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EUROPEAN TRADE UNION CONFEDERATION

CONFEDERATION EUROPEENNE DES SYNDICATS

Proposal of Sensitizers for SVHC identification under 57f:

Contribution to the practical implementation of REACH, in particular by proposing sensitizers as Substances of Very High Concern (SVHC) which, from a union perspective, should have priority for inclusion in the Candidate List and potentially in the Authorisation or Restriction Lists.

Authors:
Tatiana Santos, Rafael Gadea and Tony Musu

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1. Justification

Calculations carried out by European Trade Union Institute (ETUI) using Eurostat data (2004) on cases of occupational diseases recognised in the EU-15, suggest that 88% of recognised occupational skin disease cases and 36-89% of recognised occupational respiratory disease cases are related to chemical exposure[1]

It is also worth mentioning that, for sensitizers, the time lag between exposure and effects is relatively short compared to occupational cancers (between a few months to a few years rather than 20-30 years) and that once a person is sensitised to a chemical agent this is irreversible. In addition, there are no available threshold values of sensitizers to date. In many cases only traces of sensitizers can cause symptoms at the skin or respiratory tract.

A further analysis of occupational diseases caused by chemicals was commissioned by ETUI to the Sheffield University with the objective of assessing what could be the impact of REACH on occupational skin and respiratory diseases[2].

The number of occupational diseases caused by chemical sensitizers that could be avoided each year in Europe are estimated to be 40 000 cases for asthma, 10 000 cases for Chronic Obstructive Pulmonary Diseases (COPD) and 40 000 cases for dermatitis, using a working population figure of 200 million for EU-25.

That would add up to total average savings of 3.5 billion Euros over 10 years for the EU-25. The savings would boost social security coffers through reduced sickness benefit payments, while workers will enjoy health-related quality of life gains, and employers in all sectors will avoid productivity losses from sickness absenteeism.

A great part of the skin and respiratory occupational diseases that could be avoided thanks to REACH will come from better risk management measures implemented at the workplace. However, we believe that substitution of the most common and potent chemical sensitizers used at the workplace by safer alternatives should be promoted.

Therefore, we are convinced that there is a need for REACH authorisation and restriction procedures to also cover sensitising substances in order to reduce the incidence of occupational diseases caused by this type of chemicals. This could be done by including some sensitizers in the Candidate list by identifying them as substances of very high concern (SVHC) through the REACH article 57(f) route.

For the development of our list of sensitizers to be potentially identified as SVHC under 57(f), the starting point are the substances included in the Trade Union Priority List for

[1] Reaching, the workplace, Tony Musu, ETUI, 2006. http://hesa.etui.org/uk/publications/files/REACH-EN.pdf
[2] **The impact of REACH on occupational health** with a focus on skin and respiratory diseases. Simon Pickvance, Jon Karnon, Jean Peters, Karen El-Arifi. *School of Health and Related Research University of Sheffield, UK.* Final report, September 2005, prepared for the European Trade Union Institute for Research, Education and Health & Safety.

Authorisation under REACH[3], therefore, they all are High Production Volume Chemicals (HPVC) and have many different uses in industry (i.e. widely used).

Also, all our candidates are linked with proven occupational diseases (this is, included in Annex I of the European Schedule of Occupational Diseases[4] and/or the European Commission's study on occupational diseases published in January 2009[5] and related with wide occupational exposure (according to HazMap[6]).

Given the high incidence of both skin and respiratory occupational diseases (see Sheffield impact assessment), we have considered both skin and respiratory sensitizers.

For skin sensitizers, we have also included information related with their allergenic potency[7] that might help in order to choose the best candidates.

For respiratory sensitizers, since there are no tests guidelines, only human evidence is taken into account. We believe that when well documented this is further enough for their identification.

Based on the findings of the Sheffield Impact Assessment, cost savings from avoidance of respiratory occupational diseases are in the long run higher than costs savings from avoidance of skin occupational diseases.

Therefore, for regulatory effectiveness, respiratory sensitizers should be prioritised. This is why in this work they were given the maximum score.

2. Methodology:

The steps described hereunder have been followed in order to draw up the Trade Union's proposal for sensitizers to be included in the Candidate List:

2.1. Selection of all sensitizing substances from the Trade Union list. Therefore, all selected substances are high production volume and have known industry uses -> *126 substances remaining*

2.2. Removal of the CMR substances, cat. 1A and 1B (according to CLP[8] classification) -> *89 substances remaining*

[3] http://www.etuc.org/a/6023
[4] Commission Recommendation (19/09/2003) concerning the European Schedule of Occupational Diseases. C(2003)3297 final
[5] Information notices on occupational diseases: a guide to diagnosis. **European Commission.** Directorate-General for Employment, Social Affairs and Equal Opportunities F4 unit. Manuscript completed in January 2009: http://www.beroepsziekten.nl/sites/default/files/documents/Information-Notices-2009.pdf
[6] Haz Map: Occupational exposure to hazardous agents. http://hazmap.nlm.nih.gov/
[7] Chemical substances and contact allergy—244 substances ranked according to allergenic potency. E. Schlede et al.

2.3. **Removal of those not linked with occupational diseases** (except where they are recognized as cause of occupational diseases according with the European Commission's document[5]) -> *67 substances left*

2.4. **Removal of substances "suspected" to cause occupational diseases**[9] except where they have been identified by the mentioned European Commission's document on occupational diseases[5] (2009) -> *46 substances remaining*

2.5. **Grouping of substances**: Isomers or substances with very high structural similarities have been grouped together in order to reduce the number of entries (e.g. "alkyl acrylates" or "diisocyanates"). As a consequence, entries can be single substances but also group of substances covering a whole range of related substances. In those cases, the most hazardous substance was taken as a reference for the whole group and marked with * in the list (*please, see excel file*).

2.6. **Differentiating among**:

- skin sensitizers according to CLP Regulation
- respiratory sensitizers according to CLP Regulation
- sensitizing allergens according to REACH allergens' article[10] or the Danish EPA' Q(SAR) database[11].

2.7. **Identification of concerning properties**

It is worth to remind the sources we have used for the identification of all effects:

Carcinogenic substances:

- Substances classified as category 1A, 1B and 2 in accordance with EU Regulation 1272/2008, so called CLP Regulation (categories 1, 2 and 3 in accordance with Directive 67/548/EEC) identified in Annex VI with hazard statements[12] H350 (may cause cancer) and H351 (suspected of causing cancer).

- Substances classified by the International Agency for Research on Cancer[13] (IARC) as human carcinogens (IARC 1), that are probable human carcinogens (IARC 2A) and that are possible human carcinogens (IARC 2B).

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[8] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures.
[9] ANNEX II. Additional list of diseases suspected of being occupational in origin which should be subject to notification and which may be considered at a later stage for inclusion in Annex I to the European schedule. **Commission Recommendation of 19 September 2003 concerning the European schedule of occupational diseases** (Text with EEA relevance) (notified under document number C(2003) 3297)
[10] List of REACH Allergens. AVE e.V./KEAC Working Group (Friedhelm Diel, Michael Fischer, John Kamsteeg, Hans Schubert, Klaus-Michael Weber)
[11] http://130.226.165.14/index.html
[12] Hazard statement is a phrase assigned to a hazard class and category that describes the nature of the hazards of a substance or mixture, including, where appropriate, the degree of hazard.
[13] IARC. IARC Monographs on the evaluation of carcinogenic risks to humans. Lyon, France: International Agency for Research on Cancer (IARC). Available at: http://www.iarc.fr/. Accessed October 2009.

Mutagenic substances:

- Substances classified as mutagenic category 1A, 1B and 2 in accordance with CLP Regulation (categories 1, 2 and 3 in accordance with Directive 67/548/EEC) identified in Annex VI with hazard statements H340 (may cause genetic defects) and H341 (suspected of causing genetic defects).

Substances that are toxic for reproduction:

- Substances classified as toxic for reproduction category 1A, 1B or 2 in accordance with CLP Regulation (categories 1, 2 and 3 in accordance with Directive 67/548/EEC) identified in Annex VI with hazard statements H360 (may damage fertility or the unborn child), H361 (suspected of damaging fertility or the unborn child).

Persistent, Bioaccumulative and Toxic substances (PBT) and very Persistent and very Bioaccumulative substances (vPvB)

- PBT substances listed in the OSPAR Convention for the Protection of the Marine Environment of the North-East Atlantic[14].

- PBT/vPvB substances listed by the Technical Committee on New and Existing Substances (TC NES)[15].

Endocrine disrupters (EDC)

- Substances included in the priority list developed within the EU-Strategy for Endocrine Disrupters[16] classified as category 1 (evidence of endocrine disrupting activity in at least one species using intact animals) and category 2 (at least some in vitro evidence of biological activity related to endocrine disruption).

Neurotoxicants

- Provisional list for occupational neurotoxicants included in the review published by Vela et al[17].

Sensitizers

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14 http://www.google.es/url?sa=t&source=web&cd=2&ved=0CCIQFjAB&url=http%3A%2F%2Fwww.ospar.org%2Fhtml_documents%2Fospar%2Fhtml%2F04-12e_list_of_chemicals_for_priority_action.doc&rct=j&q=%E2%80%A2%09PBT%20substances%20listed%20in%20the%20OSPAR%20Convention%20for%20the%20Protection%20of%20the%20Marine%20Environment%20of%20the%20North-East%20Atlantic&ei=waFbTb2PO5Go8APBlK2VAg&usg=AFQjCNHutmKiYe_6bqcAcXpqik_APCWIYA&sig2=6um_MFzkTeAY1JpQTePFhg&cad=rja

15 http://ecb.jrc.ec.europa.eu/esis/

16 European Commission. Community Strategy for Endocrine Disrupters - a range of substances suspected of interfering with the hormone systems of humans and wildlife. COM (1999)706. COM (2001)262 SEC(2004)1372, and SEC(2007)1635, Brussels: European Commission, 1999-2007.

17 Vela M, Laborda R, García AM. Neurotóxicos en el ambiente laboral: criterios de clasificación y listado provisional. Arch. Prev. Riesgos Labor. 2003; 61:17-25.

- Substances classified as skin or respiratory sensitizers by CLP Regulation, identified in Annex VI with hazard statements H334 (may cause allergy or asthma symptoms or breathing difficulties if inhaled) and H317 (may cause an allergic skin reaction).

- Substances included in the "List of REACH Allergens"[18]

2.8. Prioritizing by score:

Our work aims to prioritise sensitising substances providing different scores for every health effect and/or damage potential, in a scale ranking from 1 (lowest score) to 5 (highest score).

We consider that respiratory sensitizers cause more concerning effects that skin sensitizers, and cost savings from avoidance of respiratory occupational diseases are in the long run higher than costs savings from avoidance of skin occupational diseases. Therefore, we have given the maximum score to these chemicals.

On the other hand, a study used for this work[7], ranks 244 skin sensitising substances according to allergenic potency, prioritise skin sensitizers into 3 main categories:

Table 2: Definition of categories

Category	Definition	Remarks
Category A	**Significant contact allergen** because of: (1) Proven strong contact allergenic effect in humans after short and/or almost negligible exposure taking into account existing animal data (2) Frequently proven contact allergenic effect in humans	**Data on humans demonstrate that in larger collectives 1% or more of the patients react positive and that several independent case studies and experimental data on humans are available**
Category B	**Solid-based indication for contact allergenic effects** because of: (1) Less frequently proven contact allergenic effect in humans taking into account existing positive animal data (2) The capacity of substances to induce cross-reactions in humans without being a significant allergen itself	**Data on humans demonstrate that in collectives less than 1% of the patients react positive and that independent case studies and/or experimental data on humans are available**
Category C	**Insignificant contact allergen or questionable contact allergenic effect** because of: (1) Rarely proven contact allergenic effect in humans (2) Doubtful effect in humans; no or non-appropriate animal data (3) No data on humans but positive animal data	**Data on humans include isolated positive test results and isolated case studies and experimental data**

Source: Chemical substances and contact allergy—244 substances ranked according to allergenic potency. E. Schlede, W. Aberer , T. Fuchs, I. Gerner, H. Lessmann, T. Maurer, R.

[18] AVE e.V./KEAC Working Group (Friedhelm Diel, Michael Fischer, John Kamsteeg, Hans Schubert, Klaus-Michael Weber). UMWELT & GESUNDHEIT 2/2006.

For this reason, all classified skin sensitizers that are included in category A (potent skin sensitizers), were given 4 points. Other classified skin sensitizers, were given 3 points.

In conclusion, scores were applied for classified respiratory sensitizers (5 points), for potent skin sensitizers (4 points), for other not potent skin sensitizers (3 points), for other concerning health or environment effects (2 points) and for suspected concerning health and environment effects, sensitizers not classified at European level and neurotoxicants (1 point), as shown in Table 1.

Table 1: Health and environmental effect scores used by the Trade Union List of sensitizers

Score	Effect
5 points	**respiratory sensitizers**
4 points	**potent skin sensitizers**
3 points	**other skin sensitizers**
2 points	**CMR (cat. 2)** **EDCs cat. 1**
1 point	**sensitizing substances according to allergen-REACH[18], Danish EPA[11]** **EDC cat. 2** **neurotoxicants**

Scores were applied by effect. Hence one substance that is a carcinogen according to CLP Regulation and also according to IARC, will be given the score associated with the most conservative (and maximum) designation. In those cases, a 0 has been included to the IARC scoring box.

The same rule will be applied for sensitising substances classified by EU and others identified by the REACH allergens article and or Danish EPA.

3. Results

As a result, there are 11 substances (or groups of substances) with maximum score -up to 7 points- (*please see the enclosed excel file*).

Since sensitizers are not specifically included in article 57, additional concerning effects such as CMR cat. 2, EDC properties, PBTness/vPvBness and/or neurotoxicant effects, are crucial to be taken into account for the proposal for SVHC identification.

On the other hand it is also important to specially consider substances that are both respiratory and skin sensitizers.

The main candidates for sensitizers are:

Table 3: Extract of the 11 substances with maximum score.

Name	Health effects:	Occupational disease's group	COM's occupational health effects
Diisocyanates	**Possible carcinogen** (CLP & IARC) **Potent skin sensitizer** **Respiratory sensitizer**	Isocyanates	Allergic contact dermatitis, allergic rhinitis and conjunctivitis, asthma & allergic alveolitis, fibrogenic
Cobalt (dust & fumes)	**Possible carcinogen** (IARC) **Potent skin sensitizer** **Respiratory sensitizer**	Respiratory ailments caused by the inhalation of dust from cobalt	Allergic contact dermatoses, broncho-pulmonary ailments, respiratory ailments, occupational asthma
Ethylenediamine	**Potent skin sensitizer** **Respiratory sensitizer**	Aliphatic amines and halogenated derivatives thereof	Allergic contact dermatitis, asthma, allergic rhinitis and conjunctivitis, irritant and corrosive effects, corneal oedema, disturbancies of the central nervous system
Glutaral	**Potent skin sensitizer** **Respiratory sensitizer**		Occupational allergic asthma & allergy-provoking or irritative substances
Trifluralin	**EDC** cat. 1 **Possible carcinogen** (CLP) **PBT** **Skin sensitizer**	Aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulfonated derivatives thereof	Irritant effects, hypersensitivity in the skin and respiratory tract, haematological disorders, transient liver function abnormalities, disorders of the liver ranging from reversible functional abnormalities to severe atrophy, jaundice, cancer of the bladder
Phthalic anhydrides	**Skin sensitizer** **Respiratory sensitizer**		Occupational allergic asthma
Pphenylenediamines	**Possible carcinogen** (CLP) **Possible mutagen** **Skin sensitizer**	Aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulfonated derivatives thereof	Hypersensitivity in the skin and respiratory tract
Aniline	**Possible carcinogen** (CLP) **Possible mutagen** **Skin sensitizer**	Aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulfonated derivatives thereof	Irritant effects, hypersensitivity in the skin and respiratory tract, haematological disorders, transient liver function abnormalities, disorders of the liver ranging from reversible functional abnormalities to severe atrophy, jaundice, cancer of the bladder

3,4-dichloroaniline	**EDC** cat. 1 **PBT** **Skin sensitizer**	Aromatic amines or aromatic hydrazines or halogenated, phenolic, nitrified, nitrated or sulfonated derivatives thereof	Irritant effects, hypersensitivity in the skin and respiratory tract, haematological disorders, transient liver function abnormalities, disorders of the liver ranging from reversible functional abnormalities to severe atrophy, jaundice, cancer of the bladder
Bisphenol A	**EDC** cat. 1 **Possible Reprotoxicant** **Skin sensitizer**	Phenols or counterparts or halogenated derivatives thereof	
Alkyl acrylates	**Possible carcinogen** (IARC) **Neurotoxicant** **Potent skin sensitizer**		Methyl acrilates; Occupational skin ailments caused by scientifically recognised allergy-provoking or irritative substances Occupational skin diseases are represented by allergic and irritant contact dermatitis and also contact urticaria. Allergic contact dermatitis Methyl acrylate causes sensitization of the skin.

1. **Diisocyanates:**

Names: 4-methyl-m-phenylene diisocyanate / m-tolylidene diisocyanate / 4,4'-methylenedicyclohexyl diisocyanate / hexamethylene diisocyanate / 4,4'-methylenediphenyl diisocyanate / methylenediphenyl diisocyanate / o-(p-isocyanatobenzyl)phenyl isocyanate / isophorone di-isocyanate

EC No: 209-544-5 / 247-722-4 / 225-863-2 / 212-485-8 / 202-966-0 / 247-714-0 / 227-534-9 / 223-861-6
CAS No: 584-84-9 / 26471-62-5 / 5124-30-1 / 822-06-0 / 101-68-8 / 26447-40-5 / 5873-54-1 / 4098-71-9

Major uses: additive, solvent, hardener, paints, construction material, adhesive, surface treatment, casting material, colouring agent, binder, adhesive, additive, elastomer, foaming agent, process regulator, intermediate, filler, heat transferring agent, reagent, bleaching agent, joint-less floor, moulding compound, coating agent, reprographic agent, curing agent, inks, dispersion agent, primer. MDI is used to make rigid foams, while both TDI and MDI are used to make flexible foams, elastomers, and surface coatings. The diisocyanate chemicals, e.g., TDI or MDI, along with various polyols, catalysts, blowing agents, surfactants, and other agents are needed to manufacture urethane polymers.

Isocyanates constitute a group of highly reactive chemicals used on a large scale for the production of flexible polyurethane foam.

Diisocyanates are both respiratory and skin sensitizer, but also are possible carcinogens.

They are linked with occupational diseases in the European Schedule of occupational diseases and also by the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Allergic contact dermatitis,
- Allergic rhinitis and conjunctivitis,
- Asthma,
- Allergic alveolitis,
- Fibrogenic,
- Chronic obstructive bronchopathy
- Isocyanate Hp

m-tolylidene diisocyanate has been identified[19] as a significant contact allergen (category A).

On the other hand, 4,4'-methylenedicyclohexyl diisocyanate, hexamethylene diisocyanate, 4,4'-methylenediphenyl diisocyanate and isophorone di-isocyanate have been identified[19] with solid-based indication for contact allergenic effects (category B)

Some industrial Processes with risk of exposure are:

- Burning Synthetic Polymers
- Painting (Pigments, Binders, and Biocides)
- Plastic Composites Manufacturing

Some activities with risk of exposure are:

- Painting
- Sculpturing plastics

See more info on occupational exposure at: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=49

2. **Cobalt (dust)**

EC No: 231-158-0
CAS No: 7440-48-4

Major uses: Paints, hard metal grinders and diamond polishers, electronics, cement, orthopedic prostheses, glass and paint pigments, catalysts. Emissions from burning fossil fuels, nutrient in the human diet in the form of Vitamin B12 (cyanocobalamin), radioactive cobalt is used in medicine and food/equipment irradiation, cobalt is used as a binder along with tungsten and carbon to produce tungsten carbide.

Cobalt dust is both respiratory and skin sensitizer, but also is a possible carcinogen.

It is linked with occupational diseases in the European Schedule of occupational diseases and also by the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Asthma
- Interstitial lung disease (*hard metal disease*), resulting in interstitial fibrosis.

[19] Chemical substances and contact allergy—244 substances ranked according to allergenic potency. E. Schlede, W. Aberer , T. Fuchs, I. Gerner, H. Lessmann, T. Maurer, R. Rossbacher, G. Stropp, E. Wagner, D. Kayser

- Pulmonary edema
- Echocardiographic changes
- Immunologic, occupational contact urticaria
- Contact dermatitis, allergic
- Contact urticaria

Cobalt and its salts has been identified[19] as a significant contact allergen (category A).

Some industrial Processes with risk of exposure are:

- Acid and Alkali Cleaning of Metals
- Cement Producing
- Glass Manufacturing
- Metal Machining
- Painting (Pigments, Binders, and Biocides)
- Petroleum Production and Refining

Some activities with risk of exposure are:

- Ceramics making
- Enameling
- Glassblowing
- Painting

See more info on occupational exposure at: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=37

3. Ethylenediamine

EC No: 203-468-6
CAS No: 107-15-3

Major uses: pesticide, solvent, stabilizer, process regulator, surface treatment, lubricant, additive, adhesive, reprographic agent, construction material, electroplating agent, colour, chemical intermediates in the synthesis of pharmaceutical products, pigments, ion exchange resins, emulsifiers and detergents used in the plastics industry (catalysers, hardeners), leather and photography industries, used in the manufacture of chelating agents, fungicides, waxes, polyamide resins and corrosion inhibitors. Used as an emulsifier, an inhibitor in antifreeze solutions, textile lubricants.

Ethylenediamine is both respiratory and skin sensitizer.

It is linked with occupational diseases in the European Schedule of occupational diseases and also by the European Commission's guidance.

Some aliphatic amines can easily penetrate the skin.

Occupational diseases associated with exposure to this agent are:

- Allergic contact dermatitis,
- Asthma,
- Allergic rhinitis and conjunctivitis,
- Irritant and corrosive effects,

- Corneal oedema,
- Disturbancies of the central nervous system
- Pulmonary edema

Ethylenediamine has been also identified[19] as a significant contact allergen (category A).

Some industrial Processes with risk of exposure are:

- Painting (Pigments, Binders, and Biocides)
- Photographic Processing
- Textiles Manufacturing

See more info on occupational exposure at: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=480

4. **Glutaral**

EC No: 203-856-5
CAS No: 111-30-8

Major uses: disinfectant, pesticide, preservative, cleaner. Used in hospitals and medical and dental offices in solutions for cold sterilization and automatic processing of x-rays.

Glutaraldehyde is both respiratory and skin sensitizer.

It is not linked with occupational diseases or suspected to cause them, in the European Schedule of occupational diseases, but it is described in the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Occupational allergic asthma,
- Allergy-provoking substance
- Irritative substance
- Contact urticaria
- Anamnesis
- Allergic contact dermatitis
- Toxic hepatitis

Glutaral has been also identified[19] as a significant contact allergen (category A).

Some industrial Processes with risk of exposure are:

- Photographic Processing
- Pulp and Paper Processing
- Sterilizing Equipment
- Using Disinfectants

See more info on occupational exposure at: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=97

5. Trifluralin

EC No: 216-428-8
CAS No: 1582-09-8

Major uses: food agent, herbicide

Trifluralin is only a skin sensitizer, but it is also a possible carcinogen and Persistent, Bioaccumulative and Toxic (PBT).

It is linked with occupational diseases in the European Schedule of occupational diseases and is also described in the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Irritant effects,
- Hypersensitivity in the skin and respiratory tract,
- Haematological disorders,
- Transient liver function abnormalities,
- Disorders of the liver ranging from reversible functional abnormalities to severe atrophy,
- Jaundice,
- Cancer of the bladder
- Injury to kidneys, thyroid, blood, and cns
- Contact dermatitis, allergic

Some industrial Processes with risk of exposure are:

- Farming (Pesticides and Feed Additives)

See more info on occupational exposure at: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=7586

Note: Since trifluralin is mainly used as pesticide, it might not be a good candidate for Authorisation under REACH.

6. Phthalic anhydrides

Names: phthalic anhydride / tetrahydro-4-methylphthalic anhydride / tetrahydromethylphthalic anhydride / 1,2,3,6-tetrahydrophthalic anhydride / hexahydro-4-methylphthalic anhydride
EC No: 201-607-5 / 251-823-9 / 234-290-7 / 201-605-4 / 243-072-0
CAS No: 85-44-9 / 34090-76-1 / 11070-44-3 / 85-43-8 / 19438-60-9

Major uses: rubber retarder, scorch inhibitor, plasticizer, hardener, pesticide, reagent, softener, tanning agent, light- and heat-stabilizer, construction material, adhesive, corrosion inhibitor, impregnation material, colouring, viscosity adjustor, heat transferring agent, process regulator, manufacture of basic metal, electrical machinery and apparatus and other transport equipment, intermediate, anti-scorching agent, filler, stopping material, chemical intermediate for various chemical resins, dyes, and pigments, curing agent for epoxy resins.

Phthalic anhydrides are both respiratory and skin sensitizers.

They are not linked with occupational diseases in the European Schedule of occupational diseases (only suspected originator of occupational diseases as aromatic acids - aromatic anhydrides or their halogenated derivatives**), but are described in the European Commission's guidance.**

Occupational diseases associated with exposure to this agent are:

- Occupational Allergic Asthma
- Contact dermatitis, allergic
- First degree burns on short exposure
- Skin irritant
- Conjunctivitis
- Mucous membrane irritation
- Eyes irritant and upper respiratory system

Phthalic anhydride has been identified[19] with solid-based indication for contact allergenic effects (Category B).

Some industrial Processes with risk of exposure are:

- Plastic Composites Manufacturing
- Welding Over Coatings

See more info on occupational exposure at: http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=599

7. Phenylenediamines

Names: o-phenylenediamine / m-phenylenediamine / N,N'-diphenyl-p-phenylenediamine / N-isopropyl-N'-phenyl-p-phenylenediamine

EC No: 202-430-6 / 203-584-7 / 200-806-4 / 202-969-7
CAS No: 95-54-5 / 108-45-2 / 74-31-7 / 101-72-4

Major uses: Used to dye hair and fur; also used to develop photographs and to synthesize other organic compounds, stabilizer, antioxidant, polymerization inhibitor, protection of rubbers against oxidation, ozone, flexcracking, adhesive, used to make diisocyanates for the production of polyurethane foams and other resins and polymers; also used as a corrosion inhibitor, curing agent, photographic developer, analytical reagent and intermediate for other chemical products, and to cure epoxy resins.

Phenylenediamines are only skin sensitizers, but they are also possible carcinogens and mutagens.

They are linked with occupational diseases in the European Schedule of occupational diseases and also described in the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Hypersensitivity in the skin and respiratory tract
- Occupational asthma
- Allergic contact dermatitis
- Immunologic contact urticaria
- Fatty degeneration of the liver
- Methemoglobinemia, and
- Kidney injury

Phenylenediamine has been also identified[19] as a significant contact allergen (category A).

Some industrial Processes with risk of exposure are:

- Dressing Hair
- Fur Dressing and Dyeing
- Photographic Processing
- Printing, Dyeing, or Finishing Textiles
- Plastic Composites Manufacturing

See more info on occupational exposure at:
http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=1666

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=1667

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=229

8. Aniline

EC No: 200-539-3
CAS No: 62-53-3

Major uses: solvent, used in the synthesis of dyes, rubber additives, drugs, photographic chemicals, isocyanates, and pesticides.

Aniline is only a skin sensitizer, but it is also a possible carcinogen and mutagen.

It is linked with occupational diseases in the European Schedule of occupational diseases and is also described in the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Severe Eye Irritant
- Methemoglobinemia, acute
- Hypersensitivity in the skin and respiratory tract,
- Haematological disorders,
- Transient liver function abnormalities,
- Disorders of the liver ranging from reversible functional abnormalities to severe atrophy,
- Jaundice,
- Cancer of the bladder

Some industrial Processes with risk of exposure are:

- Leather Tanning and Processing
- Shakeout, Cleaning, and Finishing

See more info on occupational exposure at:
http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=296

9. 3,4-dichloroaniline

EC No: 202-448-4
CAS No: 95-76-1

Major uses: intermediate, paints, corrosion inhibitor, thinner, used to make dyes and pesticides.

3,4-dichloroaniline is only a skin sensitizer, but it is also an endocrine disrupter and PBT.

It is linked with both occupational diseases in the European Schedule of occupational diseases and the European Commission's guidance.

Occupational diseases associated with exposure to this agent are:

- Severe Eye Irritant
- Methemoglobinemia, acute
- Hypersensitivity in the skin and respiratory tract,
- Haematological disorders,
- Transient liver function abnormalities,
- Disorders of the liver ranging from reversible functional abnormalities to severe atrophy,
- Jaundice,
- Cancer of the bladder
- Liver and kidney injury
- Toxic by inhalation, ingestion, and skin absorption
- May cause serious damage to eyes
- Corrosive substance that can cause injury to the skin, eyes, and respiratory tract
- Inhalation may cause chemical pneumonitis
- Convulsions, cyanosis, lacrimation
- Contact dermatitis, allergic

See more info on occupational exposure at:
http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=3194

10. Bisphenol A

EC No: 201-245-8
CAS No: 80-05-7

Major uses: antioxidant, plasticizer, flame retardant, pesticide, process regulator, paints, adhesive, softener, construction material, stabilizer, lubricant, additive, surface treatment, filler, anti-static agent, viscosity adjustor, insulating material, used as a chemical intermediate, mainly for epoxy resins and polycarbonate resins, used with epichlorohydrin to produce bisphenol-A diglycidyl ether, the monomer in bisphenol-A type epoxy resins.

Bisphenol A is only a skin sensitizer, but it is also a possible toxic for reproduction and an endocrine disrupter.

It is linked with occupational diseases in the European Schedule of occupational diseases.

Occupational diseases associated with exposure to this agent are:

- Contact dermatitis, allergic
- Skin, eye, and respiratory tract irritant

Some industrial Processes with risk of exposure are:

- Plastic Composites Manufacturing
- Semiconductor Manufacturing
- Welding Over Coatings

See more info on occupational exposure at:
http://hazmap.nlm.nih.gov/cgi-bin/hazmap_generic?tbl=TblAgents&id=842

11. Alkyl acrylates

Names: butyl acrylate / 2-ethylhexyl acrylate / tert-butyl acrylate / 2-hydroxyethyl acrylate / ethyl acrylate / methyl methacrylate / isobutyl acrylate / methyl acrylate / ethyl methacrylate / isobutyl methacrylate / butyl methacrylate / 2-hydroxyethyl methacrylate / 2-dimethylaminoethyl methacrylate / (1-methyl-1,2-ethanediyl)bis[oxy(methyl-2,1-ethanediyl)] diacrylate / 2-(hydroxymethyl)-2-[[(1-oxoallyl)oxy]methyl]-1,3-propanediyl diacrylate / 2-ethyl-2-[[(1-oxoallyl)oxy]methyl]-1,3-propanediyl diacrylate / hexamethylene diacrylate

EC No: 205-480-7 / 203-080-7 / 216-768-7 / 212-454-9 / 205-438-8 / 201-297-1 / 203-417-8 / 202-500-6 / 202-500-6 / 202-597-5 / 202-613-0 / 202-615-1 / 212-782-2 / 220-688-8 / 256-032-2 / 222-540-8 / 239-701-3 / 235-921-9
CAS No: 141-32-2 / 103-11-7 / 1663-39-4 / 818-61-1 / 140-88-5 / 80-62-6 / 106-63-8 / 96-33-3 / 97-63-2 / 97-86-9 / 97-88-1 / 868-77-9 / 2867-47-2 / 42978-66-5 / 3524-68-3 / 15625-89-5 / 13048-33-4

Major uses: adhesive, binder, surface treatment, construction material, filler, cleaner, reprographic agent, impregnation agent, pesticide, solvent, corrosion inhibitor, colouring agent, hydraulic fluid, additive, polishing agent, cement, coating, used in polymer manufacturing, textile and leather finishing, and paint formulation industries, monomer for plastics, protective coatings, paper treatment, used in media for electron microscope preparations; also used in UV-cured artificial nails, used to make acrylic resins for fibers, adhesives, binders, surface coatings, textiles, paper, and leather, monomers that are combined with other monomers or polymers to produce plastics used in cosmetics, medicine, dentistry, and manufacturing industries, oil additives, also used in emulsions for textiles, for leather and to make contact lenses, used artificial nails, chemical intermediate and curing agent for polymers, cross-linking agent in UV-cured inks, coatings, adhesives, and dental sealants.

Alkyl acrylates are potent skin sensitizers (category A) and also neurotoxicants.

They are not linked with occupational diseases in the European Schedule of occupational diseases (only suspected originator of occupational diseases as esters or their halogenated derivatives**), but are described in the European Commission's guidance.**

Occupational diseases associated with exposure to this agent are:

- Occupational skin ailments
- Irritative substances
- Allergic and irritant contact dermatitis
- Contact urticaria
- Methyl acrylate causes sensitization of the skin
- Pulmonary edema
- Reddening of skin
- First degree burns
- Occupational asthma
- Lachrymator
- Damage to the liver, kidneys, and lungs

Some industrial Processes with risk of exposure are:

- Painting (Pigments, Binders, and Biocides)
- Plastic Composites Manufacturing
- Burning Synthetic Polymers
- Welding Over Coatings
- Working with Glues and Adhesives
- Printing, Dyeing, or Finishing Textiles
- Silk-Screen Printing
- Leather Tanning and Processing
- Pulp and Paper Processing
- Textiles Manufacturing
- Working with Glues and Adhesives

Some activities with risk of exposure are:

- Sculpturing plastics

See more info on occupational exposure at:
http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=141-32-2&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=103-11-7&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=1663-39-4&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=818-61-1&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=140-88-5&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=80-62-6&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=106-63-8&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=96-33-3&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=97-63-2&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=97-86-9&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=97-88-1&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=97-88-1&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=42978-66-5&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=3524-68-3&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=15625-89-5&tbl=TblAgents

http://hazmap.nlm.nih.gov/cgi-bin/hazmap_search?queryx=13048-33-4&tbl=TblAgents