED) was determined for each subject before occlusive patches containing the test material (0.1 ml/cm^2) were applied for 24 h. The application sites were then irradiated with 3x the MED using a Xenon Arc Solar Stimulator (150 W), which produced UVA and UVB light. After 48 h, the treatment sites were observed for edema, erythema, and vesicular skin reactions. For the induction period, there were a total of 6 treatments (2x/wk for 3 wk) with the product and UV irradiation. The subjects then had an occlusive patch for 24 h to an untreated site adjacent to the induction site after 10 d of nontreatment. The patch was removed, and the treated site was irradiated with UVA light for 3 min before being evaluated 15 min and 24, 48, and 72 h postirradiation. The two groups did not have any photoallergic or phototoxic reactions.

OCULAR IRRITATION STUDIES

Tosylamide/Formaldehyde Resin

A finely ground powder consisting of Tosylamide/Formaldehyde Resin (100 mg) was instilled in one eye of 6 New Zealand albino rabbits and the eyes were not rinsed after exposure.[2] There was slight to moderate discharge and slight erythema but no effects on the iris or cornea as the ocular irritation had cleared. Tosylamide/ Formaldehyde Resin was concluded to be a slight ocular irritant. Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) was instilled into one eye of 3 albino New Zealand rabbits at 0.1 ml to test the ocular irritation potential. There was slight erythema of the conjunctivae and ocular discharge. After 72 h, there was no irritation or damage to the cornea or iris. Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) was considered to be a slight ocular irritant. Albino rabbits (6/product) received 0.1 ml of one of three nail polish and enamel formulations containing ~12% of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol) in one eye. For the 3 formulations, average irritation scores ranged from 14 – 40, 17 – 47, and 11 – 31 which indicated mild (>15 – 25) to moderate (>25 – 50) irritation. Most animals had no irritation or minimal conjunctival irritation, while some had lesions in the iris and cornea. The study concluded that a formulation that produced corneal and iridial lesions that did not clear by the 7th day would be considered a severe eye irritant, but it was not confirmed whether it was solely a result of Tosylamide/ Formaldehyde Resin. A nail hardener containing 8.26% consisting of Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and

butyl alcohol) was tested for ocular irritation in both wet and dry forms (0.1 ml or 100 mg) in one eye each of 6 albino rabbits. The dry product affected one rabbit who developed chemosis, conjunctival erythema, iritis, and keratitis while all 6 rabbits were affected by the wet product which led to chemosis, conjunctival erythema and iritis.

CLINICAL STUDIES

Retrospective and Multicenter Studies

Patients (n =119) were patch tested according to internationally accepted methods in a multicenter study, and the second most frequent contact allergen was Tosylamide/Formaldehyde Resin (in 10% petrolatum); 15 patients (12.6%) had cosmetic-related contact dermatitis.[3] Tosylamide/Formaldehyde Resin (in 10% petrolatum) was patch tested in 366 patients from April 1992 – June 1993. There were positive reactions in 14 of the patients, which had used nail varnishes or hardeners months to years before they had dermatitis. Once the patients had ended usage of the nail products, the dermatitis had cleared completely. The Medical Products Agency in Sweden evaluated 191 reports regarding the adverse effects of 253 cosmetics and toiletries between 1989 – 1994 (mainly in moisturizers, hair care products, and nail products). Tosylamide/Formaldehyde Resin was one of the most common ingredients mentioned (alongside preservatives and fragrances). Patients (n = 102) experienced contact dermatitis on their face, hands, neck, arms, and feet. Thirteen of the patients had a positive reaction for Tosylamide/Formaldehyde Resin, and the researchers concluded that the contact dermatitis was attributable to nail polish.

The results of a multicenter study that included Tosylamide/Epoxy Resin and retrospective studies that included Tosylamide/Formaldehyde Resin are summarized in Table 4.[24-50] In North America, a multicenter study from 1999 – 2001 reported 33.71% and 33.33% of patients had a positive reaction to Tosylamide/Epoxy Resin in petrolatum and ethanol, respectively. For Tosylamide/Formaldehyde Resin, retrospective studies conducted in Sweden, Belgium, Finland, Germany, Brazil, Thailand, Australia, and North America from 1989 – 2022 reported positive reactions to Tosylamide/Formaldehyde Resin in ~ 0.2% – 94% of patients. There were also retrospective studies for patients with eyelid dermatitis. In three retrospective studies from 1994 – 2004, 2001 – 2003, and 2020 – 2025, completed in the US, 6.5%, 3.26%, and 0.66% of patients with suspected eyelid ACD were sensitive to Tosylamide/Formaldehyde Resin, respectively. Retrospective studies were also performed on children in the US from 2001 – 2006 and in Brazil from 2003 – 2010. The Brazilian study observed 6.8% of patients having a positive reaction to Tosylamide/Formaldehyde Resin, compared with 4.6% of patients in the US study.

Case Reports

Numerous case reports describing allergic reactions to nail enamels and Tosylamide/Formaldehyde Resin were reported.[2,3] The effects included dermatitis, gingival irritation, subungual hyperkeratosis, fingernail dystrophy, eczema, pruritus, erythema, and papules with reactions occurring at various sites including the eyelids, face, neck, ears, gingivae, fingertips, shoulders, arms, trunk, and the perianal region. Positive patch test reactions to Tosylamide/Formaldehyde Resin were reported in these cases, and symptoms improved upon the discontinuation of the implicated nail products.

Case reports have been summarized in Table 5. Following the usage of nail polish or nail hardeners containing Tosylamide/Formaldehyde Resin, allergic reactions were reported in a 4-yr-old female, 6-yr-old male, 39-yr-old female, 49-yr-old female, 60-yr-old female, and 67-yr-old female. [5,51-56] The findings include atopic flexural dermatitis, dystrophy, dermatosis, eczema, erythema, erthematosquamous lesions, edema, itching dermatitis, scaling, and itchiness in the eyelid, face, glabella, neck, fingers, ala nasi, forearms, hands, and retroauricular areas as well as onycholysis, discoloration, deformation of the nail plates. All the patients had positive reactions to 10% Tosylamide/Formaldehyde Resin in petrolatum during patch testing. A 35-yr-old female with a history of ACD to epoxy resin developed dermatitis on the fingers, acute facial swelling and rashes on the neck and arms upon beginning a plastics bench mechanic job.[57] Patch testing revealed a positive reaction to Tosylamide/Formaldehyde Resin and epoxy resin. Phototesting showed sensitivity to UVB and UVA radiation, while photopatch testing was negative. A 46-yr-old female with a history of eczema developed urticated erythema and rashes upon sun exposure.[58] The patient had positive reactions to 10% Tosylamide/Formaldehyde Resin in petrolatum and had normal ranges for erythema threshold during photopatch testing. A 32-yr-old female had symptoms develop on her skin from wearing a metallic watch.[5] The patient had assumed an allergy to nickel and began using nail varnish on the back of the watch to prevent skin contact with the nickel. Upon patch-testing, the patient tested positive to 10% Tosylamide/Formaldehyde Resin in petrolatum but negative for nickel.

Occupational Exposure

In 2003, the Occupational Dermatology Research and Education Centre in Melbourne, Australia, reported 5 positive reactions out of 1500 workers (0.3%) for Tosylamide/Formaldehyde Resin.[5] From 1998 – 2002, the Centre for Occupational and Environmental Health at the University of Manchester, England, had no cases for Tosylamide/Formaldehyde Resin in the EPIDERM occupational skin surveillance database or Occupational Physicians Reporting Activity database out of 6067 and 5546 cases, respectively. No further details were provided.

RISK ASSESSMENT

Margin of exposure (MOE) is a quantitative ratio calculated for cosmetic ingredients by dividing the point of departure (POD) obtained for an ingredient in an animal experiment by the estimated systemic exposure dose (SED) for the ingredient in humans, generally according to US Environmental Protection Agency (EPA) and European Commission (EC) Scientific Committee on Consumer Safety (SCCS) guidelines. An MOE value greater than 100 has traditionally been considered an indication of safety. The basis for this MOE value of 100 comes from two multiplication factors: a 10-fold factor for extrapolating data from test animals to human beings (interspecies extrapolation), and an additional 10-fold for differences among the human population (intraspecies extrapolation). Notably, the MOE value is sometimes referred to as the margin of safety (MOS) despite the parameters being definitionally different.

Tosylamide/Formaldehyde Resin

Systemic exposure to Tosylamide/Formaldehyde Resin from nail polish/enamel use was estimated using a nail polish product amount of 1.0 g/application and an adult use frequency of 104 applications/yr, as reported in the 2025 Dutch National Institute for Public Health and the Environment (RIVM) Cosmetics Fact Sheet,[59] together with the maximum reported concentration of use of 13.9% from the Council's 2025 survey[17] (Table 6). The 1.0 g product amount accounts for application to both fingernails and toenails and for two coats of nail polish. Considering the natural barrier properties of the nail plate and differences in physicochemical properties between skin and nails, a 50% default penetration is considered a conservative assumption for estimating systemic exposure through the nail plate when relevant ingredient and formulation-specific information is unavailable.[59] At 13.9%, the estimated exposure was 139 mg/application, corresponding to a time-averaged exposure of 39.61 mg/d and an SED of 0.33 mg/kg bw/d, assuming a 60 kg adult body weight.

In a 90-d dietary study, beagle dogs were administered Tosylamide/Formaldehyde Resin at 0, 1000, 3000, or 10,000 ppm.[2] No treatment-related effects were identified at 1000 or 3000 ppm, whereas minor changes in body weight gain, hematological parameters, and liver-to-body-weight ratios were reported at 10,000 ppm. Accordingly, 3000 ppm was conservatively selected as an assessor-derived NOAEL. Using the US EPA default dog food factor of 0.025 kg diet/kg bw/d,[33] the 3000 ppm dietary concentration corresponds to approximately 75 mg/kg bw/d. Comparison of this POD with the SED of 0.33 mg/kg bw/d resulted in an MOE of 227 (Table 6). The calculated MOE value was greater than 100 and is considered protective.

Tosylamide/Epoxy Resin

Systemic exposure to Tosylamide/Epoxy Resin from nail product use was estimated using the RIVM product use parameters described above,[59] together with the maximum reported concentrations of use of 6.3% in basecoats and undercoats, 9% in nail polish and enamels, and 5% in topcoats from the Council's 2025 survey[17] (Table 7).

RIVM notes that nail polish may be used alone or in combination with a basecoat and/or topcoat and provides separate product-use parameters for these product types.[60] For a conservative aggregate exposure scenario, concurrent use of basecoat, nail polish/enamel, and topcoat was assumed, with Tosylamide/Epoxy Resin present at the respective maximum reported concentrations. The combined exposure was 124.5 mg/application, corresponding to a time-averaged exposure of 35.5 mg/d using the RIVM adult use frequency of 104 applications/yr. This scenario conservatively combines the maximum concentrations reported for all three product categories and does not imply that these concentrations necessarily occur concurrently in actual use.

Using the same conservative 50% default nail plate penetration assumption described above,[59] the estimated SED was 0.296 mg/kg bw/d, assuming a 60 kg adult body weight. For comparison, a 10% dermal absorption assumption was also applied, supported by a published percutaneous absorption skin permeation modeling indicating that percutaneous absorption of cosmetic ingredients with molecular weights > 500 Da is expected to be less than 10%.[59,61] Application of this value resulted in an SED of 0.0591 mg/kg bw/d. Further refinement using an ingredient-specific, model-derived nail plate penetration value of 0.4%,[59] corresponding to an integrated adjustment factor of 0.004 based on physicochemical and formulation-related properties, resulting in an SED of 0.00236 mg/kg bw/d.

A suitable Tosylamide/Epoxy Resin-specific repeated-dose toxicity POD was not identified; therefore, the assessment was limited to characterization of systemic exposure, and a quantitative MOE was not calculated.

SUMMARY

Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin are reported to function as dispersing agents, film formers, and plasticizers. The Panel published a review of the safety of Tosylamide/Formaldehyde Resin (known then as Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/Formaldehyde Resin-80) in 1986. Based on the available data presented in the report, the Panel concluded that Toluenesulfonamide/Formaldehyde Resin and Toluenesulfonamide/ Formaldehyde Resin-80, are safe as cosmetic ingredients in the present practices of use and concentration (as described in the report). In September 2004, the Panel reaffirmed the 1986 conclusion, as published in 2006. In accordance with its Procedures, the Panel evaluates the conclusions of previously issued reports approximately every 15 years, and it has been at least 15 years since this assessment has been reviewed. During an annual priorities-setting discussion at the March 2023 meeting, the Panel noted a potential sensitization concern following exposure to Tosylamide/Epoxy Resin, as epoxides are

often strong sensitizers. Also at that meeting, the Panel mentioned that Tosylamide/Epoxy Resin should be further prioritized due to its increasing use in nail polishes as a replacement for Tosylamide/Formaldehyde Resin. Due to this relationship in cosmetic use (and **not** to similarities in chemical structures), these two ingredients are presented together in this amended report.

According to RLD obtained from the FDA in 2025, Tosylamide/Formaldehyde Resin and Tosylamide/Epoxy Resin are reported to be in used in 239 and 2173 formulations, respectively. In response to the 2025 Council survey, the maximum concentration of use reported is 13.9% Tosylamide/Formaldehyde Resin in nail polish and enamel formulations. The maximum concentration of use for Tosylamide/Epoxy Resin is 9% in nail polish and enamel formulations

In two different studies, Sprague Dawley rats (5/sex) were given either a single oral dose of 2000 mg/kg bw or 5000 mg/kg bw of Tosylamide/Epoxy Resin. Toxicity was not observed in either group and the overall $LD_{50} > 5000$ mg/kg.

Approximately 80% of ACD reactions associated with nail polish occur on the eyelids, face, lips, and neck. Tosylamide/Formaldehyde Resin can be a potent allergen due to its stable chemical structure that does not change between liquid and dried states. Residual monomers and other water-soluble by products may remain in dried nail polish and contribute to allergic reactions. In a study of 25 nail polish brands marketed as allergen-free or hypoallergenic, 15 contained at least one component of triggering ACD with 44% of the brands containing Tosylamide/Formaldehyde Resin.

Tosylamide/Epoxy Resin was slightly irritating to the skin of groups of 3 New Zealand albino rabbits at 0.5 g in a 0.9% saline solution and at a 60% (w/w) concentration. In an LLNA and GPMT, Tosylamide/Formaldehyde Resin was not a sensitizer (concentration not provided). Tosylamide/Epoxy Resin was not a sensitizer in an LLNA study when tested at concentrations up to 50%.

In North America, a multicenter study from 1999 – 2001 reported 33.71% and 33.33% of patients had a positive reaction to Tosylamide/Epoxy Resin in petrolatum and ethanol, respectively. For Tosylamide/Formaldehyde Resin, retrospective studies conducted in Sweden, Belgium, Finland, Germany, Brazil, Thailand, Australia, and North America from 1989 – 2022 reported positive reactions to Tosylamide/Formaldehyde Resin in ~ 0.2% – 94% of patients. There were also retrospective studies for patients with eyelid dermatitis. In three retrospective studies from 1994 – 2004, 2001 – 2003, and 2020 – 2025, completed in the US, 6.5%, 3.26%, and 0.66% of patients with suspected eyelid ACD were sensitive to Tosylamide/Formaldehyde Resin, respectively. Retrospective studies were also performed on children in the US from 2001 – 2006 and in Brazil from 2003 – 2010. The Brazilian study observed 6.8% of patients having a positive reaction to Tosylamide/Formaldehyde Resin, compared with 4.6% of patients in the US study.

Following the usage of nail polish or nail hardeners containing Tosylamide/Formaldehyde Resin, allergic reactions were reported in a 4-yr-old female, 6-yr-old male, 32-yr-old female, 39-yr-old female, 49-yr-old female, 60-yr-old female, and 67-yr-old female. The findings include atopic flexural dermatitis, dystrophy, dermatosis, eczema, erythema, erthematosquamous lesions, edema, itching dermatitis, scaling, and itchiness in the eyelid, face, glabella, neck, fingers, ala nasi, forearms, hands, and retroauricular areas as well as onycholysis, discoloration, deformation of the nail plates. All the patients had positive reactions to 10% Tosylamide/Formaldehyde Resin in petrolatum during patch testing. A 46-yr-old female with a history of eczema developed urticated erythema and rashes upon sun exposure. The patient had positive reactions to 10% Tosylamide/ Formaldehyde Resin in petrolatum and had normal ranges for erythema threshold during photopatch testing. A 35-yr-old female with a history of ACD to epoxy resin developed dermatitis on the fingers, acute facial swelling and rashes on the neck and arms upon beginning a plastics bench mechanic job. Patch testing revealed a positive reaction to Tosylamide/ Formaldehyde Resin and epoxy resin. Phototesting showed sensitivity to UVB and UVA radiation, while photopatch testing was negative. A 32-yr-old female had symptoms develop on her skin from wearing a metallic watch. The patient had assumed an allergy to nickel and began using nail varnish on the back of the watch to prevent skin contact with the nickel. Upon patch testing, the patient tested positive to 10% Tosylamide/Formaldehyde Resin in petrolatum but negative for nickel.

Tosylamide/Formaldehyde Resin produced 5 positive reactions among 1500 workers (0.3%) in the Occupational Dermatology Research and Education Centre in Melbourne, Australia in 2003, while the Centre for Occupational and Environmental Health at the University of Manchester, England had no cases for Tosylamide/Formaldehyde Resin in two different databases consisting of 6067 and 5546 cases from 1998 - 2002.

CIR staff performed an MOE calculation for Tosylamide/Formaldehyde Resin as used in nail polishes at 13.9%. When assuming 50% nail penetration, the resulting MOE was 227; this value is greater than 100 and is considered protective. An MOE calculation could not be made for Tosylamide/Epoxy Resin due to insufficient information to identify a repeated-dose toxicity POD. However, SEDs were calculated for 50, 10, and 0.4% nail penetration which were 0.296, 0.0591, and 0.00236 mg/kg bw/d, respectively.

PREVIOUS DISCUSSION

Discussion from Original Report Published in 1986

Although the clinical data were limited to studies with products, it is the Panel's opinion that the combined animal and clinical data were sufficient to assess the safety of Tosylamide/Formaldehyde Resin.[2]

DISCUSSION

To be determined.

CONCLUSION

To be determined.

TABLES

Table 1. Chemical properties

Property	Value	Reference
Tosylamide/Formaldehyde Resin		
Physical Form	Hard resin	2
Color	Clear	2
Odor	Faint formaldehyde	2
Specific Gravity (@ 25 ºC)	1.35	2
Log K_{ow}	≥ 4.98 (KOWWIN v1.68 estimate)	8
Viscosity (kg/(s x m))		2
@ 100ºC	10	
@ 120ºC	0.88	
@ 140ºC	0.18	
Vapor pressure (mmHg @ 150ºC)	< 0.1	2
Melting Point (ºC)	82	12
Water Solubility	Practically insoluble	2
Other Solubility	Soluble in alcohols, ethers, ketones, esters, and aromatic hydrocarbons	2
Tosylamide/Formaldehyde Resin (80% in a blend of butyl acetate and butyl alcohol)		
Physical Form	Soft, viscous liquid	2
Specific Gravity (@ 25ºC)	~1.256	2
Viscosity (cps)	6000 – 11,000	2
Vapor pressure (mmHg @ 25ºC)	10	2
Water Solubility (@ 25ºC)	Insoluble	2
Other Solubility	Miscible with common organic solvents and thinners except for aliphatic petroleum hydrocarbons	2
Tradename mixture (aq.) containing ~74% Tosylamide/Epoxy Resin		
Physical Form	Liquid	9
Color	Clear	9
Odor	Strong, esteric	9
Specific Gravity (@ 20ºC)	1.2	9
Viscosity (cps)	750 - 1000	9
Vapor pressure (mmHg @ 20ºC)	8.4	9
Water Solubility (@ 20ºC)	0.68%	9
Tosylamide/Epoxy Resin		
Physical Form	Viscous liquid	6
Color	White to pale yellow	6
Odor	Very mild, esteric	10
Molecular Weight (number average; Da)	< 1000	6
Specific Gravity (@ 25 ºC)	1.27	10
Log K_{ow}	≥ 5.16 (KOWWIN v1.68 estimate)	8
Boiling Point (ºC)	> 200	10
Water Solubility	Not readily soluble	10

Table 2. Frequency and concentration of use according to likely duration and exposure and by product category

	Tosylamide/Formaldehyde Resin		Tosylamide/Epoxy Resin	
	# of Uses	Max Conc of Use	# of Uses	Max Conc of Use
	RLD (2025)[15,16]	% (2025) [17]	RLD (2025) [15,16]	% (2025) [17]
Totals*	**239**	**10.2 - 13.9**	**2173**	**3.4 - 9**
summarized by likely duration and exposure**				
Duration of Use				
Leave-On	*240*	*10.2-13.9*	*2106*	*3.4-9*
Rinse-Off	*NR*	*NR*	*37*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Unknown	*NR*	*NR*	*40*	*NR*
Exposure Type				
Baby Products	NR	NR	NR	NR
Children's Makeup	NR	NR	1	NR
Eye Area	NR	NR	NR	NR
Incidental Ingestion	25	NR	66	NR
Mucous Membrane	25	NR	66	NR
Incidental Inhalation-Spray	NR	NR	3	NR
Incidental Inhalation-Airbrush	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR
Dermal Contact	NR	NR	15	NR
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	15	NR
Nail	215	10.2-13.9	2047	3.4-9
Other Preparations (Unknown Exposure Type)	NR	NR	40	NR
as reported by product category				
Fragrance Preparations				
Perfumes	NR	NR	3	NR
Hair Coloring Preparations				
Hair Dyes and Colors (all types requiring caution statements and patch tests)	NR	NR	12	NR
Hair Bleaches	NR	NR	3	NR
Makeup Preparations (not eye or children's)				
Leg and Body Paints	NR	NR	6 (traditional application)	NR
Lipstick and Lip Glosses	25	NR	65	NR
Other Makeup Preparations	NR	NR	6 (traditional application)	NR
Makeup Preparations for Children (not eye)				
Children's Lipsticks and Lip Glosses	NR	NR	1	NR
Manicuring Preparations				
Basecoats and Undercoats	2	NR	34	3.4-6.3
Nail Extenders	NR	NR	4	NR
Nail Polish and Enamel	207	10.2-13.9	1956	9
Nail Polish and Enamel Removers	NR	NR	22	NR
Other Manicuring Preparations	6	NR	31	5 (top coat)
Other Preparations (i.e., those preparations that do not fit another category)	NR	NR	40	NR

NR – not reported

l.o. – leave-on; r.o. – rinse-off

*The sum of the counts given for duration of use and by exposure type, and the sum of the frequency reported by product category, may not equal the sum of total uses because each ingredient may be used in cosmetic formulations that are reported under more than one product category.

**Likely duration and exposure are derived from survey data based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders.

Table 3. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population	Protocol	Results	Reference
IRRITATION						
ANIMAL						
Tosylamide/Epoxy Resin	saline solution	0.5 g	New Zealand albino rabbit (n = 3)	Test substance was applied to an area of ~6.25 cm^2 and occluded for 4 h with gauze before being washed. Area was evaluated for erythema and edema using the Draize scale 30 min, 24, 48, 72 h, and 7 d post treatment.	Tosylamide/Epoxy Resin was slightly irritating to the skin.	6
Tosylamide/Epoxy Resin	mineral oil	unspecified amount (60% w/w)	New Zealand albino rabbit (n = 3)	Test substance was applied in a dry paste and observations for erythema, edema, and desquamation were made.	Primary dermal irritation index was calculated to be 2.7. Light erythema, edema, and desquamation were observed; the erythema and edema resolved within 10 d. Tosylamide/Epoxy Resin was slightly irritating to the skin.	7
HUMAN						
Tosylamide/Epoxy Resin	NR	NR	10 subjects	NR	Tosylamide/Epoxy Resin was not irritating to the skin.	24
SENSITIZATION						
ANIMAL						
Tosylamide/Formaldehyde Resin	NR	NR	Mice and guinea pigs (no further information provided)	134 chemicals were reviewed including Tosylamide/Formaldehyde Resin. No exact details on the protocol for the LLNA or guinea pig sensitization testing were provided in the paper.	Tosylamide/Formaldehyde Resin was not a sensitizer.	23
Tosylamide/Epoxy Resin	NR	10, 25, and 50%	Mice (no further information provided)	LLNA study was performed using the test substance (no further information provided)	Tosylamide/Epoxy Resin produced a stimulation index of 1.8, 2.4, and 2.9 respectively. The test substance was not considered a sensitizer up to 50% concentration.	6

GPMT – guinea pig maximization test; LLNA - local lymph node assay; NR – not reported

Table 4. Multicenter and retrospective studies

# Patients	Concentration, ingredient, and test vehicle	Protocol	Known Allergy to Nail Products?	Location	Years	Results	Reference
MULTICENTER STUDIES							
41	10% Tosylamide/Epoxy Resin in petrolatum and 10% Tosylamide/Epoxy Resin in ethanol	Patients with a history of a positive patch test to DGEBA underwent patch test with series of 23 chemicals including bisphenol-A epoxy resins (including Tosylamide/Epoxy Resin), bisphenol-F epoxy resins, and epoxy acrylates using the protocol of the NACDG. The reactions were evaluated on days 2 and 5 or 7 and graded according to the NACDG protocol scale.	Unknown	North America	1999 – 2001	31.71% (13 out of 41) of patients had positive reactions to Tosylamide/Epoxy Resin in petrolatum 33.33% (13 out of 39) of patients had positive reactions to Tosylamide/Epoxy Resin in ethanol	[24]
RETROSPECTIVE STUDIES							
18	10% Tosylamide/ Formaldehyde Resin in petrolatum	In a case series that took place over a period of time, patients had contact allergies to nail varnish located most frequently on the neck, eyelids, other parts of the face and hands, and periungual areas. Patch testing was done according to the Swedish standard test series.	Yes	Sweden	1989 – 1991	94% (17 out of 18) of patients had a positive reaction to Tosylamide/Formaldehyde Resin and the nail varnishes brought in by the patients.	[25]
92	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients with ACD and chronic vulval complaints were patch tested with a European Standard series with Belgian additions for other allergens.	Unknown	Belgium	1990 – 2003	1.1% (1 out of 92) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[26]
269	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested using the plastics and glues series from the clinic.	Unknown	Finland	1991 - 1996	0.4% (1 out of 269) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[27]
525	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested using a modified European standard series.	Unknown	Finland	1991 – 1996	1.1% (6 out of 525) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[27]
1018	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested with standard series of the German Contact Dermatitis Research group.	Unknown	Germany	1993 – 1995	0.29% (3 out of 1018) of patients had positive reactions to Tosylamide/Formaldehyde Resin that were clinically relevant (8 patients had clinically irrelevant reactions) However, these 11 patients did not have any positive reactions to formaldehyde (1% aq). Due to the low incidence of sensitization, the study gave a recommendation of not including Tosylamide/Formaldehyde Resin in the standard series.	[28]
157	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients with ACD from nail varnish were patch tested using the Brazilian Cosmetic Standard Series.	Unknown	Brazil	1996 – 2006	90% (141 out of 157) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[29]
1582 female patients 611 male patients	10% Tosylamide/ Formaldehyde Resin in petrolatum	The data for the female and male patients with at least one allergic reaction to a NACDG standard screening allergen with cosmetic use was analyzed.	Unknown	North America	2001 – 2004	6.1% (97 out of 1582) of female patients had a positive reaction to Tosylamide/Formaldehyde Resin. 0.5% (exact number not mentioned out of 611) of male patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[30]
755	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients with ACD from a nail care product were patch-tested with the top 5 NACDG screening allergens associated with nail care products.	Yes	North America	2001 – 2016	36.2% (273 out of 755) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[31]

Table 4. Multicenter and retrospective studies

# Patients	Concentration, ingredient, and test vehicle	Protocol	Known Allergy to Nail Products?	Location	Years	Results	Reference
7408	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested according to Skin and Cancer foundation baseline series performed according to ICDRG guidelines.	Unknown	Australia	2002 – 2017	0.78% (68 out of 7408) patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[32]
792	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested using the Brazilian Cosmetic Standard Series.	Unknown	Brazil	2003 – 2010	10.4% (82 out of 792) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[33]
678	10% Tosylamide/ Formaldehyde Resin in an unspecified vehicle	Patients with suspected ACD were patch tested using Finn chambers with reactions read on days 2, 3, and 7.	Unknown	Thailand	2004 – 2008	1.1% (exact number not mentioned out of 678) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[34]
5078	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested with NACDG standard screening tray.	Unknown	North America	2007 – 2008	1% (exact number not mentioned out of 5078) had a positive reaction to Tosylamide/Formaldehyde Resin. The calculated SPIN for this ingredient was 44.	[35]
1195	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested using Brazilian Cosmetic Standard Series and cosmetic series.	Unknown	Brazil	2010 – 2016	105 patients (out of 1195) had a positive reaction confirming ACD. 1.34% (16 out of 1195) had a positive reaction to Tosylamide/Formaldehyde Resin.	[36]
4859	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested with NACDG standard screening tray	Unknown	North America	2013 – 2014	0.9% (43 out of 4859) had a positive reaction to Tosylamide/Formaldehyde Resin. The calculated SPIN for this ingredient was 30.	[37]
768	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested using the Brazilian Cosmetic Standard Series and cosmetic series.	Suspected	Brazil	2013 – 2017	251 patients (out of 768) that had a positive reaction confirming ACD. 4.6% (35 out of 768) had a positive reaction to Tosylamide/Formaldehyde Resin. 82.9% (29 out of 35) of the reactions were clinically relevant in the patients.	[38]
175	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients with hand dermatitis were patch tested using the Brazilian Standard Battery.	Unknown	Brazil	2016 – 2022	4.6% (8 out of 175) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[39]
4113	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested with NACDG standard screening tray.	Unknown	North America	2019 – 2020	0.2% (10 out of 4113) had a positive reaction to Tosylamide/Formaldehyde Resin. The calculated SPIN for this ingredient was 7.	[40]
3056	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested with NACDG standard screening tray.	Unknown	North America	2021 – 2022	0.2% (6 out of 3056) had a positive reaction to Tosylamide/Formaldehyde Resin. The calculated SPIN for this ingredient was 4.	[41]
174	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested using a modified European standard series.	Unknown	Finland	Exact timeframe unknown but information was over the course of 3 yr	0.6% (1 out of 174) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[42]
			EYELID DERMATITIS				
888	10% Tosylamide/Formaldehyde Resin in petrolatum	Patients with contact dermatitis patch tested using Finn chambers and had their reactions read at 48 and 72 h. From the patients that reacted to Tosylamide/Formaldehyde Resin, these patients were patch tested to their personal dried nail polishes.	Suspected	Italy	1987 – 1992	1.35% (12 out of 888) of patients had sensitization to Tosylamide/Formaldehyde Resin. For the 12 patients that reacted to Tosylamide/Formaldehyde Resin that received further patch testing to their personal dried nail polishes, 92% (11 out of 12) had a positive reaction.	[43]

Table 4. Multicenter and retrospective studies

# Patients	Concentration, ingredient, and test vehicle	Protocol	Known Allergy to Nail Products?	Location	Years	Results	Reference
46	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch-tested with NACDG standard screening tray and other relevant trays when appropriate. Of the test population, 46 patients with suspected ACD of the eyelids were tested with a variety of allergens.	Unknown	US	1994 – 2004	6.5% (3 out of 46) patients with suspected eyelid ACD had positive reactions to Tosylamide/Formaldehyde Resin.	[44]
16	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested with the extended European baseline series which determined who had a nail varnish allergy (located mainly on the eyelids).	Yes	Turkey	1996 – 2008	81.25% (13 out of 16) of patients reacted to nail products 87.5% (14 out of 16) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[45]
215	Tosylamide/Formaldehyde Resin at an unspecified concentration and in an unspecified vehicle	Patients with eyelid dermatitis were patch-tested to products and ingredients in the products used.	Yes	US	2001 – 2003	8.37% (18 out of 215) of patients reacted to nail products 3.26% (7 out of 215) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[46]
268	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients that were patch-tested with the NACDG 65 screening allergens selected for routine use. Patients that met the study criteria of only having eyelid dermatitis were then patch tested using the top 26 relevant allergens for pure eyelid dermatitis.	Unknown	North America	2003 – 2004	1.5% (4 out of 268) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[47]
152	Tosylamide/Formaldehyde Resin at an unspecified concentration and in an unspecified vehicle	Patients with eyelid dermatitis were patch-tested using an 80-allergen standard series, supplemental personal care product, preservative, and emulsifier series, and additional series depending on clinical history.	Yes	US	2020 – 2025	0.66% (1 out of 152) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[48]
			CHILDREN				
65	10% Tosylamide/ Formaldehyde Resin in petrolatum	A case series of patients patch-tested with NACDG standard series and patient's own personal care products/medicaments.	Unknown	US	2001 – 2006	4.6% (3 out of 65) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[49]
73	10% Tosylamide/ Formaldehyde Resin in petrolatum	Patients were patch tested using the Brazilian Cosmetic Standard Series.	Unknown	Brazil	2003 – 2010	6.8% (5 out of 73) of patients had a positive reaction to Tosylamide/Formaldehyde Resin.	[50]

ACD - allergic contact dermatitis; DGEBA - bisphenol A diglycidyl ether; ICDRG – International Contact Dermatitis Research Group; NACDG - North American Contact Dermatitis Group; SPIN - significance-prevalence index number

Table 5. Case reports with products containing Tosylamide/Formaldehyde Resin

Suspected product/ingredient causing adverse effects	Subjects	Protocol/Study Description	Results	Reference
Nail varnish	4-yr-old female	The patient developed eyelid dermatitis and atopic flexural dermatitis from having her nails painted regularly	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum. Discontinued use of products containing Tosylamide/Formaldehyde Resin resulted in an improvement of atopic dermatitis.	[51]
Nail varnish	6-yr-old male	The patient had a 2-mo history of itchy eczematous lesions on the eyelids, face, lateral sides of the neck and periungual areas of the fingers. The patient's mother had applied bitter nail varnish to prevent nail biting.	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum and bitter nail varnish. Application of a nail varnish remover and topical corticosteroid ointment led to a complete clearance in eczema with no recurrence at the follow-up.	[52]
Nail varnish	39-yr-old female	The patient exhibited an itchy rash on lower and upper eyelids, glabella, ala nasi, and retroauricular areas for 2 - 3 yr.	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum.	[53]
Nail hardener	49-yr-old female	The patient had itching dermatitis and erthemato-squamous lesions on the fingers and toes. The patient has a history of applying a nail hardener that would cause non-inflammatory onycholysis, discoloration, and deformation of the nail plate.	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum.	[56]
Nail varnish	60-yr-old female	The patient had a 4-yr history of fingernail dystrophy and finger-tip dermatosis. The patient has a history of gel and glue-on nails 2 yr before stopping and has been using nail varnish for the most recent 2 yr before coming it for patch testing.	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum.	[55]
Nail varnish	67-yr-old female	The patient had erythema, edema, scaling on the glabella and neck that developed over 1-yr (started from the eyelids).	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum, nail lacquer patient used, 2-hydroxyethyl acrylate, and 2-hydroxyethyl methacrylate. Avoiding the original nail varnish used led to an 80% improvement after 6 wk.	[54]
Nail varnish	35-yr-old female	The patient had a 4-yr history of ACD to epoxy resin. She developed dermatitis of the fingers, acute facial swelling and rashes along the neck and arms upon starting a job as a plastics bench mechanic. The patient was patch tested to the North American Standard series, corticosteroids, plastic and glue derivative, and her personal products. The patient also underwent photo testing and photopatch testing.	The patient had a 1+ reaction at 24 h to the epoxy resin that became a 2+ reaction at 7 d and a 2+ reaction to Tosylamide/Formaldehyde Resin after 48 h and 7 d. Phototesting revealed a UVB MED OF 10 mJ/cm^2 and UVA MED of 0.5 J/cm^2. Photopatch testing was negative.	[57]
Nail varnish	46-yr-old female	The patient had a history of eczema on her forearms and hands. The patient noticed that she started becoming sensitive to the sun where 20 min of sun exposure could induce urticated erythema that would become a rash lasting for weeks. The patient underwent monochromator phototesting, repeat patch and photopatch testing.	For repeat patch testing, the patient had a positive patch tests at 48 and 96 h to 10% Tosylamide/Formaldehyde Resin in petrolatum in 1999 and 2006. For photopatch testing, 24-h erythema thresholds were within normal ranges Patient practiced allergen avoidance and implemented photoprotective measures. The patient was symptom free in 2007.	[58]
Nickel	32-yr-old female	The patient had symptoms from wearing a metallic watch and had assumed an allergy to nickel. To counteract the symptoms, the patient used nail varnish on the back of the watch to prevent skin contact with the nickel. The patient was patch-tested using the modified European standard series.	Positive patch test to 10% Tosylamide/Formaldehyde Resin in petrolatum and had a negative reaction to nickel.	[5]

ACD - allergic contact dermatitis; MED – minimal erythemal dose

Table 6. MOE calculation for Tosylamide/Formaldehyde Resin in nail polish/enamels

Parameter	Value / Calculation	Reference
Nail polish amount	1.0 g/application	[60]
Adult frequency of use	104 applications/yr	[60]
Maximum concentration in product	13.9%	[17]
Tosylamide/Formaldehyde Resin application	1.0 g × 13.9% = 139 mg/application	
Time-averaged Tosylamide/Formaldehyde Resin amount	139 × 104 / 365 = 39.61 mg/day	
Nail penetration	50%	
Body weight	60 kg	
SED	39.61 × 0.50 / 60 = 0.330 mg/kg bw/d	[59]
POD*	75 mg/kg bw/d	[2,62]
MOE	POD/SED = 227	

*The 75 mg/kg bw/d is an estimated equivalent dose corresponding to 3000 ppm, selected from the 90-d dog study, using the US EPA default dog food factor of 0.025 kg diet/kg bw/d.

Table 7. Aggregate exposure assessment for Tosylamide/Epoxy Resin across nail-product coats

Parameter	Value / Calculation	Reference
Base coat amount	0.23 g/application	[60]
Maximum use concentration, base coat	6.3%	[17]
Exposure from base coat	0.23 g × 6.3% = 14.49 mg/application	
Nail polish amount	1.0 g/application	[60]
Maximum use concentration, nail polish/enamels	9%	[17]
Exposure from nail polish/enamel	1.0 g × 9% = 90.0 mg/application	
Top coat amount	0.40 g/application	[60]
Maximum use concentration, top coat	5%	[17]
Exposure from top coat	0.40 g × 5% = 20.0 mg/application	
Total Tosylamide/Epoxy Resin/application	14.49 + 90.0 + 20.0 = 124.49 mg/application	
Adult frequency of use	104 applications/yr	[17]
Time-averaged use amount	124.49 × 104 / 365 = 35.47 mg/d	
Body weight	60 kg	
50% nail penetration	SED = 0.296 mg/kg bw/d	[59]
10% nail penetration	SED = 0.0591 mg/kg bw/d	[59,61]
0.4% nail penetration	SED = 0.00236 mg/kg bw/d	[59]

Note: The 50% value is a conservative default for nail-plate penetration when relevant ingredient- and formulation-specific information is unavailable. The 10% value is a conservative dermal absorption estimate supported by published skin-permeation modeling indicating that cosmetic ingredients with molecular weights >500 Da are expected to have very low absorption and less than 10%.[59,61] The 0.4% value is a model-derived nail-plate penetration estimate for Tosylamide/Epoxy Resin, based on its high molecular weight (740 Da), vapor pressure, low water solubility, and other physicochemical and formulation-related properties.[59]

REFERENCES

1. Personal Care Products Council. 2026. *International Cosmetic Ingredient Dictionary*. https://incipedia.personalcarecouncil.org/winci/. Date Accessed: March 11, 2026.
2. Elder RL (ed). Final report on the safety assessment of toluenesulfonamide/formaldehyde resin. *Journal of the American College of Toxicology*. 1986;5(5):471–490.
3. Chen M. 2004. Re-review of Tosylamide/Formaldehyde Resin (formerly called Toluenesulfonamide/Formaldehyde Resin). [Unpublished re-review document reviewed by the Panel at the September 2004 Panel meeting].
4. Andersen FA (ed). Annual review of cosmetic ingredient safety assessments-2004/2005. *Int J Toxicol*. 2006;25 (S2):59.
5. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2005. Final Report on Hazard Classification of Common Skin Sensitisers. https://www.industrialchemicals.gov.au/sites/default/files/Common%20skin%20sensitisers.pdf. Date Accessed: August 3, 2026.
6. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2008. Full Public Report: Tosylamide / Epoxy Resin. https://www.industrialchemicals.gov.au/sites/default/files/LTD1329%20Public%20Report%20PDF.pdf. Date Accessed: Aug 3, 2026.
7. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2013. Full Public Report: Polymer in Polytex NX-55. https://www.industrialchemicals.gov.au/sites/default/files/LTD1669%20Public%20Report%20PDF.pdf. Date Accessed: Aug 3, 2026.
8. U.S. Environmental Protection Agency. 2026. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. https://www.epa.gov/tsca-screening-tools/download-epi-suitetm-estimation-program-interface-v411. Date Accessed: August 28, 2026.
9. Estron Chemical. 2020. GHS Compliant Safety Data Sheet: Polytex NX-55. https://estron.com/wp-content/uploads/2010/05/Polytex-NX-55-10-27-20-GHS-SDS.pdf. Date Accessed: Aug 5, 2026.
10. Estron Chemical. 2020. GHS COMPLIANT SAFETY DATA SHEET: Polytex E-100. https://estron.com/wp-content/uploads/2010/05/Polytex-E-100-10-29-20-GHS-SDS.pdf. Date Accessed: Aug 5, 2026.
11. PubChem. 2026. Toluenesulfonamide formaldehyde resin. https://pubchem.ncbi.nlm.nih.gov/compound/159985. Date Accessed: Mar 24, 2026.
12. CAS Common Chemistry. 2026. Formaldehyde-p-toluenesulfonamide copolymer (CAS RN 25035-71-6). https://commonchemistry.cas.org/detail?cas_rn=25035-71-6. Date Accessed: Aug 5, 2026.
13. Jackson EM. Formalehyde in personal care products. *Skin Pharmacol Physiol*. 2012;25(5):236–240.
14. U.S. Food and Drug Administration. Federal Food, Drug, and Cosmetic Act Section 612 Title 21.
15. US Food and Drug, Administration (FDA) Office of Colors & Cosmetics (OCAC). 2025. Data from: Registration and Listing of Cosmetic Product Facilities and Products. College Park, MD [Obtained under the Freedom of Information Act].
16. Hicks J., Eisenmann C., Nikitakis J., Kim D., Flores W. 2025. Personal Care Products Council (PCPC) RLD Mapping Project Report. Washington, DC [Analysis results provided as a courtesy to CIR].
17. Personal Care Products Council. 2025. Concentration of Use by FDA Product Category: Tosylamide/Epoxy Resin and Tosylamide/Formaldehyde Resin. [Unpublished data submitted by the Personal Care Products Council on March 31st, 2025].
18. EUR-Lex. Commission Implementing Decision (EU) 2022/677 of 31 March 2022 laying down rules for the application of Regulation (EC) No 1223/2009 of the European Parliament and of the Council as regards the glossary of common ingredient names for use in the labelling of cosmetic products (Text with EEA relevance). https://eur-lex.europa.eu/eli/dec_impl/2022/677/oj/eng. Date Accessed: Jun 24, 2026.
19. Orton DI, Wilkinson JD. Cosmetic allergy: Incidence, diagnosis, and management. *Am J Clin Dermatol*. 2004;5(5):327–337.
20. Chou M, Dhingra N, Strugar TL. Contact sensitization to allergens in nail cosmetics. *Dermatitis*. 2017;28(4):231–240.
21. Pascoe D, Moreau L, Sasseville D. Emergent and unusual allergens in cosmetics. *Dermatitis*. 2010;21(3):127–137.
22. Lazzarini R, Hafner MFS, Lopes ASA, Oliari CB. Allergy to hypoallergenic nail polish: Does this exist? *An Bras Dermatol*. 2017;92(3):421–422.

23. Basketter DA, Lea LJ, Cooper K, et al. Threshold for classification as a skin sensitizer in the local lymph node assay: A statistical evaluation. *Food Chem Toxicol*. 1999;37(12):1167–1174.

24. Lee HN, Pokorny CD, Law S, Pratt M, Sasseville D, Storrs FJ. Cross-reactivity among epoxy acrylates and bisphenol F epoxy resins in patients with bisphenol A epoxy resin sensitivity. *Am J Contact Dermat*. 2002;13(3):108–115.

25. Lidén C, Berg M, Färm G, Wrangsjö K. Nail varnish allergy with far-reaching consequences. *Br J Dermatol*. 1993;128(1):57–62.

26. Nardelli A, Degreef H, Goossens A. Contact allergic reactions of the vulva: A 14-year review. *Dermatitis*. 2004;15(3):131–136.

27. Kanerva L, Jolanki R, Alanko K, Estlander T. Patch-test reactions to plastic and glue allergens. *Acta Derm Venereol*. 1999;79(4):296–300.

28. Fuchs T, Gutgesell C. Is contact allergy to toluene sulphonamide-formaldehyde resin common? *Br J Dermatol*. 1996;135(6):1013–1014.

29. Lazzarini R, Duarte I, de Farias DC, Santos CA, Tsai AI. Frequency and main sites of allergic contact dermatitis caused by nail varnish. *Dermatitis*. 2008;19(6):319–322.

30. Warshaw EM, Buchholz HJ, Belsito DV, et al. Allergic patch test reactions associated with cosmetics: Retrospective analysis of cross-sectional data from the North American Contact Dermatitis Group, 2001-2004. *J Am Acad Dermatol*. 2009;60(1):23–38.

31. Warshaw EM, Voller LM, Silverberg JI, et al. Contact dermatitis associated with nail care products: Retrospective analysis of North American Contact Dermatitis Group data, 2001-2016. *Dermatitis*. 2020;31(3):191–201.

32. Lee S, Maor D, Palmer A, Nixon RL. Declining prevalence of allergic contact dermatitis caused by toslyamide/formaldehyde in nail polish. *Contact Dermatitis*. 2018;79(3):184–185.

33. Rodrigues DF, Neves DR, Pinto JM, Alves MFF, Fulgêncio ACF. Results of patch-tests from Santa Casa de Belo Horizonte dermatology clinic, Belo Horizonte, Brazil, from 2003 to 2010. *An Bras Dermatol*. 2012;87(5):800–803.

34. Boonchai W, Desomchoke R, Iamtharachai P. Trend of contact allergy to cosmetic ingredients in Thais over a period of 10 years. *Contact Dermatitis*. 2011;65(6):311–316.

35. Fransway AF, Zug KA, Belsito DV, et al. North American Contact Dermatitis Group patch test results for 2007-2008. *Dermatitis*. 2013;24(1):10–21.

36. Duarte I, Mendonça RF, Hafner MFS. Allergic contact dermatitis in private practice: Evolution in 16 years. *Int j exp clin res*. 2017;2017(08):1–5.

37. DeKoven JG, Warshaw EM, Belsito DV, et al. North American Contact Dermatitis Group patch test results 2013-2014. *Dermatitis*. 2017;28(1):33–46.

38. Villarinho ALCF, Melo MdGM, Teixeira LR. Application of the Brazilian patch test panel in the diagnosis of allergic contact dermatitis to cosmetics. *An Bras Dermatol*. 2022;97(5):656–660.

39. Endlich LRdFG, Samorano LP, Nunes RS, Reis VMSD. Hand dermatitis: A 6-year experience in a tertiary referral Brazilian hospital. *An Bras Dermatol*. 2025;100(3):439–446.

40. DeKoven JG, Warshaw EM, Reeder MJ, et al. North American Contact Dermatitis Group patch test results: 2019-2020. *Dermatitis*. 2023;34(2):90–104.

41. Houle M, DeKoven JG, Atwater AR, et al. North American Contact Dermatitis Group patch test results: 2021-2022. *Dermatitis*. 2025;36(5):464–476.

42. Kanerva L, Jolanki R, Estlander T. Allergic and irritant patch test reactions to plastic and glue allergens. *Contact Dermatitis*. 1997;37(6):301–302.

43. Tosti A, Guerra L, Vincenzi C, Piraccini BM, Peluso AM. Contact sensitization caused by toluene sulfonamide-formaldehyde resin in women who use nail cosmetics. *Am J Contact Dermat*. 1993;4(3):150–153.

44. Amin KA, Belsito DV. The aetiology of eyelid dermatitis: A 10-year retrospective analysis. *Contact Dermatitis*. 2006;55(5):280–285.

45. Ozkaya E, Ekinci A. Metal contact sites: A hidden localization for nail varnish allergy? *Clin Exp Dermatol*. 2010;35(4):137.

46. Guin JD. Eyelid dermatitis: A report of 215 patients. *Contact Dermatitis*. 2004;50(2):87–90.

47. Rietschel RL, Warshaw EM, Sasseville D, et al. Common contact allergens associated with eyelid dermatitis: Data from the North American Contact Dermatitis Group 2003-2004 study period. *Dermatitis*. 2007;18(2):78–81.

48. Alley DR, Abi H, Hylwa S, Neeley A, Ophaug S, Lee K. Eyelid dermatitis: A 5-year retrospective review from a metropolitan contact dermatitis clinic. *Dermatitis*. 2026:17103568261463215.

49. Jacob SE, Brod B, Crawford GH. Clinically relevant patch test reactions in children--a United States based study. *Pediatr Dermatol*. 2008;25(5):520–527.

50. Rodrigues DF, Goulart EMA. Patch test results in children and adolescents. study from the Santa Casa de Belo Horizonte dermatology clinic, Brazil, from 2003 to 2010. *An Bras Dermatol*. 2015;90(5):671–683.

51. Jacob SE, Stechschulte SA. Tosylamide/formaldehyde resin allergy--a consideration in the atopic toddler. *Contact Dermatitis*. 2008;58(5):312–313.

52. Ozkaya E, Mirzoyeva L. Tosylamide/formaldehyde resin allergy in a young boy: Exposure from bitter nail varnish used against nail biting. *Contact Dermatitis*. 2009;60(3):171–172.

53. Pongpairoj K, Morar N, McFadden JP. 'Seborrhoeic dermatitis' of the head and neck without scalp involvement - remember nail varnish allergy. *Contact Dermatitis*. 2016;74(5):306–307.

54. Yokota M, Thong H, Hoffman CA, Maibach HI. Allergic contact dermatitis caused by tosylamide formaldehyde resin in nail varnish: An old allergen that has not disappeared. *Contact Dermatitis*. 2007;57(4):277.

55. Coe J, Robinson R, Wilkinson SM. Nail dystrophy mimicking psoriatic disease caused by contact allergy to nail varnish allergens including copolymers. *Contact Dermatitis*. 2021;85(5):600–602.

56. Mestach L, Goossens A. Allergic contact dermatitis and nail damage mimicking psoriasis caused by nail hardeners. *Contact Dermatitis*. 2016;74(2):112–114.

57. Kwok T, Rosen CF, Storrs FJ, Lobel E, DeKoven JG. Persistent photosensitivity after allergic contact dermatitis to epoxy resin. *Dermatitis*. 2013;24(3):124–130.

58. Rose RF, Goulden V, Wilkinson SM. The spontaneous resolution of photosensitivity and contact allergy in a patient with chronic actinic dermatitis. *Photodermatol Photoimmunol Photomed*. 2009;25(2):114–116.

59. Yin XJ, Hewitt NJ, Erler S, et al. Safety assessment for nail cosmetics: Framework for the estimation of systemic exposure through the nail plate. *Regul Toxicol Pharmacol*. 2024;148:105588.

60. National Institute for Public Health and the Environment (RIVM) of the Netherlands. 2025. Cosmetics Fact Sheet. https://www.rivm.nl/bibliotheek/rapporten/2025-0099.pdf.

61. Kroes R, Renwick AG, Feron V, et al. Application of the threshold of toxicological concern (TTC) to the safety evaluation of cosmetic ingredients. *Food Chem Toxicol*. 2007;45(12):2533–2562.

62. US Environmental Protection Agency. 2004. Toxicological Review of Boron and Compounds (CAS no. 7440-42-8). https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P1006CK9.TXT.

Distributed for Comment Only -- Do Not Cite or Quote
JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY
Volume 5, Number 5, 1986
Mary Ann Liebert, Inc., Publishers

9

Final Report on the Safety Assessment of Toluenesulfonamide/ Formaldehyde Resin

Toluenesulfonamide/Formaldehyde Resin (TSFR) is used in such cosmetic products as fingernail polishes and enamels at concentrations up to 10%.

TSFR was practically nontoxic to rats when given orally as a 70% solution in acetone and when applied to the skin of rabbits as a 40% suspension in corn oil. TSFR in the form of a finely ground powder was nonirritating to rabbit skin and slightly irritating to the rabbit eye. The undiluted material was nonirritating to rabbit skin, slightly irritating to the rabbit eye, and practically nontoxic to rabbits by dermal application. No significant treatment-related effects were observed in a subchronic oral study in dogs. TSFR was negative in the Ames test for mutagenicity.

In clinical studies, 10% TSFR in dimethyl phthalate was nonirritating and nonsensitizing to the skin. Nail products containing up to 12% TSFR were nonsensitizing, nonphotosensitizing, and essentially nonirritating to the human skin. Reports of nail polish dermatitis of allergic origin have been attributed to TSFR and other liquid thermoplastic resins.

It is concluded that Toluenesulfonamide/Formaldehyde Resin (TSFR) and Toluenesulfonamide/Formaldehyde Resin-80% (TSFR-80) are safe as cosmetic ingredients in the present practices of use and concentration.

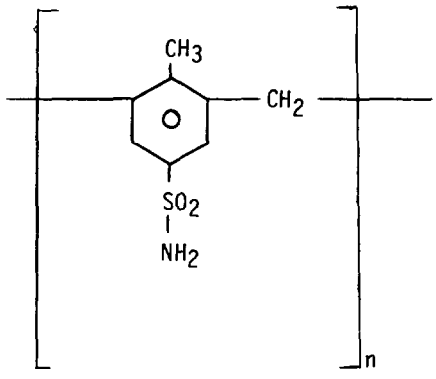
CHEMISTRY

Definition and Structure

Toluenesulfonamide/Formaldehyde Resin,* hereafter referred to as TSFR, is the polymer that conforms generally to the structure:[1]

*The safety of formaldehyde as a cosmetic ingredient has been previously reviewed.[4]

Distributed for Comment Only -- Do Not Cite or Quote



Other names for TSFR (CAS Nos.: 1338-51-8, 25035-71-6, 9008-60-0) include Santolite MHP,* Santolite MS-80 percent,* p-Toluenesulfonamide-Formaldehyde Resin, o-Toluenesulfonamide Formaldehyde Resin, Benzenesulfonamide, 4-Methyl-, Polymer with Formaldehyde, and Benzenesulfonamide, ar-Methyl-, Polymer with Formaldehyde.[2,3]

Properties

TSFR is available to cosmetic manufacturers as both a liquid and a solid. The solid form of TSFR is a hard, practically colorless material with a faint formaldehyde odor. It is soluble in alcohols, ethers, ketones, esters, and aromatic hydrocarbons. It is insoluble in aliphatic hydrocarbons and practically insoluble in water. The resin is neither a primary oxidant nor a reducing agent, and it is not reactive with water or air under ambient conditions.[2,6] Additional chemical and physical data are presented in Table 1.

TSFR-80 is a soft, viscous liquid. This solution consists of approximately 80% solids in a mixture of butyl acetate and butyl alcohol. The product is insoluble in water at 25°C, and it is miscible with all common organic solvents and thinners except aliphatic petroleum hydrocarbons. TSFR-80 is "compatible" with both nitrocellulose and cellulose acetate and forms "brittle compositions" with both of these materials; addition of a plasticizer makes such combinations permanently flexible. TSFR-80 is a combustible material. It is neither a primary oxidant nor a reducing agent and is not reactive with water or air under ambient conditions.[5,7,8] Additional chemical and physical data are presented in Table 2.

Method of Manufacture

TSFR is prepared by the condensation of aryl sulfonamides with formaldehyde.[2,9] TSFR-80 is formed by the condensation of formaldehyde with aromatic sulfonamides.[5,9] These aryl and aromatic sulfonamides were not identified.

Doviak[10] reported that when formaldehyde and p-toluene sulfonamide were employed in equimolecular proportions, they condensed to form a viscous mass, which on heating to 110°C, yielded a hard, colorless resin.

*Santolite MHP and Santolite MS-80% are registered trademarks.[5]

TABLE 1. Chemical and Physical Data for Toluenesulfonamide/Formaldehyde Resin

		Reference
Appearance	Hard, clear resin	2,6
Molecular formula	$(C_7H_9NO_2S\text{-}CH_2)_x$	3
Odor	Faint formaldehyde	6
Acid value	Approximately 1	2
Refractive index of 25 g in 75 g of butyl acetate at 25°C	1.4275–1.4325 1.430	2 6
Specific gravity at 25/25°C	1.35	2,6
Vapor pressure at 150°C	<0.1 mm Hg	6
Softening point	60°C–70°C 62°C	2 6
Flash point	171.1°C (340°F) Cleveland open cup	6
Fire point	229.4°C (445°F) Cleveland open cup	6
Viscosity at 100°C at 120°C at 140°C	 10,000 cps 880 cps 180 cps	 2,6

TABLE 2. Chemical and Physical Data for Toluenesulfonamide/Formaldehyde Resin-80%

		Reference
Appearance	Liquid (soft, viscous resin)	5,7,8
Odor	Strong butyl acetate	8
Identification	Positive; close match to a standard IR spectrum	5
Specific gravity 25°/25°C	1.23–1.24 1.256	5 8
Refractive index at 25°C	1.535–1.540	5
Vapor pressure at 25°C	~10 mm Hg	8
Viscosity at 25°C	6000–11000 cps	8
Flash point	32.2°C (90°F) (Tag closed cup and Cleveland open cup)	8
Solids[a] (100% minus % solvents)	78.8–81.2% in butyl acetate and butyl alcohol	5

[a]The various solids were not specified.

Distributed for Comment Only -- Do Not Cite or Quote

Impurities

TSFR and TSFR-80 are known to contain free formaldehyde. The formaldehyde content of TSFR-80 is <0.2%.[6,8] Data relating to other possible impurities were not available.

In a review of the safety of formaldehyde as a cosmetic ingredient, the CIR Expert Panel concluded that the concentration of formaldehyde in cosmetic products should not exceed 0.2%.[4]

NONCOSMETIC USE

TSFR and TSFR-80 are used in various indirect food contact applications. Both compounds are regulated by the U.S. Department of Agriculture as acceptable components of packaging material in contact with meat or poultry food products prepared under federal inspection.[6,8] They are also permitted as components of cellophane food packaging material (up to a limit of 0.6% by weight of the cellophane) and as components of adhesives used in food packaging articles.[11,12] Federal regulations additionally permit TSFR to be used as a side seam cement in articles intended for food contact[13] and as a component of paper and paperboard in contact with aqueous and fatty foods.[14]

TSFR-80 is also used as a solvent for nitrocellulose and cellulose acetate and in spraying, dipping, or brushing lacquers to make clear, odorless coatings.[9]

COSMETIC USE

Purpose in Cosmetics

Aryl sulfonamide-formaldehyde resins were first introduced into nail varnish films in about 1938.[15] Two commercially available resins of the aryl sulfonamide-formaldehyde type are TSFR and TSFR-80. TSFR-80 is softer and produces films of "greater flexibility" than TSFR. Both of these resins are used in nail lacquers and other nail preparations to impart high gloss and good flow properties and to increase the hardness of nitrocellulose films. They also increase the moisture resistance of nitrocellulose films, thereby reducing the incidence of water spotting and whiteness of such films.[2,15] TSFR and TSFR-80 are also employed in nail formulations to increase the flexibility and toughness of both ethyl and nitrocellulose, and "to increase the flow at elevated temperatures with polyvinyl acetate resins, imparting quick tack."[2]

Product Formulation

Data submitted to the Food and Drug Administration (FDA) in (or before) 1981 by cosmetic firms participating in the voluntary cosmetic registration program indicated that TSFR and TSFR-80 were used in a total of 211 and 356 of the registered cosmetic products, respectively (Tables 3 and 4). Product types formulated with these two resins included nail basecoats and undercoats, nail polish and enamel, and other manicuring preparations. Reported concentrations of the

Distributed for Comment Only -- Do Not Cite or Quote

TABLE 3. Product Formulation Data for Toluenesulfonamide/Formaldehyde Resin[16,17]

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)				
			>10–25	>5–10	>1–5	>0.1–1	≤0.1
Nail basecoats and undercoats	44	31	–	10	21	–	–
Nail polish and enamel	767	172	1	151	11	8	1
Other manicuring preparations	50	8	–	3	5	–	–
1981 TOTALS		211	1	164	37	8	1

TABLE 4. Product Formulation Data for Toluenesulfonamide/Formaldehyde Resin-80%[16,17]

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)				
			>10–25	>5–10	>1–5	>0.1–1	≤0.1
Nail basecoats and undercoats	44	5	–	4	1	–	–
Nail polish and enamel	767	344	2	227	74	32	9
Other manicuring preparations	50	7	1	2	2	–	2
1981 TOTALS		356	3	233	77	32	11

two resins in these products ranged from ≤0.1% to >10–25%, with the majority of products containing the resins in the concentration range of >5–10%.[16,17]

Voluntary filing of product formulation data with FDA by cosmetic manufacturers and formulators must conform to the format of concentration ranges and product categories as described in Title 21 Part 720.4 of the Code of Federal Regulations.[18] Since certain cosmetic ingredients are supplied to the formulator at less than 100% concentration, the concentration reported by the formulator may not necessarily reflect the actual concentration found in the finished cosmetic product; the actual concentration in such an instance would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of a "concentration range" provides opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing a two- to ten-fold error in the assumed ingredient concentration.

Exposure to TSFR

The fingernail, the toenail, the nail cuticle, and the skin surrounding the nail are the areas directly exposed to TSFR and TSFR-80. However, parts of the body readily accessible to the nail may also be exposed. Such areas may include the

Distributed for Comment Only -- Do Not Cite or Quote

eye region, the face and neck, and the vulva.[19] Nail products formulated with TSFR and TSFR-80 can be applied as often as several times per week. Nail polish and enamel may typically remain in contact with the nail until removed by a solvent-based enamel remover. Cosmetics formulated with TSFR and TSFR-80 have the potential for repeated application over many years.

Typical Nail Polish Composition

The major use of TSFR and TSFR-80 is in nail polish and enamel (Tables 3 and 4). Most nail polish* formulations typically consist of the following constituents[10,19]:

1. A film former (such as ethylcellulose, nitrocellulose, cellulose acetate, cellulose acetate-butyrate, methacrylate polymers, vinyl polymers, or sucrose acetate isobutyrate)
2. Resins to improve gloss and adhesion of the film (such as TSFR)
3. Plasticizers to give the film pliability, minimize shrinkage, and soften and plasticize the film former (such as camphor or dibutyl phthalate)
4. Solvents and diluents to stabilize viscosity and to keep the film former, resin, and plasticizer in a liquid state (such as esters, glycol ethers, nitroparaffins, alcohols, xylene, or toluene)†
5. Thixotropic agents for nonsettling and flow on shaking (clay modified by quaternary ammonium compounds)
6. Coloring substances (such as fluorescent and nonfluorescent dyes, guanine, or inorganic and organic pigments)

TSFR and TSFR-80 are moderately stable to light and soluble in the majority of solvents and diluents usually employed. Because of the low viscosity of TSFR and TSFR-80 formulations, "large amounts" of these resins can be used in lacquer products without adversely affecting the ease of application of the lacquer, or the hardness or flexibility of the coating.[10,15]

Suggested formulas for various nail products containing TSFR and TSFR-80 have been described in the published literature.[10,15,20–23]

TOXICOLOGY

Acute Oral Toxicity

The acute oral toxicity of TSFR was investigated using five Sprague-Dawley albino rats (two males and three females). The test material was administered as 70.0% solution in acetone in a single 7.94 g/kg oral dose. Reduced appetite and activity were observed for 2–4 days. No animals died over a 14-day observation period, and the "viscera appeared normal" at gross examination.[24]

*The term "nail polish" is often used to denote nail enamel, nail lacquer, nail varnish, top coat, and/or basecoat.[10,15,19]

†These solvents may cause false-positive irritant reactions if not permitted to evaporate before the nail lacquer is applied under a patch to the skin.[19]

Distributed for Comment Only -- Do Not Cite or Quote

A single oral dose of 5 g/kg TSFR-80 (50% solution in "3A alcohol") was administered to five male Sprague-Dawley albino rats. Animals were subsequently observed for 14 days. Reduced activity and appetite were noted for 2–3 days. All animals survived and "viscera appeared normal" at gross examination.[25]

Three different nail polish and enamel formulations were evaluated for acute oral toxicity. The products (A, B, and C)* were tested at 100% concentration, and each was formulated with approximately 12% TSFR-80. Each product was given by stomach tube at a dose of 15.0 g/kg to five female albino rats (five rats per product). Three of the 15 rats died within 2 days following the single dose. Of the three rats that died, two died following administration of formulation A, and one died following exposure to formulation C. The surviving animals generally had normal weight gain over the 7-day observation period. The exception was a single rat that had weight loss. This animal was exposed to formulation C. The acute oral LD_{50} of each product was considered >15 g/kg.[26–28]

A nail hardener (product D) containing 8.26% TSFR-80 was evaluated for acute oral toxicity according to the procedures outlined in Title 16 Part 1500.3(b)(6)(i)(A) of the Code of Federal Regulations.[29] A single dose of 5 g/kg body weight of the wet product was given by oral intubation to each of 10 albino rats. No deaths occurred over a 14-day observation period.[30]

Ocular Irritation

TSFR (100 mg) in the form of a finely ground powder was instilled into one eye of each of six New Zealand albino rabbits. The treated eyes were not rinsed with water after exposure. Untreated eyes served as controls. Slight erythema of the conjunctivae and slight to moderate discharge were observed 1, 24, and 48 h after instillation. Ocular irritation had cleared by the 72-h evaluation. No effects on the cornea or iris were noted. The investigator concluded that the test material was a "slight" ocular irritant.[24]

The ocular irritation potential of undiluted TSFR-80 was assessed in three albino New Zealand rabbits. The test material was instilled in a single 0.1 ml dose into one eye of each rabbit. Slight erythema of the conjunctivae and ocular discharge were noted at the 1-, 24-, and 48-h evaluations. Irritation had dissipated by the 72-h evaluation. No damage to the cornea or iris was reported. It was concluded that undiluted TSFR-80 was a "slight" ocular irritant.[25]

Ocular irritation was evaluated in rabbits exposed to cosmetic formulations containing approximately 12% TSFR-80. Eighteen albino rabbits were assigned to three groups of six. Each group of six rabbits was tested with one of three different nail polish and enamel products (A, B, and C). The test material (0.1 ml) was instilled into one eye of each of the six rabbits; the untreated eye served as control. Treated eyes received no water rinse. Irritation of the cornea, iris, and conjunctivae was assessed 1, 2, 3, 4, and 7 days postinstillation according to the procedures described by Draize.[31] All 18 rabbits developed ocular irritation.

*The formulations referred to in the text as "A, B, C, D, and E" are repeatedly mentioned in this report. Thus, products A, B, C, D, and E, as discussed in this section, are the same A, B, C, D, and E as discussed in other sections of the report.

Distributed for Comment Only -- Do Not Cite or Quote

Average irritation scores (max = 110) on Days 1, 2, 3, 4, and 7 postinstillation were as follows: product A: 40, 38, 24, 14, 14; product B: 47, 37, 25, 17, 25; product C: 31, 25, 17, 12, 11. Scores of >15–25 and >25–50 were indicative of mild and moderate irritation, respectively. Corneal lesions were present throughout the observation period and were the major contributing factor to the average irritation score. On the final day of observation (Day 7), 13 of the 18 treated animals had no irritation or minimal conjunctival irritation; the remaining 5 animals had lesions of the cornea and iris. Of the 5 rabbits with injury of the cornea and/or iris on Day 7, 2 animals treated with product A had lesions, 2 exposed to product B had lesions, and 1 exposed to product C had lesions.[32–34] According to Draize,[31] "a preparation which has elicited corneal and iridial lesions which have not cleared by the seventh day is considered a severe eye irritant." It was not ascertained in this study whether or not the observed ocular irritation was a result of TSFR.

A nail hardener (product D) containing 8.26% TSFR-80 was tested for ocular irritation. The procedures outlined in Title 16 Parts 1500.3(c)(4) and 1500.42 of the Code of Federal Regulations were used to evaluate both wet and dry forms of the product.[29,35] The test material (0.1 ml or 100 mg) was instilled into one eye of each of six albino rabbits; the untreated eye served as control. Treated eyes received no water rinse following instillation of the test material. Ocular reactions were evaluated at 24, 48, and 72 h. One of six rabbits developed conjunctival erythema and chemosis, iritis, and keratitis to the dry product. All six rabbits exposed to the wet product developed iritis, conjunctival erythema, and chemosis; three of these latter six animals also had keratitis. It was not specified at which evaluation these ocular reactions were observed.[30]

Dermal Toxicity

TSFR was applied as a 40% solution/suspension in corn oil to the skin of five New Zealand albino rabbits (three males and two females). Single doses of either 2.0, 3.16, 5.01, or 7.94 g/kg were applied for 24 h. Two animals were tested at the highest dose, and one rabbit was tested at each of the other doses. Reduced appetite and activity were observed for 2–4 days. No animals died during the 14-day observation period after exposure. At gross examination, the "viscera" appeared normal.[24]

TSFR-80 was applied undiluted to the skin of three New Zealand albino rabbits. Doses of 5.01 g/kg and 7.94 g/kg were applied to one male and to one male and one female, respectively. No deaths occurred over a 14-day observation period after the single 24-h exposure. Reduced appetite and activity were observed for 2–5 days, and no lesions were found at necropsy.[25]

The procedures outlined in Title 16 Parts 1500.3(c)(1)(ii)(c) and 1500.40 of the Code of Federal Regulations were used to assess the acute dermal toxicity of a nail hardener (product D) containing 8.26% TSFR-80.[29,36] A 2 g/kg per body weight dose of the wet product was applied under an "impervious sleeve" to either the clipped skin (five rabbits) or the clipped and abraded skin (five rabbits). After 24 h, the sleeves were removed. No deaths were observed over a 2-week period.[30]

Distributed for Comment Only -- Do Not Cite or Quote

Skin Irritation

TSFR was applied as a finely ground powder (0.5 g moistened with water) under an occlusive patch to the intact and abraded clipped skin of six New Zealand albino rabbits. After 24 h, the patches were removed and the treated sites were scored for erythema and edema. Skin reactions were also evaluated 48, 72, and 168 h after the single 24-h exposure. No irritation was observed.[24]

No irritation was observed when undiluted TSFR-80 (0.5 ml) was applied for 24 h to the intact skin of three New Zealand albino rabbits. Skin erythema and edema were evaluated 4, 24, 48, 72, and 168 h after the single exposure.[25]

The skin-irritating property of three different nail polish and enamel products was assessed by means of a single insult occlusive patch test. The three formulations (A, B, and C) each contained approximately 12% TSFR-80. Each product (0.5 ml) was placed on a filter disc from which the solvents were allowed to evaporate. The filter disc was then placed in contact with the clipped skin of the back of each of nine female albino rabbits (9 rabbits per product). The filter disc was secured by means of an occlusive plastic sheet wrapped around the trunk of the animal. After 24 h, the occlusive wrappings were removed, and the test sites were scored for erythema and edema. Four of the 27 rabbits had minimal skin erythema 2 h after removal of the occlusive dressing. Of these four rabbits, one had been exposed to formulation A, one had been treated with formulation B, and two had been exposed to formulation C. One rabbit treated with formulation C had minimal skin erythema at the 24-h evaluation. All of the other treated rabbits had no irritation at the 2- or 24-h evaluations. The skin irritation potential of the three products was considered minimal.[37-39]

Skin irritation to a nail hardener (product D) containing 8.26% TSFR-80 was assessed according to the methods described in Title 16 Parts 1500.3(c)(4) and 1500.41 of the Code of Federal Regulations.[29,40] The wet product (0.5 ml) was applied for 24 h under an occlusive patch to the intact and abraded skin of each of six rabbits. Skin reactions were evaluated 24, 48, and 72 h after application. The results were not specified; however, it was reported that the product was a "nonirritant" under conditions of this test.[30]

Subchronic Toxicity

Purebred beagle dogs were given TSFR in the diet at concentrations of 0, 1000, 3000, or 10,000 ppm for 90 days. The three treatment groups and the nontreated control group each consisted of 4 male and 4 female dogs (32 animals total). No deaths were reported throughout the study. Food consumption, behavior, blood chemistry parameters, and results of urinalyses of treated dogs were comparable to those of the untreated control group. At gross and microscopic examination of tissues and organs, no treatment-related lesions were found. "Slight to moderate body weight gain suppression" was noted among females fed 10,000 ppm TSFR; males at this same dietary concentration had body weight gains "somewhat lower" than those of untreated males, "although the gains were within normal limits for dogs of this age." Body weight gains at the two lower concentrations (1000 and 3000 ppm) were comparable to those of untreated controls. Erythrocyte counts, hemoglobin concentrations, and hematocrit values

Distributed for Comment Only -- Do Not Cite or Quote

among females fed 10,000 ppm were "slightly lower than those of untreated females"; however, "the values remained within or were slightly lower than the normal range." Hematological parameters for males administered 10,000 ppm TSFR were comparable to those of untreated males; no treatment related hematological effects were noted at 1000 or 3000 ppm. "Slightly elevated" liver:body weight ratios were observed in all males and one of four females given 10,000 ppm; however, "the liver to brain weight ratios for these 5 dogs did not exceed normal limits and liver enlargement was considered minimal." "Liver weights and ratios" in the 1000 ppm and 3000 ppm treatment groups "were considered normal." Remaining organ weight data "revealed no treatment related abnormalities" at any of the concentrations tested. In this study, the following parameters were determined: (1) hematological studies: total and differential leukocyte count, erythrocyte count, hemoglobin, and hematocrit; (2) blood chemistry studies: blood urea nitrogen, serum glucose, serum alkaline phosphatase, serum glutamic-oxalacetic transaminase, serum glutamic-pyruvic transaminase, serum sodium, serum potassium, serum chloride, serum calcium, and serum magnesium; and (3) urinalyses: albumin, glucose, pH, specific gravity, and microscopic elements. Weights of the following organs were obtained: liver, kidneys, heart, brain, spleen, gonads, adrenal glands, thyroid, and pituitary gland. Microscopic examination was made of the following tissues and organs: adrenal glands, aorta, bone marrow, brain, caecum, colon, esophagus, gallbladder, gonads, heart, kidneys, liver, lungs, lymph nodes, muscle, pancreas, peripheral nerve, pituitary gland, prostate gland, salivary gland, small intestine, spinal cord, spleen, stomach, trachea, thyroid, uterus, and urinary bladder.[41]

Mutagenicity

No mutagenicity was observed when TSFR, TSFR-80, and butyl acetate were tested with and without metabolic activation in the Ames assay with five *Salmonella* strains[42] (Table 5).

TABLE 5. Results of Mutagenicity Studies[a(42)]

Material tested	*Solvent*	*Metabolic activation*	*Dose*	*Result*
TSFR	DMSO	Yes	6 doses ranging from 20 to 1000 μg	Negative
TSFR	DMSO	No	7 doses ranging from 20 to 1500 μg; doses of 2000 to 3500 μg were toxic	Negative
TSFR-80	DMSO	Yes	7 doses ranging from 20 to 1500 μg; doses of 2000 to 3500 μg were toxic	Negative
TSFR-80	DMSO	No	7 doses ranging from 20 to 1500 μg; doses of 2000 to 3500 μg were toxic	Negative
Butyl acetate	As is	Yes	5 doses ranging from 1.764 to 44.1 mg; a dose of 88.2 mg was toxic	Negative
Butyl acetate	As is	No	6 doses ranging from 1.764 to 88.2 mg; doses of 132.3 to 308.7 mg were toxic	Negative

[a]*Salmonella typhimurium* indicator strains used included TA98, TA1535, TA100, TA1537, and TA1538.

Distributed for Comment Only -- Do Not Cite or Quote

CLINICAL ASSESSMENT OF SAFETY

Skin Irritation, Sensitization, and Photosensitization

The skin irritation, sensitization, and photosensitization potential of various nail products containing 4.9–12.0% TSFR-80 were assessed in clinical studies. Results of these investigations indicated that these cosmetic products were nonsensitizing, nonphotosensitizing, and essentially nonirritating to the human skin. TSFR in dimethyl phthalate also was nonirritating and nonsensitizing. These assays are described below; results are summarized in Table 6.

A 10% w/v solution of TSFR in dimethyl phthalate was not an irritant, fatiguing agent, or sensitizer when applied to the intact and abraded skin of 50 subjects in a Shelanski Repeated Insult Patch Test. The induction phase consisted of 15 serial applications, followed 10–14 days later by a challenge application.[6,43]

A single insult occlusive patch procedure was used to evaluate the skin-irritating effects of three different nail polish and enamel products. All three products (A, B, and C) were formulated with 12% TSFR-80. Each product was placed on a Blenderm patch from which the solvents were allowed to evaporate. The patch was then applied to the forearm or upper arm of 18 panelists. The patch remained in place either 24 or 48 h. Skin responses were evaluated 2 and 24 h after patch removal. No irritation was observed in the 36 panelists treated with products A or B.[44,45] One of 18 subjects developed minimal skin erythema to product C.[46]

A nail hardener (product D) containing 8.26% TSFR-80 caused no skin irritation when applied to the nails of 51 subjects for 4 weeks in a controlled use study.[47] The areas examined included the fingernails, nailbeds, nail folds, and surrounding skin.

A modified Shelanski and Shelanski repeat insult patch test was used to determine the skin irritation and sensitization potential of a nail polish (product E) containing 4.9% TSFR-80.[55] The wet product was applied for 24 h by means of a patch every Monday, Wednesday, and Friday for a total of 10 induction applications. After a 2–3 week nontreatment period, a challenge patch was applied for 48 h. Reactions were graded according to the scoring system described by Wilkinson and Moore.[15] No skin irritation or sensitization was noted in any of the 53 panelists.[48]

Ninety-seven panelists (96 females and 1 male, aged 16–70) were tested with a nail strengthener containing 7.4% TSFR-80 for skin irritation and sensitization. Subjects with known skin diseases were excluded from the study. Approximately 0.1 ml of the product was dispensed onto a patch one-half hour before application to allow for evaporation of the volatile ingredients. Induction patches containing the test material were applied to the same site of the upper back for 24 h every Monday, Wednesday, and Friday for 3 consecutive weeks. A challenge patch was applied for 24 h to a previously untreated site on Tuesday of the sixth week. Challenge reactions were assessed 24 and 48 h after patch removal. Two subjects developed skin reactions at the treatment site during the induction phase. One of these individuals had mild erythema after the ninth induction patch. The second subject had barely perceptible to mild skin erythema after the sixth, seventh, and eighth induction patches. No skin reactions were observed to

Distributed for Comment Only -- Do Not Cite or Quote

TABLE 6. Clinical Studies with Products Containing Toluenesulfonamide/Formaldehyde Resin-80

Type of test	*Material tested*	*TSFR or TSFR-80 concentration (%)*	*No. of subjects*	*Procedure*	*Result*	*Reference*
Skin irritation/ sensitization	TSFR in dimethyl phthalate	10 (TSFR)	50	Shelanski repeat insult patch test: 15 induction applications to abraded and intact skin; after 10–14 day nontreatment period, challenge patch applied	No skin irritation or sensitization	6,43
Skin irritation	Nail polish and enamel[a] (product A)	12 (TSFR-80)	18	Single insult occlusive patch	No skin irritation	44
Skin irritation	Nail polish and enamel[a] (product B)	12 (TSFR-80)	18	Single insult occlusive patch	No skin irritation	45
Skin irritation	Nail polish and enamel[a] (product C)	12 (TSFR-80)	18	Single insult occlusive patch	One subject developed minimal skin erythema	46
Skin irritation	Nail hardener[b] (product D)	8.26 (TSFR-80)	51	Applied to nails daily for 4 weeks	No irritation of the skin surrounding the nails	47
Skin irritation/ sensitization	Nail polish[b] (product E)	4.9 (TSFR-80)	53	Modified Shelanski and Shelanski repeat insult patch test: product applied to skin by 24-h patch every Mon., Wed., Fri. for 3 weeks; after 2–3 week nontreatment period, 48-h challenge patch applied	No skin irritation or sensitization	48
Skin irritation/ sensitization	Nail strengthener[a]	7.4 (TSFR-80)	97	Repeat insult patch test: product applied to skin every Mon., Wed., Fri. for 3 weeks; after 2 week nontreatment period, 24-h challenge patch applied	Two subjects developed mild skin erythema during induction phase; no sensitization reactions observed	49

Distributed for Comment Only -- Do Not Cite or Quote

Skin irritation/ sensitization	Nail color[a]	6.5 (TSFR-80)	148	Draize-Shelanski-Jordan repeat insult patch test: product applied to skin every Mon., Wed., Fri. for 3 weeks; after 2 week nontreatment period, 2 consecutive 48-h challenge patches applied	No skin irritation or sensitization	50
Skin irritation/ sensitization	Nail color[a]	9.0 (TSFR-80)	203	Draize-Shelanski-Jordan repeat insult patch test: product applied to skin every Mon., Wed., Fri. for 3 weeks; after 2 week nontreatment period, 2 consecutive 48-h challenge patches applied	One subject developed faint skin erythema during induction phase; no skin sensitization observed	51
Skin irritation/ sensitization/ photosensitization	Nail polish[b] (product E)	4.9 (TSFR-80)	101	Schwartz and Peck[52] with UV exposure: For induction phase, set of open and closed patches applied to skin for 48 h; after 10 day nontreatment period, open and closed challenge patches applied for 48 h; treated sites exposed to UV irradiation during induction and challenge phases	One subject developed weak nonvesicular reaction to closed patch during induction phase; no other irritation, sensitization, or photosensitization reactions observed	48
Phototoxicity/ photosensitization	Nail color[c]	9.0 (TSFR-80)	30	Exposure to product and UV irradation repeated twice weekly for 3 weeks for a total of 6 induction treatments; after 10-day nontreatment period, product was applied under occlusion to previously untreated site; challenge site irradiated with UV light for 3 minutes	No phototoxic or photoallergic skin reactions observed	53

Distributed for Comment Only -- Do Not Cite or Quote

TABLE 6. (Continued)

Type of test	*Material tested*	*TSFR or TSFR-80 concentration (%)*	*No. of subjects*	*Procedure*	*Result*	*Reference*
Phototoxicity/ photosensitization	Nail color[c]	9.0 (TSFR-80)	28	Exposure to product and UV irradiation repeated twice weekly for 3 weeks for a total of 6 induction treatments; after 10-day nontreatment period, product was applied under occlusion to previously untreated site; challenge site irradiated with UV light for 3 minutes	No phototoxic or photoallergic skin reactions observed	54

[a]Test material was applied dry, i.e., solvents were allowed to evaporate prior to application.
[b]Test material was applied wet, i.e., solvents were not allowed to evaporate prior to application.
[c]Not specified whether or not solvents were allowed to evaporate prior to application.

Distributed for Comment Only -- Do Not Cite or Quote

the single challenge patch. It was concluded that the nail strengthener "did not exhibit any potential for inducing allergic sensitization."[49]

A Draize-Shelanski-Jordan repeat insult patch test was conducted to evaluate the skin irritation and sensitization potential of two different nail color products. One formulation contained 6.5% TSFR-80 and was evaluated on 148 subjects (89 females, 59 males).[50] The second nail product contained 9.0% TSFR-80 and was evaluated on 203 subjects (144 females, 59 males).[51] All panelists were between the ages of 18 and 65. Only subjects with no known skin diseases or allergies were selected for testing. Impermeable dry patches containing the test material were applied to the upper back on Monday, Wednesday, and Friday for 3 consecutive weeks for a total of nine induction exposures. After a 2-week nontreatment period, two consecutive 48-h challenge patches were applied to sites adjacent to the original induction site. Skin responses were scored on a scale of 0 (no reaction) to 4 (bullae or extensive erosion). The product containing 6.5% TSFR-80 produced "no significant reactions" during the induction phase. One subject developed a single 1+ reaction (macular, faint erythema involving 25% of the test area) during the induction phase to the product containing 9.0% TSFR-80. No skin sensitization was observed to either nail color product.[50,51]

One hundred one panelists were exposed in a modified Schwartz-Peck prophetic patch test to a nail polish (product E) containing 4.9% TSFR-80.[52] For the induction phase, a set of open and closed patches containing the wet product was applied for 48 h to the skin. Ten days after the induction exposure, a similar set of open and closed challenge patches was applied. The treated sites were exposed to UV irradiation during both induction and challenge phases. Skin reactions were evaluated according to the grading system described by Wilkinson et al.[56] One subject developed a weak, nonvesicular skin reaction to the closed induction patch. No other irritation, sensitization, or photoreactions were observed.[48] Test methodology for the UV exposure was not reported.

No phototoxicity or photosensitization was observed in groups of 30 or 28 human subjects exposed to UV irradiation and two nail color products each containing 9% TSFR-80. Before testing, the minimal erythemal dose (MED) of each panelist was determined in accordance with the procedures outlined in the Federal Register.[57] Occlusive patches containing the test material were applied to the back for 24 h (0.1 ml/cm^2). Upon removal of the patch, the site was irradiated with three times the individual's MED using a Xenon Arc Solar Simulator (150 W). The lamp was filtered to produce a continuous spectrum in the UVA and UVB region (290–400 nm). Forty-eight hours after UV exposure, the treated sites were scored for erythema, edema, and vesicular skin reactions. Exposure to product and UV irradiation was repeated twice weekly for 3 weeks for a total of six induction treatments. Following a 10-day nontreatment period, an occlusive patch containing the test material was applied for 24 h to a previously untreated site adjacent to the induction site. After removal of the patch, the challenge site was irradiated for 3 minutes. In this instance, a Schott WG 345 glass filter was placed over the lamp to remove UVB light. Challenge responses were evaluated 15 minutes, 24 h, 48 h, and 72 h postirradiation. No phototoxic or photoallergic reactions were detected in either of the two groups.[53,54] It was not specified whether or not the solvents of the two nail colors were allowed to evaporate before testing.

Distributed for Comment Only -- Do Not Cite or Quote

Nail Polish Dermatitis

Nail polish dermatitis of allergic origin rarely occurs in the region of the fingernails or toenails but occurs instead on parts of the body accessible to the nails. Four areas typically involved in nail polish dermatitis are the eyelids, the lower half of the face, the sides of the neck, and the upper chest. Areas less frequently involved are the bridge of the nose, forehead, retroauricular zone, shoulder, and vulva. Sometimes, widespread areas may be involved, resulting in generalized dermatitis.[19] Because dermatitis occurs most frequently at distant sites that come in contact with the moist nail lacquer, Fisher[58] described nail lacquer dermatitis as an "ectopic" dermatitis.

Although any ingredient in the nail polish may account for "distant allergic eczematous contact dermatitis," liquid TSFR and other thermoplastic resins are considered the primary causative agents.[19,59] According to Fisher,[59] TSFR is the most common cause of nail polish dermatitis, whereas the film formers (usually nitrocellulose), plasticizers, solvents, and coloring agents in nail enamels are only rarely the cause of allergic contact dermatitis. Many nail enamels contain synthetic resins that are applied in a "partially polymerized liquid state."[59] Fisher[58,59] and Baran[19] claim that as TSFR-80 and other liquid thermoplastic resins dry, they become less sensitizing to the skin, and when completely dry, these resins are only very weak allergens. Fisher[58,59] suggests that individuals who are allergic to a nail polish can use that same polish provided the fingers do not contact the skin until the product has dried.

Case Reports

Wilkinson and Moore[15] reported that some nail lacquer users develop a skin sensitivity to aryl sulfonamide-formaldehyde resins. It was suggested that such persons use a nail varnish that does not include these resins.

Three women who acquired a dermatitis of the neck, face, and/or eyelids from various nail lacquers containing TSFR were studied. All three patients had positive patch test reactions to nail lacquers and to TSFR.[58]

Patients identified as "contact dermatitis cases" were patch tested with various cosmetic materials. Patches containing the materials were applied to the upper back for 48 h. Sixteen of the 8093 patients tested developed "cutaneous reactions" to TSFR. The concentration of TSFR and the test vehicle were not specified.[60]

Two women developed onycholysis of the fingernails following use of a hardener and polish containing TSFR. Both patients were patch tested with a standard patch test tray and to the nail hardener and polish. In both subjects, a "2+ reaction" was observed to the nail hardeners, TSFR, and 2% formaldehyde in petrolatum. Two months after discontinuance of the use of nail hardeners, all nails had regrowth and were "almost normal" in appearance.[61] The authors suspected that one of the nail products was the cause of the onycholysis.

Brauer[62] reported a number of deficiencies in the previous report by Paltzik and Enscoe.[61] He suggested that Paltzik and Enscoe did not prove "instances of onycholysis resulting from toluene sulfonamide/formaldehyde-containing products."

Distributed for Comment Only -- Do Not Cite or Quote

SUMMARY

Toluenesulfonamide/Formaldehyde Resin (TSFR) is available to cosmetic manufacturers in liquid (80% "solids" in a mixture of butyl acetate and butyl alcohol) and solid forms. It is prepared by the condensation of aryl or aromatic sulfonamides with formaldehyde.

TSFR has several indirect food additive uses. It is used as a "side seam cement" for articles intended for food contact, as a component of paper and paperboard in contact with food, and as a component of cellophane packaging material intended for food contact. TSFR-80 is used as a solvent for nitrocellulose and cellulose acetate and is used in lacquers to make clear coatings.

TSFR and TSFR-80 are used in such cosmetic products as nail basecoats and undercoats, nail polish and enamel, and other manicuring preparations. They impart high gloss, moisture resistance, and flow characteristics to these products, as well as increase the hardness of nitrocellulose and ethyl cellulose films. Data submitted to the FDA in 1981 under the voluntary cosmetic registration program indicated that TSFR and TSFR-80% were used in approximately 567 of the registered nail products. The majority of formulations contained this resin in the concentration range of > 5 to 10%.

The fingernail, toenail, nail cuticle, and skin surrounding the nail are the areas directly exposed to cosmetics containing TSFR and TSFR-80. The wet nail may also come in contact with such areas as the eye region, the face, the neck, and the vulva.

In acute studies, TSFR was practically nontoxic to rats when given orally as a 70% solution in acetone and was practically nontoxic to rabbits when applied to the skin as a 40% suspension in corn oil. TSFR in the form of a finely ground powder was nonirritating to rabbit skin and slightly irritating to the rabbit eye. No significant treatment-related effects were observed in a subchronic oral study in which beagle dogs were administered 1000, 3000, or 10,000 ppm TSFR. TSFR was nonmutagenic in the Ames assay.

In acute studies with TSFR-80, the undiluted material was nonirritating to rabbit skin, slightly irritating to the rabbit eye, and practically nontoxic to rabbits by dermal application. TSFR-80 also was practically nontoxic to rats when given orally as a 50% solution in alcohol. Nail polish and enamel formulations containing approximately 12% TSFR-80 were nontoxic to rats by oral administration, severely irritating to the rabbit eye, and minimally irritating to rabbit skin. TSFR-80 was negative in the Ames test for mutagenicity.

In clinical studies, 10% TSFR in dimethyl phthalate was nonirritating and nonsensitizing to the skin. Nail products containing approximately 4.9–12.0% TSFR-80 were nonsensitizing, nonphotosensitizing, and essentially nonirritating to the human skin.

Reports in the literature suggest that nail polish dermatitis of allergic origin rarely occurs in the region of the fingernails or toenails but rather on parts of the body accessible to the nails. Because dermatitis occurs most frequently at sites that come in contact with the wet nail lacquer, nail lacquer dermatitis is referred to as an "ectopic" dermatitis.

Although any ingredient in the nail polish may account for allergic contact dermatitis, it is reported that TSFR-80 and other liquid thermoplastic resins are

Distributed for Comment Only -- Do Not Cite or Quote

the probable primary causative agents. These resins are applied to the nail in a partially polymerized liquid state. It is claimed that as these resins dry, they become less sensitizing to the skin. When completely dry, they are purported to be only very weak allergens.

DISCUSSION

Although the clinical data were limited to studies with products, it is the Panel's opinion that the combined animal and clinical data were sufficient to assess the safety of TSFR and TSFR-80.

CONCLUSION

On the basis of the available data, the CIR Panel concludes that Toluenesulfonamide/Formaldehyde Resin (TSFR) and Toluenesulfonamide/Formaldehyde Resin-80% (TSFR-80) are safe as cosmetic ingredients in the present practices of use and concentration.

ACKNOWLEDGMENT

Jonathon T. Busch, Senior Scientific Analyst, prepared the literature review and Technical Analysis of this report. Word processing for the report was performed by Karen Swanson.

REFERENCES

1. ESTRIN, N.F., CROSLEY, P.A., and HAYNES, C.R. (1982). *CTFA Cosmetic Ingredient Dictionary*. Washington, D.C.: Cosmetic, Toiletry and Fragrance Assoc., p. 320.
2. COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION (CTFA). (July 12, 1984). Submission of data by CTFA. Cosmetic Ingredient Chemical Description. Toluenesulfonamide/Formaldehyde Resin. CTFA Code No. 2-43-18.*
3. NATIONAL LIBRARY of MEDICINE. (1984). Medlars Computerized Data Base. Dept. of Health and Human Services. Bethesda, Md., Computer File: Chemline.
4. COSMETIC INGREDIENT REVIEW. (1984). Final report on the safety assessment of formaldehyde. J. Am. Coll. Toxicol. 3(3), 157–184.
5. ESTRIN, N.F., HAYNES, C.R., and WHELAN, J.M. (1982). *Cosmetic Ingredient Descriptions. CTFA Compendium of Cosmetic Ingredient Composition. Toluenesulfonamide/Formaldehyde Resin*. Washington, D.C.: The Cosmetic, Toiletry and Fragrance Association, Inc.
6. MONSANTO COMPANY. (January 27, 1983). Monsanto Material Safety Data Sheet. MSDS No. 001338518. Santolite MHP Resin.*
7. PLANT, A.F. (1982/1983). *Chemcylopedia*. Washington, D.C.: American Chemical Society. Vol. 1, p. 143.
8. MONSANTO COMPANY. (October 1, 1982). Monsanto Material Safety Data Sheet MSDS No. M00006698. Santolite MS-80 percent Resin.*

*Available upon request: Director, Cosmetic Ingredient Review, Suite 810, 1110 Vermont Ave. NW, Washington, DC 20005.

9. HAWLEY, G.G. (1971). *The Condensed Chemical Dictionary*, 8th ed. New York: Van Nostrand Reinhold Company, Santolite, p. 773.
10. DOVIAK, W.C. (1972). Nail lacquers and removers, Chap. 29 in: M.S. Balsam and E. Sagarin (eds.). *Cosmetics–Science and Technology*, 2nd ed. New York: Wiley-Interscience, Vol. 2, pp. 521–541.
11. CODE OF FEDERAL REGULATIONS (CFR). (Revised as of April 1, 1984). Title 21 Part 177.1200. Cellophane. Washington, D.C.: U.S. Government Printing Office.
12. CFR. (Revised as of April 1, 1984). Title 21 Part 175.105. Adhesives. Washington, D.C.: U.S. Government Printing Office.
13. CFR. (Revised as of April 1, 1984). Title 21 Part 175.300. Resinous and polymeric coatings. Side seam cements. Washington, D.C.: U.S. Government Printing Office.
14. CFR. (Revised as of April 1, 1984). Title 21 Part 176.170. Components of paper and paper-board in contact with aqueous and fatty foods. Washington, D.C.: U.S. Government Printing Office.
15. WILKINSON, J.B., and MOORE, R.J. (1982). *Harry's Cosmeticology*, 7th ed. New York: Chemical Publishing, Chap. 22, pp. 369–393.
16. FOOD AND DRUG ADMINISTRATION (FDA). (December 22, 1981). Cosmetic product formulation data: Ingredients used in each product category. Computer printout. Washington, D.C.
17. FDA. (January 5, 1982). (a) Frequency of Trade Name Ingredients in the Cosmetic Product File, and (b) Frequency of Common, Usual, or Chemical Names in the Cosmetic Product File. Computer printout. Washington, D.C.
18. CFR. (Revised as of April 1, 1984). Title 21 Part 720.4. Voluntary filing of cosmetic product ingredient and cosmetic raw material composition statement. Information requested about cosmetic products.
19. BARAN, R. (1982). Pathology induced by the application of cosmetics to the nail, in: P. Frost and S.N. Horwitz (eds.). *Principles of Cosmetics For The Dermatologist*. St. Louis, Mo.: C.V. Mosby Co., Chap. 24, pp. 181–184.
20. DUFFY, J.A. (August 11, 1981). Nail enamel composition. U.S. Patent No. 4283324. Avon Products Inc.
21. BENKENDORF, S., CALAMITO, F.A., and ZACCARIA, C.M. (December 20, 1983). Nitrocellulose fingernail lacquer containing gelatin and acrylic copolymers. U.S. Patent No. 4421881.
22. ISODA, T. (October 26, 1979). Perfumed nail lacquers. Jpn. Kokai Tokkyo Koho Patent No. 79138134. Isehan K.K.
23. KALOPISSIS, G. (November 19, 1974). Colored nail polishes. U.S. Patent No. 3849547. Oreal S.A.
24. YOUNGER LABORATORIES, INC. (March 27, 1974). Submission of data by Monsanto Co. Toxicologic investigation of Santolite MHP. Project No. Y-74-24. Acute oral, acute dermal, acute eye and primary skin irritation.*
25. YOUNGER LABORATORIES, INC. (July 12, 1974). Submission of data by Monsanto Co. Toxicologic investigation of Santolite MS 80 percent. Acute oral, acute dermal, acute eye and primary skin irritation.*
26. CTFA. (May 6, 1980). Submission of unpublished data by CTFA. Acute oral toxicity. CTFA Code No. 2-43-1.*
27. CTFA. (May 6, 1980). Submission of unpublished data by CTFA. Acute oral toxicity. CTFA Code No. 2-43-3.*
28. CTFA. (May 8, 1980). Submission of unpublished data by CTFA. Acute oral toxicity. CTFA Code No. 2-43-2.*
29. CFR. (Revised as of April 1, 1984). Title 16 Part 1500.3 Sections: (b)(6)(i)(A); (c)(1)(ii)(C); and (c)(4). Definitions. Washington, D.C.: U.S. Government Printing Office.
30. CTFA. (March 23, 1984). Submission of unpublished data by CTFA. CIR safety data test summary response form. Oral intubation; dermal toxicity; skin irritation; ocular irritation. CTFA Code No. 2-43-19).*
31. DRAIZE, J.H. (1959). *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics*. Austin, Texas: Association of Food and Drug Officials of the U.S., Texas State Dept. of Health.
32. CTFA. (April 21, 1980). Submission of unpublished data by CTFA. Eye irritation. CTFA Code No. 2-43-4.*
33. CTFA. (April 21, 1980). Submission of unpublished data by CTFA. Eye irritation. CTFA Code No. 2-43-5.*
34. CTFA. (April 21, 1980). Submission of unpublished data by CTFA. Eye irritation. CTFA Code No. 2-43-6.*
35. CFR. (Revised as of April 1, 1984). Title 16 Part 1500.42. Test for eye irritants. Washington, D.C.: U.S. Government Printing Office.
36. CFR. (Revised as of April 1, 1984). Title 16 Part 1500.40. Method of testing toxic substances. Washington, D.C.: U.S. Government Printing Office.
37. CTFA. (March 31, 1980). Submission of unpublished data by CTFA. Primary skin irritation. CTFA Code No. 2-43-7.*
38. CTFA. (March 31, 1980). Submission of unpublished data by CTFA. Primary skin irritation. CTFA Code No. 2-43-8.*

Distributed for Comment Only -- Do Not Cite or Quote

39. CTFA. (March 31, 1980). Submission of unpublished data by CTFA. Primary skin irritation. CTFA Code No. 2-43-9.*
40. CFR. (Revised as of April 1, 1984). Title 16 Part 1500.41. Method of testing primary irritant substances. Washington, D.C.: U.S. Government Printing Office.
41. INDUSTRIAL BIO-TEST LABORATORIES, INC. (February 14, 1975). Final Report to Monsanto Co. Submission of data by Monsanto Co. Ninety-day subacute oral toxicity study with Santolite MHP Technical in beagle dogs. BTL No. 73-68. IBT 611-04770.*
42. CTFA. (September 5, 1985). Submission of unpublished data by CTFA. Mutagenicity studies on butyl acetate, Santolite MHP and Santolite 80.
43. INDUSTRIAL BIOLOGY RESEARCH AND TESTING LABORATORIES. (June 6, 1985). Letter to Dr. R. Emmet Kelley (Monsanto Co.) from Morris V. Shelanski (Industrial Bio-Test Labs) regarding Santolite MHP: Percutaneous absorption and repeat insult patch test.*
44. CTFA. (June 26, 1980). Submission of unpublished data by CTFA. Skin irritation potential. Human patch test. CTFA Code No. 2-43-10.*
45. CTFA. (June 26, 1980). Submission of unpublished data by CTFA. Skin irritation potential. Human patch test. CTFA Code No. 2-43-11.*
46. CTFA. (June 26, 1980). Submission of unpublished data by CTFA. Skin irritation potential. Human patch test. CTFA Code No. 2-43-12.*
47. CTFA. (March 19, 1984). Submission of unpublished data by CTFA. CIR safety data test summary response form. Controlled use study. CTFA Code No. 2-43-20.*
48. CTFA. (February 24, 1984). Submission of unpublished data by CTFA. CIR safety data test summary response form. Schwartz and Peck prophetic patch test. Repeat insult patch test. Shelanski and Shelanski CTFA Code No. 2-43-21.*
49. CTFA. (February 17, 1978). Submission of unpublished data by CTFA. Allergic contact sensitization test. Test No. 036-78. Nail strengthener No. 13841-01. CTFA Code No. 2-43-14.*
50. CTFA. (June 2, 1980). Submission of unpublished data by CTFA. CIR Safety data test summary response form. Draize-Shelanski-Jordan RIPT. CTFA Code No. 2-43-15.*
51. CTFA. (Nov. 16, 1982). Submission of unpublished data by CTFA. CIR safety data test summary response form. Draize-Shelanski-Jordan RIPT. CTFA Code No. 2-43-13.*
52. SCHWARTZ, L., and PECK, S.M. (1944). The patch test in contact dermatitis. Public Health Rep. **59,** 546–557.
53. CTFA. (August 1, 1979). Submission of unpublished data by CTFA. CIR safety data test summary response form. Photopatch test. CTFA Code No. 2-43-17.*
54. CTFA. (September 10, 1979). Submission of unpublished data by CTFA. CIR safety data test summary response form. Photopatch test. CTFA Code No. 2-43-16.*
55. SHELANSKI, H.A., and SHELANSKI, M.V. (1953). A new technique of human patch tests. Proceedings of the Scientific Section of the Toilet Goods Assoc. No. 19, May, 46–49.
56. WILKINSON, D.A., FREGERT, S., MAGNUSSON, B., et al. (1970). Terminology of contact dermatitis. Acta Dermatovener (Stockholm) **50,** 287–292.
57. FEDERAL REGISTER. (1978). Sunscreen Drug Products for Over-The-Counter Drugs. August 25: 38206–38369.
58. FISHER, A.A. (1981). Allergen replacement (alternatives) in the management of contact dermatitis. Cutis **28**(4), 368–370, 372.
59. FISHER, A. (1973). *Contact Dermatitis*. Philadelphia: Lea & Febiger, p. 232.
60. EIERMANN, H.J., LARSEN, W., and MAIBACH, H.I. (1982). Prospective study of cosmetic reactions. J. Acad. Dermatol. **6**(5), 909–917.
61. PALTZIK, R.L., and ENSCOE, I. (1980). Oncholysis secondary to toluenesulfonamide formaldehyde resin used in a nail hardener mimicking onychomycosis. Cutis **25**(June), 647–648.
62. BRAUER, E.W. (1980). Letter to the Editor. Onycholysis secondary to toluene sulfonamide formaldehyde resin. Cutis **26**(6), 588.

Distributed for Comment Only -- Do Not Cite or Quote

monitoring of exposure to toluene in human volunteers. *Appl. Occup. Environ. Hyg*. 13:127–132.

Taskinen, H., A. Antilla, M. L. Lindbohm, M. Sallmen, et al. 1989. Spontaneous abortions and congenital malformations among the wives of men occupationally exposed to organic solvents. *Scand. J. Work. Environ. Health.* 15:345–352.

Tassaneeyakul, W., D. J. Birkett, J. W. Edwards, M. E. Veronese, et al. 1996. Human cytochrome P450 isoform specificity in the regioselective metabolism of toluene and *o*-, *M*-, and *p*-xylene. *J. Pharmacol. Exp. Therapeut.* 276:101–108.

Thiel, R., and I. Chahoud. 1997. Postnatal development and behaviour of Wistar rats after prenatal toluene exposure. *Arch. Toxicol.* 71:258–265.

Thrall, K. D., K. K. Weitz, and A. D. Woodstock. 2002. Use of real-time breath analysis and physiologically based pharmacokinetic modeling to evaluate dermal absorption of aqueous toluene in human volunteers. *Toxicol. Sci.* 68:280–287.

Toyonaga, N., E. Adachi-Usami, and H. Yamazaki. 1989. Clinical and electrophysiological findings in three patients with toluene dependency. *Doc. Ophthalmol.*73:201–207.

Truchon, G., R. Tardiff, and J. Brodeur. 1996. Gas chromatographic determination of urinary *o*-cresol for the monitoring of toluene exposure. *J. Anal. Toxicol.* 20:309–312.

Ukai, H., T. Watanabe, H. Nakatsuka, T. Satoh, et al. 1993. Dose-dependent increase in subjective symptoms among toluene-exposed workers. *Environ. Res.* 60:274–289.

Unger, E., A. Alexander, T. Fritz, N. Rosenberg, et al. 1994. Toluene abuse: Physical basis for hypointensity of the basal ganglia on T2-weighted MR images. *Radiology* 193:473–746.

Urban, P., and E. Lukáš. 1990. Visual evoked potentials in rotogravure printers exposed to toluene. *Br. J. Indust. Med.* 47:819–823.

Verma, Y., and S. V.S. Rana. 2003. Gender differences in the metabolism of benzene, toluene and trichloroethylene in rat with special reference to certain biochemical parameters. *J. Environ. Biol.* 24:135–140.

Von Euler, G., K. Fuxe, T. Hansson, and P. Eneroth. 1989. Persistent effects of neonatal toluene exposure on regional brain catecholamine levels and turnover in the adult male rat. *Toxicology* 54:1–16.

Von Euler, G., K. Fuxe, T. Hansson, and J.Å. Gustafsson. 1988a. Effects of toluene treatment in vivo and in vitro on the binding characteristics of [^{3}H]neurotensin in rat striatal membranes. *Toxicology* 49:149–154.

Von Euler, G., K. Fuxe, T. Hannsson, and S. O. Ogren,. 1988b. Effects of chronic toluene exposure on central monoamine and peptide receptors and their interactions in the adult male rat. *Toxicology.* 52:103–126.

Von Euler, G., E. Hansson, and K. Fuxe. 1989. Toluene treatment in vitro and calcium regulated protein phosphorylation in primary astroglial cell cultures from the rat striatum. *Toxicol. In Vitro* 3:235–240.

Von Euler, G., S. O. Ogren, S. C. Bondy, and M. McKee. 1991. Subacute exposure to low concentrations of toluene affects dopamine-mediated locomotor activity in the rat. *Toxicology* 67:333–349.

Von Euler, G., S.O Ogren, P. Eneroth, and K. Fuxe. 1994. Persistent effects of 80 ppm toluene on dopamine-regulated locomotor activity and prolactin secretion in the male rat. *NeuroToxicology* 15:621–624.

Von Euler, G., S. O. Ogren, X. M. Li, and K. Fuxe et al. 1993. Persistent effects of subchronic toluene exposure on spatial learning and memory, dopamine-mediated locomotor activity and dopamine D_2 agonist binding in the rat. *Toxicology* 77:223–232.

Von Euler, M., T. M. Pham, M. Hillefors, and B. Bjelke. 2000. Inhalation of low concentrations of toluene induces persistent effects on a learning retention task, beam-walk performance, and cerebrocortical size in the rat. *Exp. Neurol.* 163:1–8.

Vrca, A., D. Bozicevic, V. Karacic, and R. Fuchs. 1995. Visual evoked potentials in individuals exposed to long-term low concentrations of toluene. *Arch. Toxicol.* 69:337–340.

Vrca, A., V. Karacic, D. Bozicevic, and V. Bosikov. 1996. Brainstem auditory evoked potentials in individuals exposed to long-term low concentrations of toluene. *Am. J. Ind. Med.* 30:62–66.

Wada, H. 1989. Single toluene exposure and changes of response latency in shock avoidance performance. *Neurotoxicol. Teratol.* 11:265–272.

Wada, H.. 1999. Toluene and temporal discrimination in rats: Effects on accuracy, discriminability, and time estimation. *Neurotoxicol. Teratol.* 21:709–718.

Wada, H., T. Hosokawa, and K. Saito. 1988. Repeated toluene exposure and changes of response latency in shock avoidance learning. *Neurotoxicol. Teratol.* 10:387–391.

Wang, G., G. Maranelli, L. Perbellini, and G. Guglielmi. 1993. Reference values for blood toluene in the occupationally nonexposed general population. *Int. Arch. Occup. Environ. Health* 65:201–203.

Wang, R. S., T. Nakajima, S. S. Park, and H. V. Gelboin. 1993. Monoclonal antibody-directed assessment of toluene induction of rat hepatic cytochrome P450 isozymes. *Biochem. Pharmacol.* 46:413–419.

Washington, W. J., A. Wilson, C. Lyons, and D. Dennie. 1989. Lack of toluene-induced dominant lethals in rats. *Ohio J. Sci.* 89:2–4.

Wiebelt, H. and N. Becker. 1999. Mortality in a cohort of toluene exposed *employees (Rotogravure printing plant workers). J Occup. Environ. Med.* 41:1134–1139.

Wiley, J. L., A. S. Bale, and R. L. Balster. 2003. Evaluation of toluene dependence and cross-sensitization to diazepam. *Life Sci.* 72:3023–3033.

Wilkins-Haug, L., and P. A. Gabow. 1991. Toluene abuse during pregnancy: Obstetric complications and perinatal outcomes. *Obstet. Gynecol.* 77:504–509.

Wood, R. W., and V. A. Colotla. 1990. Biphasic changes in mouse motor activity during exposure to toluene. *Fundam. Appl. Toxicol.* 14:6–14.

Wood, R. W., and C. Cox. 1995. A repeated measures approach too the detection of the acute behavioral effects of toluene at low concentrations. *Fundam. Appl. Toxicol.* 25:293–301.

Xiong, L., J. D. Matthes, J. Li, and J. R. Jinkins. 1993. MR imaging of "spray heads": Toluene abuse via aerosol paint inhalation. *Am. J. Neuroradiol.* 14:1195–1199.

Yamada, K. 1993. Influence of lacquer thinner and some organic solvents on reproductive and accessory reproductive organs in the male rat. *Biol. Pharm. Bull.* 16:425–427.

Yamaguchi, H., Y. Kidachi, and K. Ryoyama. 2002. Toluene at environmentally relevant low levels disrupts differentiation of astrocyte precursor cells. Arch. *Environ. Health* 57:232–238.

Yelian, F. D., and W. R. Dukelow. 1992. Cellular toxicity of toluene on mouse gamete cells and preimplantation embryos. *Arch. Toxicol.* 66:443–445.

Zavalic, M., Z. Mandic, R. Turk, A. Bogandi-Sare, et al. 1998a. Assessment of color vision impairment in male workers exposed to toluene generally above occupational exposure limits. *Occup. Med.* 48:175–180.

Zavalic, M., Z. Mandic, R. Turk, A. Bogandi-Sare, et al. 1998b. Qualitative color vision impairment in toluene-exposed workers. *Int. Arch. Occup. Environ. Health.* 71:194–200.

TOLUENESULFONAMIDE/FORMALDEHYDE RESIN

A safety assessment of Toluenesulfonamide/Formaldehyde Resin (including Toluenesulfonamide/Formaldehyde Resin-80) was published in 1986 with the conclusion that these ingredients were safe as cosmetic ingredients in the present practices of use and concentration (Elder 1986). Studies available since that time, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. Based on its consideration of the available data, the Panel decided to not reopen this safety assessment.

The terminology for this ingredient in the *International Cosmetic Ingredient Dictionary and Handbook* has changed—Tosylamide/Formaldehyde Resin is the current terminology (Gottschalck and McEwen 2004).

Distributed for Comment Only -- Do Not Cite or Quote

TABLE 27
Historical and current cosmetic product uses and concentrations for Tosylamide/Formaldehyde Resin

Product category	1981 uses (Elder 1986)	2002 uses (FDA 2002)	1981 use concentrations (Elder 1986) %	2003 use concentrations (CTFA 2004) %
	Tosylamide/Formaldehyde Resin			
Nail care products				
Basecoats and undercoats	31	—	1–10	8–11
Nail polishes and enamels	172	29	≤0.1–25	7–13
Other	8	—	1–10	7–8
Total uses/ranges for Tosylamide/Formaldehyde Resin	**211**	**29**	**≤0.1–25**	**7–13**
	Tosylamide/Formaldehyde Resin-80			
Nail care products				
Basecoats and undercoats (44)	5	—	1–10	—
Nail polishes and enamels (767)	344	—	≤0.1–25	—
Other (50)	7	—	≤0.1–25	—
Total uses/ranges for Tosylamide/Formaldehyde Resin-80	**356**	**29**	**≤0.1–25**	—

Tosylamide/Formaldehyde Resin was used in 211 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from ≤0.1%–25% (Elder 1986). In 2002, stearyl alcohol was reportedly used in 29 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2003 indicated that Toluene was used in a range from 7%–13% (CTFA 2004).

Tosylamide/Formaldehyde Resin-80 was used in 356 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from ≤0.1%–25% (Elder 1986). In 2002, there were no reports of use (FDA 2002), nor did an industry survey in 2003 indicated any current use concentrations (CTFA 2004).

Table 27 provides the available data on usage and use concentration as a function of cosmetic product category. The most current information now represents the present practices of use and concentration.

Case reports of allergic reaction to nail care products containing Tosylamide/Formaldehyde Resin were consistent with the data in the original safety assessment.

REFERENCES

Berne, B., A. Boström, A. F. Grahfén, and M. Tammela. 1996. Adverse effects of cosmetics and toiletries reported to the Swedish Medical Products Agency 1989–1994. *Contact Dermatitis* 34:359–362.

Cosmetic, Toiletry, and Fragrance Association (CTFA). 2004. Survey of Tosylamide/Formaldehyde Resin usage. Unpublished data submitted by CTFA.[28] 1 page.

de Groot, A., D. P. Bruynzeel, J. D. Bos, et al. 1988. The allergens in cosmetics. *Arch Dermatol*. 124:1525–1529.

De Wit, F. S., A. C. de Groot, J. W. Weyland, and J. D. Bos 1988. An outbreak of contact dermatitis from toluenesulfnamide Formaldehyde resin in a nail hardener. *Contact Dermatitis*. 18:280–283.

Duarte, I., R. Lazzarinin, and C. M. Kobata 2003. Contact dermatitis in adolescents. *Am. J. Contact Dermatitis* 14:200–204.

Elder, R. L. 1986. Final report on the safety assessment of Toluenesulfonamide/Formaldehyde Resin. *J. Am. Coll. Toxicol.* 5:471–490.

Giorgini, S., C. Brusi, S. Francalanci, et al. 1994. Prevention of allergic contact dermatitis from nail vanishes and hardeners. *Contact Dermatitis* 31:325–326.

Gottschalck, T., and G. N. McEwen, Jr. 2004.*International cosmetic ingredient dictionary and handbook*. Washington, DC: CTFA.

Guin, J. D., K. Baas, and P. Nelson-Adesokan. 1998. Contact sensitization to cyanoacrylate adhesive as a cause of severe onychodystorphy. *Int. J. Dermatol.* 37:31–36.

Hausen, B. M., M. Milbrodt, and W. A. Koenig. 1995. The allergens of nail polish. (I). Allergenic constituents of common nail polish and toluenesulfonamide-Formaldehyde resin (TS-F-R). *Contact Dermatitis* 33:157–164.

Lazarov, A. 1999. Perianal contact dermatitis caused by nail lacquer allergy. *Am. J. Contact Dermatitis* 10:43–44.

Staines, K. S., D. H. Felix and A. Forsyth. 1998. Desquamative gingivitis, sole manifestation of tosylamide/formaldehyde resin allergy. *Contact Dermatitis* 39:90.

Vilaplana, J., and C. Romaguera. 2000. Contact dermatitis from tosylamide/formaldehyde resin with photosensitivity. *Contact Dermatitis* 42:311–312.

TRAGACANTH GUM

A safety assessment of Tragacanth Gum was published in 1987 with the conclusion that these ingredients were safe as cosmetic ingredients in the present practices of use and concentration (Elder 1987). Studies available since that time, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. Based on its consideration of the available data, the Panel decided to not reopen this safety assessment.

[28] Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

Distributed for Comment Only -- Do Not Cite or Quote

C I R

September 9-10, 2004

Memorandum

To: CIR Expert Panel

From: Melody Chen
Scientific Analyst and Writer

Subject: Re-review of Tosylamide/Formaldehyde Resin (formerly called Toluenesulfonamide/Formaldehyde Resin)

In 1986, CIR issued a Final Report that "Toluenesulfonamide/Formaldehyde Resin (TSFR) and Toluenesulfonamide/Formaldehyde Resin-80% (TSFR-80) are safe as cosmetic ingredients in the present practices of use and concentration." A search for new literature since the original safety assessment yielded 8 references. All of them concern patients with allergic reactions to Tosylamide/Formaldehyde Resin (the current name). TSFR-80 is no longer listed as a separate ingredient.

A table with the historical and current uses and concentrations for TSFR and TSFR-80 has been included (Tables 1, 2). TSFR uses dropped from 211 to 29 in nail care products between 1981 and 2002; use concentrations appear to have stayed the same. No current uses were reported for TSFR-80, down from 356 in 1981.

The original report is attached.

The Panel should decide whether the new data warrant an amended conclusion.

Table 1. Historical and current cosmetic product uses and concentrations for Tosylamide/Formaldehyde Resin

Product Category (Total number of formulations)	1981 uses (Elder, 1986)	2002 uses (FDA, 2002)	1981 concentrations (Elder, 1986) (%)	2003 concentrations (CTFA, 2004) (%)
	Tosylamide/Formaldehyde Resin			
Nail care products				
Basecoats and undercoats (44)	31	-	1-10	8-11
Nail polishes and enamels (767)	172	29	≤0 1-25	7-13
Other (50)	8	-	1-10	7-8
Total uses/ranges for TSFR	**211**	**29**		

Table 2. Historical and current cosmetic product uses and concentrations for Toluenesulfonamide/Formaldehyde Resin-80%

Product Category (Total number of formulations)	1981 uses (Elder, 1986)	2002 uses (FDA, 2002)	1981 concentrations (Elder, 1986) (%)	2003 concentrations (CTFA, 2004) (%)
	Toluenesulfonamide/Formaldehyde Resin-80%			
Nail care products				
Basecoats and undercoats (44)	5	-	1-10	-
Nail polishes and enamels (767)	344	-	≤0 1-25	-
Other (50)	7	-	≤0 1-25	-
Total uses/ranges for TSFR-80	**356**			

Distributed for Comment Only -- Do Not Cite or Quote

Tosylamide/Formaldehyde Resin

Tosylamide/Formaldehyde Resin, called Toluenesulfonamide/Formaldehyde Resin (TSFR) until 1991 along with Toluenesulfonamide/Formaldehyde Resin-80% (TSFR-80) (Nikitakis et al. 1991) is a polymer used in nail varnishes. In 1986, the CIR Expert Panel concluded that TSFR and TSFR-80 were safe as cosmetic ingredients (Elder 1986). A search for new literature since the original safety assessment yielded 8 references. Their summaries are given below.

Eight female patients who were allergic to a particular brand of nail hardener containing 9.1% Tosylamide/Formaldehyde Resin. All patients had dermatitis on the face, the ears, the neck or the chest. The patients were patch tested with the nail hardener (all reacted to it). All reacted to Tosylamide/Formaldehyde Resin (10% pet). After stopping the use of the nail hardener and nail lacquers containing Tosylamide/Formaldehyde Resin, the dermatitis cleared in all patients, and no recurrences have been reported (de Wit et al. 1988).

In 119 patients with cosmetic allergies, a total of 53 allergens were found. Patients were patch tested according to internationally accepted methods in a multicenter study. The most frequent contact allergen was Kathon CG, reacting in 33 patients (27.7%). Second was Tosylamide/Formaldehyde Resin (10% pet), causing cosmetic related contact dermatitis in 15 patients (12.6%) (de Groot et al. 1988).

Tosylamide/Formaldehyde Resin was patch tested in 10% pet. in 366 patients and 14 were positive. All the positive cases were female and ranged from 16 to 59 years of age. All patients reported that they had used 1 or more nail varnishes or

hardeners or months or years before the onset of dermatitis. In all patients, dermatitis cleared completely upon stopping the use of nail products (Giorgini et al. 1994).

In spring 1994, 12 female patients with proven nail polish allergy were patch tested. All but 3 reacted to Tosylamide/Formaldehyde Resin. They had been tested with 20 other nail polish components and only 2 fractions were positive. These contained a monomer and a dimer created during the condensation of Tosylamide/Formaldehyde Resin (Hausen et al. 1995).

In Sweden, the Medical Products Agency evaluated 191 reports concerning adverse effects of 253 cosmetics and toiletries between 1989 and 1994. The most common offending ingredients were fragrances, Tosylamide/Formaldehyde Resin, and preservatives. The adverse effects reported, related to the different product categories, were moisturizes (99 cases) (51%), hair care products (30 cases) (16%) and nail products (23 cases) (12%) (Berne et al. 1996).

A 27 year old woman with a history of using nail varnish complained of constant soreness and redness of the gingivae, particularly around the upper incisors. Patch tests to the European standard series showed positive results to Tosylamide/Formaldehyde Resin 10% pet (+++). The patient admitted to habitual biting of the nails such that the varnish was in contact with her gingival surfaces. She was given advice about an alternative nail varnish and 3 months later, the patient reported a dramatic improvement in her gingivitis and was symptom-free (Staines et al. 1998).

A 54 year old woman was seen in January 1992 because of eczematous change over her fingertips, subungual hyperkeratosis, and dystrophy of her fingernails. She also had scattered areas of eczema over the arms, shoulders, and trunk. She was

patch tested to her nail polish, Tosylamide/Formaldehyde Resin, the Chemotechnique acrylate series, hydroquinone, and a standard screening series of 30 antigens. She had 2+ reaction to her nail polish and 3+ reactions to Tosylamide/Formaldehyde Resin which were accompanied by a flare in her eczema with nummular patches and fingermarks. Her nails grew out normally from the base, and after several months were found to have essentially recovered (Guin et al. 1998).

A 50 year old woman exhibited perianal pruritus for a year. For 6 months, she had been complaining of eyelid pruritus as well. Contact dermatitis was suspected and patch tests were performed with the standard series, the cosmetic series, the plastic and glue series, and the patient's own cosmetics (including 3 of her nail varnishes). None of the patch tests were positive except for the nail varnishes and Tosylamide/Formaldehyde Resin. The patient was advised to stop using nail varnishes. One month later, the pruritis at the perianal and eyelid areas had decreased and after 2 months it had subsided completely (Lazarov 1999).

A 55 year old woman had pruritus on the neck increase to erythema and papules was patch tested for Tosylamide/Formaldehyde Resin (10% pet) with positive reactions. After this, she stopped using nail varnish, and with topical corticosteroids, the whole condition disappeared within 20 days (Vilaplana and Romaguera 2000).

In a study of 102 patients with contact dermatitis between 10 and 19 years of age where 93 (91%) were female, and 9 (9%) were male, the main location for the dermatitis was in the face in 70 patients (36%), hands in 64 (32.5%), neck in 20 (10%), arms in 12 (6%) and feet in 10 (5%). Among the 102 adolescents, 13 cases (12.7%) tested positive for Tosylamide/Formaldehyde Resin. The authors concluded that the

contact dermatitis was attributable to nail polish (Duarte et al. 2003).

References

Berne B, A Boström, AF Grahfén, and M Tammela. (1996) Adverse effects of cosmetics and toiletries reported to the Swedish Medical Products Agency 1989-1994. Contact Dermatitis 34: 359-362.

de Groot A, DP Bruynzeel, JD Bos, et al. (1988). The allergens in cosmetics. Arch Dermatol. 124: 1525-1529.

De Wit FS, AC de Groot, JW Weyland, and JD Bos (1988) an outbreak of contact dermatitis from toluenesulfnamide Formaldehyde resin in a nail hardener. Contact Dermatitis 18: 280-283.

Duarte I, R Lazzarinin, and CM Kobata (2003). Contact dermatitis in adolescents. American Journal of Contact Dermatitis. 14: 200-204.

Elder, RL (1986). Final report on the safety assessment of Toluenesulfonamide/Formaldehyde Resin. JACT 5: 471-490.

Giorgini S, C. Brusi, S Francalanci, et al. (1994). Prevention of allergic contact dermatitis from nail vanishes and hardeners. Contact Dermatitis. 31: 325-326.

Guin JD, K Baas, and P Nelson-Adesokan. (1998). Contact sensitization to cyanoacrylate adhesive as a cause of severe onychodystorphy. International Journal of Dermatology. 37: 31-36.

Hausen BM, M Milbrodt and WA Koenig. (1995). The allergens of nail polish. (I). Allergenic constituents of common nail polish and toluenesulfonamide-Formaldehyde resin (TS-F-R). Contact Dermatitis. 33: 157-164.

Lazarov, A. (1999). Perianal contact dermatitis caused by nail lacquer allergy. American Journal of Contact Dermatitis. 10: 43-44.

Nikitakis JM, GN McEwen, JA Wenninger (1991) CTFA International Cosmetic Ingredient Dictionary. 4th edn. CTFA, Inc.

Staines KS, DH Felix and A Forsyth (1998). Desquamative gingivitis, sole manifestation of tosylamide/formaldehyde resin allergy. Contact Dermatitis. 39:90.

Vilaplana J and C Romaguera. (2000). Contact dermatitis from tosylamide/formaldehyde resin with photosensitivity. Contact Dermatitis 42: 311-312.

Concentration of Use by FDA Product Category[1]*

Tosylamide/Epoxy Resin
Tosylamide/Formaldehyde Resin

Ingredient	Product Category	Maximum Concentration of Use
Tosylamide/Epoxy Resin	Basecoats and under coats (manicuring preparations)	3.4-6.3%
Tosylamide/Epoxy Resin	Nail polish and enamels	9%
Tosylamide/Epoxy Resin	Other manicuring preparations Top coat	5%
Tosylamide/Formaldehyde Resin	Nail polish and enamels	10.2-13.9%

Information collected in 2025
Table prepared: March 31, 2025

[1] The new FDA cosmetic product categories under MoCRA were used for this survey.