PreventPartner

Literature and model study on absorption routes of toxic substances in smoke caused by fire

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Project leader and contact	Jolanda Willems MBA, certified toxicologist and occupational hygienist (Coöperatie PreventPartner), Jolanda.willems@preventpartner.nl
Performance of research	Jolanda Willems MBA, certified toxicologist and occupational hygienist (Coöperatie PreventPartner) Dr. Ellen Wissink, certified occupational hygienist (Coöperatie PreventPartner) Dr Remko Houba, occupational hygienist and researcher (IRAS, NKAL and Coöperatie PreventPartner) Dr. Frans Greven, registered toxicologist-researcher, GAGS, GGD Groningen
Client	This study was carried out by Coöperatie PreventPartner on behalf of the Institute for Physical Safety (IFV). Contact at the IFV: Ronald Heus

Summary

The Institute for Physical Safety (IFV) has asked the centre of Expertise on Toxic Substances of PreventPartner to provide insight into the most common substances that are released in a fire, what effects these substances can cause in the body and which absorption routes are relevant. An underlying question from the fire service for this study to consider is whether the measures that are now being taken to minimise risks are effective.

This study only focuses on the potential hazards of substances that occur in fire smoke. However, the potential dangers of substances in fire smoke in themselves have no bearing on the actual risk of these substances in fire situations.

To answer the study questions, the following steps have been taken:

1. Selection of the most important (hazardous) substances that can occur in fire smoke.

2. Classification of substances by exposure route (through respiratory tract, skin and mouth) and single/repeated exposure.

3. Classification of substances in hazard classes.

The study was conducted through a combination of expert sessions, surveys of the literature and the use of models. 32 of the most common substances in smoke have been assessed. For this purpose, substances are classified in hazard classes for each exposure route. This is a broad-brush approach.

It is concluded that in the case of one-off (high) exposure the main absorption route is inhalation. The chance of effects caused by these substances that occur during one-off (high) exposure through the skin is seen as small. There are only a limited number of substances that can be absorbed through the skin and that have the potential to cause effects with a one-off (high) exposure.

Even with repeated exposure to substances in smoke from fire, inhalation seems to be the most important absorption route for most substances. The absorption route through the skin is only of importance for a limited number of substances, but it is a real route for these substances. Skin absorption should therefore certainly be included in future risk assessments. The ingestion route through the mouth is seen as the least relevant route, since ingestion by mouth will only take place indirectly through hand-to-mouth contact in relatively small quantities.

As far as the relationship between inhalation and skin hazards is concerned, the absorption of smoke through inhalation is the greatest danger. The risk of unexpected/accidental inhalation of smoke arises if, for example, the mask is removed too soon, if the mask does not connect properly to the face and/or if the person is unprotected at too small a distance from the fire.

It is recommended to make even more sure that inhalation of smoke is prevented, to further reduce hand contact and skin contact with substances and to monitor whether measures taken are effective.

There is also a recommendation to perform follow-up studies in order to get a good picture of the actual risk of substances in smoke caused by fire by combining the actual exposure with the potential hazards of substances.

Contents

1 Introduction

1.1 Reason for the study

In 2015, the Occupational Employment Safety Knowledge Centre (KCAV) compiled a review of the literature of the risks that firefighters run of contracting cancer when they are exposed to smoke during firefighting activities and which substances in smoke could be carcinogenic[1,2].

A number of gaps were found in the knowledge about exposure to smoke-carried substances for firefighting personnel in the Netherlands.

The Institute for Physical Safety (IFV) accordingly asked the Centre of Expertise on Toxic Substances of PreventPartner to provide insight into the most common substances that are released during a fire, what effects they can produce in the body and which routes are particularly relevant. An underlying question from the fire service for this study to consider is whether the measures that are now being taken to minimise risks are effective. To answer these questions, it is necessary to look more broadly than just at carcinogenic substances. From the literature it is known that substances in smoke can also cause other health effects. So substances are not exclusively assessed for carcinogenic properties but also for other health effects.

A wide range of substances is released during fires. These can be both unburned products - for example organic liquids which evaporate due to the heat of the fire and spread along with the smoke plume in gas form - and reaction products, such as carbon monoxide, soot particles and PAHs (polycyclic aromatic hydrocarbons) that originate in the burning process. The group of reaction products usually represents the majority. The formation of combustion products depends on the materials in the fire and the conditions; oxygen supply, temperature, influence of building, weather conditions, etc. All of these factors affect the source strength (that is, the amount of a substance that is released for each time unit) of the components formed. Fire is a complex process and conditions are generally not constant. As a result, the source strength of a component can vary greatly over time. There are also different types of fires or stages in which a fire can occur[3].

This study is part of a research program in which two other studies are running. In one study, the contamination, permeability and cleanability of firefighter's clothing is investigated. The other study focuses on the influence of stress on skin barrier function and the extent to which exposure to substances through skin absorption is possible when carrying out fire-fighting tasks.

1.2 Objective and question

In this study the following questions are addressed:

- What are the pathways of the most important toxic substances that occur in fire smoke?
- Is skin absorption a real route on exposure to toxic substances that occur in fire smoke?

If skin absorption is a real route,

- What is the importance of this absorption route in relation to other routes of absorption (through the breath and through the mouth)?
- What are the most critical substances for absorption through the skin?

Because the fire service always in principle wears respiratory protection when fighting fires, skin absorption appears to be an important route of exposure to substances in smoke caused by fire. We know from the literature, however, that firefighters can still be exposed to smoke through inhalation, despite wearing respiratory protection[4,5,6]. It is not excluded that exposure can occur due to, for example, leakage of the mask or the removal of the mask too rapidly. For these reasons, the inhalatory absorption route (absorption through inhalation) has been included in this study.

Ingestion through the mouth is also a possible absorption route, because sometimes persons eat, drink and smoke during or immediately after a deployment. So this exposure route has also been included in the study. Hand-mouth contact allows unnoticed substances to be absorbed into the body. This can take place in various ways[7]:

- by ingestion of dust that precipitates in the mouth and nose area and is swallowed with the mucus;
- by drinking (e.g. through the cup);
- through eating and smoking with unwashed hands that have been in contact with substances and then act as a source;
- through nail biting and nose picking;
- through the accidental ingestion of harmful liquids or solids (only incidental).

1.3 Demarcation of the study

The concepts of hazard and risk are often used interchangeably. However, it is important to draw a distinction here. By "hazards" is meant the intrinsic properties of substances, such as the toxicity and a number of physical factors such as water solubility, molecular size and similar. *Hazard* means the potential of substances to cause health damage.

This report focuses on the potential hazards of substances, and specifically of substances that occur in fire smoke. These hazards are viewed for each intake route (through the airways (inhalation), the skin and the mouth). However, the potential dangers of the substances in fire smoke have no bearing on the actual *risk* of these substances in fire situations. The actual risk depends on many further factors, including the exposure time of the substances, the exposure quantity and the effectiveness of the protective measures taken. This study does not include an extensive analysis of these factors.

This report also does not address hazards/risks of specific toxic substances that can be released in fires at BRZO companies or other companies/vehicles where specific substances are present. These scenarios are included in the emergency response plans. This study concerns substances that occur in smoke during regular fires.

1.4 How to read the report

In Chapter 2 the study method is explained. Chapter 3 presents the results of the assessment of the hazards for each absorption route of the most common substances in smoke caused by fire. Chapter 4 contains the discussion and assessment. Chapter 5 gives the conclusions of the study, and the recommendations are provided in Chapter 6.

2 Study method

To answer the study questions, the following steps have been taken:

1. Selection of the most important (hazardous) substances that can occur in fire smoke.
2. Classification of substances by exposure route and single/repeated exposure.
3. Classification into hazard classes.

The study was conducted by a combination of expert sessions, surveys of the literature and the use of models. An overview of the various expert sessions is included in Annex 1.

2.1 Selection of substances

Based on a review of the literature[3.8.9] we examined who has done research in the past few years on substances in smoke caused by fire in the Netherlands. These research bodies were approached with the question whether they want to contribute through an expert session to the selection of the most important substances that occur in fire smoke. During the expert session, the studies carried out were assessed and on the basis of the results a list of the most common substances in smoke from fire was drawn up (see §3.1).

2.2 Classification of substances by exposure route and single/repeated exposure

As the next step in the study, data were collected about the selected substances, including:

- Unique number of a substance, the so-called CAS number.
- Physical properties, such as boiling point, water solubility.
- Warning phrases, so-called Hazard phrases (H-phrases)[10.11]. The H-phrases are determined on the basis of a number of properties of a substance, on the basis of which a substance is classified in a hazard class.
- A possible H-notation of substances. An H-notation is a warning sentence that is given to substances to warn that skin absorption can be an important absorption route.
- Limit values (both for one-off exposure and for repeated exposure).

Annex 2 contains an overview of the meaning of all H-phrases and a general description of the toxicity of substances.

Subsequently, on the basis of the H-phrases assigned to the substances, it was assessed whether the substances could pose a hazard through the various exposure routes (through respiration, through the skin and through the mouth). In Figure 1 an overview is given for the first classification of substances[10,11]. The choice for classification is explained in the following sections. For substances for which no H-phrases are available - for example dust fractions - the assessment was carried out on the basis of the literature.

Figure 1: First hazard classification of substances that occur in fire smoke

Classification of hazards of the selected substances

Inhalation		Skin		Mouth
Possible risk with one-off exposure through inhalation	**Possible risk of repeated exposure through inhalation**	**Possible risk with one-off exposure through absorption through the skin**	**Possible risk of repeated exposure by absorption through the skin or cause skin cancer**	**Possible risk of repeated exposure through the mouth**
Direct absorption by airways (effect elsewhere or direct effect on airways) H330, H331, H332, H335, H336, EUH071, H340, H360 H370, H371	Absorption by airways (effect elsewhere or direct effect on airways) H330, H331, H332, H334, H340, H341, H350, H351 H360, H361, H370, H372, H273, EUH017	H310, H311, H312 and/or "H" notation If relevant absorption by skin also includes 360, 370 and H371	H 310, H311, H312, H340, H317 and/or "H" notation If admission: H340, H341, H350, H351, H360F, H361, H372, H373	Direct effect or uptake by gastrointestinal tract or effect elsewhere Only for non-gaseous substances H 300, H301, H302 H 340, H341, H350, H351, H36F, H360, H372, H373
↓	↓	↓	↓	↓
Classification in 4 classes based on H-phrases and limit values (alarm limit values) that are used in emergencies Testing literature	Classification in 4 classes based on H-sentences Testing literature	Classification in 4 classes → inclusion in combination with hazard classification Testing literature	Classification in 4 classes → inclusion in combination with hazard classification Assessment of the literature and model (Skinperm) Skin cancer → direct classification in class based on H-sentence	Classification in 4 classes based on H-sentences Testing literature

2.2.1 Selection based on H-phrases

In the classification in Figure 1, a distinction is drawn for each exposure route between one-off exposure and repeated exposure.

When estimating hazards given one-off exposure presuppose that firefighters are very noticeably exposed to smoke as a result of an incident. For inhalation, the so-called intervention values are included in the assessment in this case as an extra check on the chosen classification.

In the case of one-off exposure to substances in fires due to fire, the absorption route through the mouth was not included in the assessment, because no direct effects were reported in the literature of intake by mouth with a one-off exposure.

As already mentioned in the introduction, in the assessment of repeated exposure it is assumed that firefighters - despite the fact that they are generally protected against smoke by means of respiratory protection - can nevertheless be repeatedly exposed to substances in smoke caused by fire through inhalation.

In the event of repeated exposure, absorption by mouth is included, because contact with food during the course of eating, drinking and smoking can in fact take place through this route.

2.2.2 Classification into hazard classes

Then a structured assessment schedule was drawn up, arranged in four groups for each intake route: red, orange, yellow or green, where red represents the greatest hazard and green a small or non-existent hazard.

This is also referred to by the term "control banding". Control banding is a broad-brush method for classifying substances into hazard classes in a relatively rapid and well-organised way, so that on this basis insight can be gained into which substances pose the greatest and least risk for each exposure route. The use of control banding is a common method in the assessment of hazardous substances. This method is used, for example, in the models COSHH and Stoffenmanager[12, 13].

Because it concerns a specific situation - namely exposure of the fire service to substances in smoke during regular fires - a hazard classification has been made in the control banding that is specific to this situation. Here, substances are not only classified on the basis of the hazard phrases, but the following items have also been taken into account:

- the potential for absorption of substances in the body;
- concentration (range) of a substance in smoke in combination with the absorption potential.

The following choices have been made:

- With **inhalation** for one-off, incidental exposure, the "worst case" situation has been assumed. This means that for substances that are present in smoke in a fire, 100% absorption is assumed in the body. In the case of repeated exposure, consideration has been given to the fact that in principle respiratory protection is used, but that (unnoticed) exposure can take place, for example due to leakage of the mask;
- With the **skin** it is taken into account whether a substance can be absorbed through the

skin. In addition, it is taken into account that substances do not come directly onto the skin (this means direct contact with liquid), but indirectly through smoke. This means that there are smaller quantities than in direct contact with a (liquid) substance.

- With the **mouth** the recording potential has been taken into account. Absorption by mouth is not obvious, but can take place through hand-mouth contact. There are always small quantities involved. So only an assessment for repeated exposure has been performed. No evidence has been found in the literature that ingestion could pose a hazard/risk in the event of a one-off (high) exposure to smoke from fire.

It is important to emphasise once again that the actual risk of the substances depends, in particular, on the concentration of the substances in smoke and the duration of exposure, which can vary for each fire/location.

A more detailed explanation of the choices made during the application of the classification of the substances is included in Annex 3.

Hazard classification and skin absorption

With certain substances, skin exposure and absorption may contribute to the total internal toxic stress. The process of skin absorption/skin intake is a complex matter, which is divided into three parts. First there is the penetration, the transition of the substance in the state in which it comes into contact with the skin to the horny layer (the outer layer of the skin). The second step is the diffusion through the horny layer. The third step is transport through the underlying tissue to the small blood vessels, where the substance is absorbed into the blood.

The final amount of dust that is absorbed is determined by the permeation rate, the size of the contact surface, the duration of the exposure, the properties of a substance (molecular size, water solubility), the form of administration, the conditions under which the skin exposure takes place and the quality of the skin[14]. The aggregation state of the substance is very important. Substances must first be dissolved if they are to penetrate the skin rapidly.

During this study, it was examined on the one hand by means of surveys of the literature whether absorption of substances through the skin could occur with the selected substances and whether the substances could potentially contribute to the total internal toxic stress. On the other hand, a model has been used to determine whether skin absorption is a relevant factor in relation to absorption through inhalation.

<u>Review of the literature</u>

In addition to a selection of Hazard-phrases (H-phrases), the surveys of the literature looked at whether the substances had a skin notation (H-notation). A skin notation is assigned when, for a substance under certain conditions, the contribution through the skin to the total toxic stress can be greater than through other forms of exposure[15]. The skin notation indicates that for a given substance there is a potential risk of skin absorption and that the substance can then cause effects elsewhere in the body (the so-called systemic effects). The skin notation does not say anything about the actual risk of skin exposure and skin absorption. This risk depends on many factors in the workplace, including the duration of exposure, the method of exposure and, for example, the presence of other substances - in particular irritant, sensitising or corrosive substances.

Model

In an expert session, it was determined which model can best be used for the assessment of the degree of uptake by the skin compared to absorption by inhalation. IH Skinperm[16] was chosen as the most suitable tool.

In contrast to other available tools (such as the ECETOC-TRA Worker tool - skin module and RiskOfDerm), IH SkinPerm focuses on the assessment of the actual absorption of substances through the skin, the amount that becomes available systemically (in the body).[18]. Possible evaporation of the substance during the contamination and the process of skin absorption are discounted in the assessment.

The IH SkinPerm model provides an estimate of the importance of absorption through the skin compared with absorption through inhalation. This is expressed as the "dermal/respiratory uptake ratio".

A marginal note to be made is that IH SkinPerm can only be used within this current study to classify substances based on the potential for skin absorption. An exact estimate of the skin absorption for each substance cannot be made, because the fire services are specific factors that can strongly influence the skin absorption of a substance. This is particularly the case when substances come under a pack and are enclosed there (occlusion). The conditions under a pack (heat, sweat that forms a layer of water on the skin, etc.) can indicate a different order of priority for the skin absorption, because water solubility can then be significant. The chosen approach in this study therefore does not look at exact skin absorption of the substances, but assumes the skin absorption compared to absorption through inhalation (inhalation recording) at a given air concentration.

IH SkinPerm[16]

IH SkinPerm is an Excel application for estimating skin absorption. IH SkinPerm is a work product of the AIHA Exposure Assessment Strategies Committee (EASC) and the Dermal Project Team (DPT) in collaboration with Wil ten Berg, author of the original SkinPerm model.

In order to arrive at an estimate of skin absorption (skin permeation), only a limited number of physicochemical properties of the substance are required in the model, such as the molecular weight, the water solubility, the octanol-water partition coefficient and the vapour pressure.

These substance properties have been selected from the attached fabric database of IH SkinPerm or have been looked up in the literature if not available[17].

The same exposure situation was chosen for all substances in order to make a good comparison between the substances. See Annex 5 for further explanation of the calculation.

2.2.3 Classification method

For the classification of the substances in the case of fire smoke, as described in section 2.2., control banding is used.

The classification of this control banding has been submitted to the Expert Group (see Annex 1). The control banding is shown in Tables 1 to 5. Annex 3 provides further support for this classification.

In addition to control banding, a literature search was performed for all substances, looking at the described hazards of the substances and reported practical cases. Use has been made of information in the toxicological database Cheminfo[19].

One-off exposure

Table 1: Inhalation absorption, effects on one-off exposure to smoke (local and systemic effects)

Class	Hazard:
	Limit value ALV*) ≥ 1000 mg/m^3 or no relevant H-phrases
	Limit value ALV ≥ 100- <1000 mg/m^3 *(ALV value is prioritised over H-phrases)* or H332 *(harmful on inhalation)* or If inhalation recording: H371, H335, H336
	Limit value ALV > 25- <100 mg/m^3 *(ALV value is prioritised over H-phrases)* or H331 *(toxic on inhalation),* EUH071 *(corrosive to airways)* or If inhalation recording: H370
	Limit value ALV <25 mg/m^3 (ALV value is prioritised over H-phrases) or H330 (lethal on inhalation) Or H334 (test in literature that this applies to one-off exposure)

*) ALV: Alarm limit value - the air concentration above which irreparable or other serious health effects can occur, or where persons are less able to bring themselves to safety due to exposure to the substance. The intervention values used are derived for a duration of exposure of one hour[20].

Table 2: Absorption through the skin, effects of one-off exposure to smoke (local and systemic effects)

Class	**Hazard**
	No or low skin absorption, inhalation is the most important factor or No H-notation and no harmful effects described in literature by skin absorption, or Skin absorption is important or greatest factor with regard to inhalation recording in combination with H312 *(harmful in contact with the skin),* or H314, H315
	Skin absorption important or largest factor in relation to inhalation recording in combination with: H311 (toxic on contact with the skin) or H371
	Skin absorption important or largest factor with regard to inhalation recording

	in combination with: H310 *(lethal on contact with the skin),* or H370
	Not applicable to the substances in smoke

For both skin and inhalation, H360 is included in order to be able to comment on the influence of substances on fertility (reprotoxicity).

<u>One-off exposure</u>

Table 3: Inhalation absorption, effects of one-off exposure to smoke (local and systemic effects)

Hazard class	Hazard:
	No H-phrases present, or H332 *(harmful on inhalation)* If ingestion by inhalation (inhalation recording): H335 *(irritation)*, H336 *(drowsiness)*
	H331 *(toxic on inhalation)* H373 *(can cause damage to organs)* (if effect on lungs and/or inhalation) EU071 *(corrosive to respiratory tract*, if effect is also described for long-term exposure) H361F
	H330 *(lethal on inhalation)* H372 *(causes damage to organs)* (if effect on lungs and/or inhalation recording) H334 *(allergy, asthma symptoms)* H341, (suspicious mutagen) H351 (suspected carcinogenic) H360F *(influence on fertility)* (or suspected carcinogenic or mutagenic substance in literature)
	H340 *(mutagenic)* H350 *(carcinogenic)* (or proven carcinogenic or mutagenic substance in literature)

Table 4: Ingestion by mouth, effects of repeated exposure to smoke (local and systemic effects)

Hazard class	Hazard
	No H-phrases or H302 in dust form *(harmful if swallowed)*
	H301 in dust form *(toxic if swallowed)* H351 if possible carcinogenic to digestive tract itself If ingestion digestive tract: H341, H351, H360F *(influence on fertility)* (or possibly CMR substance in literature), H373
	H300 in dust form *(lethal if swallowed)* H350 if carcinogenic to digestive tract itself If ingestion digestive tract:

	H340 *(mutagenic)*, H350 *(carcinogenic)*, (or proven CM substance in literature), H372
	Not applicable to the substances in smoke

Table 5: Absorption through the skin, effects of repeated exposure to smoke (local and systemic effects)

Hazard class	**Hazard**			
	Skin absorption important or largest factor with regard to inhalation*),	**Skin absorption relevant factor with regard to inhalation, but not dominant*)**	**Inhalation is the most important factor, skin absorption is low, but present*)**	**Direct effect on the skin**
	In combination with H312,	in combination with H311, H312 or H373		
	in combination with H311 *(toxic on contact with the skin)*, H361F or H373 (if relevant for skin),	in combination with H310 *(lethal on contact with the skin)*, H372 *(causes damage to organs -* if relevant for skin), H341, H351 or H360F *(influence on fertility)* OR possible, carcinogenic, mutagenic or reproductive toxicity in literature.	in combination with H340 (mutagenic), H350 carcinogenic) OR proven carcinogenic or mutagenic material in literature.	H317 *(skin allergy)*
	- in combination with H310 *(lethal on contact with the skin)*, H372 *(causes damage to organs -* if relevant for skin), H341, H351, H360F *(influence on fertility)* OR possible carcinogenic, mutagenic or reproductive toxicant in	in combination with H340 (mutagenic), H350 (carcinogenic) OR proven carcinogenic or mutagenic material in literature		

	literature			
	- in combination with H340 (mutagenic), H350 (carcinogenic) OR proven carcinogenic, mutagenic or reproductive toxicity in literature)			H350 Carcinogenic to the skin itself

*) model, literature and/or H notation

2.2.4 Effects

Lastly, the most important effects for each substance (group) have been described. The following approach has been used for this:

- Effects on one-off exposure (breathing and skin) are roughly divided into five different groups (so-called toxidromes[21]), such as direct caustic effect on the lungs, direct effect on cell respiration and/or direct effect on the central nervous system. For the effect on the lungs, the water-solubility of the substance has also been examined. Water-soluble substances have an effect area at the top of the lungs, while insoluble or less soluble substances can penetrate deep into the alveoli (see also Annex 4).
- Effects on repeated exposure have been mapped using the available information from Cheminfo[19], possibly supplemented with specific literature[22, 23].

3 Result

3.1 Selection of substances

In 2007, Mennen and Van Belle[9] produced an overview of the most important harmful components that are released in a fire in the Dutch context. This overview is based on measurement data from the Environmental Accident Service (MOD) collected in more than fifty fires and on data from a limited review of the literature on emission factors, determined on the basis of combustion experiments and measurement data of fires. An overview has been produced of the most harmful components that occur in smoke during fires with different types of materials (e.g. plastics, rubber, wood, oil, chemicals and waste). There is also, by means of a qualitative scale, a determination of the order of magnitude of the emission.

In 2009, this overview was updated and expanded on the basis of information obtained through working visits, consulting experts and surveys of the literature[3].

In order to arrive at a selection of the most important harmful components that occur in smoke caused by regular fires, these studies were used as a basis. Of all substances reported by Mennen, the most important substances were selected in an expert session.

Table 6 gives an overview of the 32 selected substances. For a number of substances they can occur as a group of substances in fire smoke, such as the polycyclic aromatic hydrocarbons (PAHs). Out of these groups so-called marker substances have been chosen; these are substances with the most dangerous properties. Annex 5 contains as background information an overview of the most important physical properties of these substances.

In addition to specific substances, dust particles are generally included. They are divided according to size. The size of dust particles is important because it determines where the particles end up in the airways and/or whether they can also be absorbed by the body. For this the following classification is used:

- PM 10 → particles smaller than <10 μm; these particles mainly end up in the upper airways.
- PM 2.5 → particles smaller than <2.5 μm; these particles can penetrate into the alveoli.
- Ultrafine (nanoparticles) → particles smaller than 0.1 μm (in length or width); they penetrate the alveoli and can also be absorbed into the body.

Table 6: Overview of the 32 selected substances

Substances	**Substances treated as marker substances for an entire group**
• CO - Carbon monoxide • NO2 - Nitrogen dioxide • HCN - Hydrogen cyanide (hydrocyanic acid) • SO2 - Sulphur dioxide • HCL - Hydrochloride (Hydrochloric acid)	Hydrocarbons: • Benzene • Styrene • Xylene • Toluene • Ethylbenzene • Hexane

• Phosgene • Perfluoroisobutene (PFIB) • HF - Hydrogen fluoride • Phosphorous pentoxide *A separate group that has been named are dust particles in general on the basis of their size:* • Ultrafine dust/nanoparticles • PM 2.5 • PM 10	• (mono) Chlorobenzene • Phenol Polycyclic aromatic hydrocarbons: • Benzo [a] pyrene • Pyrene Aldehydes and ketones: • Acrolein • Formaldehyde • Acetaldehyde Isocyanates: • TDI - 2,4-toluene diisocyanate • Methyl isocyanate • Phenyl isocyanate Dioxins and furans: • TCDD (2,3,7,8-Tetrachlorodibenzodioxin) • Furan • Dibenzofuran Metal: • Lead

3.2 Top 32 substances with hazard for each absorption route

Based on the assessment method as described in Chapter 2, the following hazard classification has been made for each substance and for each exposure route.

Table 7: Top 32 substances in smoke caused by fire with hazard classification for each absorption route

Name	**Inhalation - one-off exposure**	**Inhalation - repeated exposure**	**Skin - one-off exposure (absorption)**	**Skin - repeated exposure**	**Mouth - repeated exposure**
CO - Carbon monoxide					
NO_2 - Nitrogen dioxide					
HCN - Blue acid					
SO_2 - Sulphur dioxide					
HCL - hydrochloric acid					
Hydrocarbons					
– Benzene					
– Styrene					
– Xylene					
– Toluene					
– Ethylbenzene					

– Hexane					
– (mono) Chlorobenzene					
– Phenol					
Aldehydes and ketones					
– Acrolein					
– Formaldehyde					
– Acetaldehyde					
Isocyanates					
– TDI - 2,4-toluene diisocyanate					
– Methyl isocyanate					
– Phenyl isocyanate					
Phosgene					
Perfluoroisobutene (PFIB),					
HF - Hydrogen fluoride					
Ultrafine dust/nanoparticles					
PM 2.5					
PM 10					
BUSINESS PACK					
– Benzo [a] pyrene					
– Pyrene					
Dioxins and furans					
– TCDD – (Tetrachlorodibenzodioxin)					
– Furan					
– Dibenzofuran					
Metal					
– Lead					
Phosphorous pentoxide					

3.3 One-off exposure

Health effects may occur with one-off exposure to substances in fire smoke. The results of the hazard classification of the substances are shown below for each admission route.

3.3.1 Through inhalation

The most critical substances in one-off (high) exposure to substances in smoke from fire are the substances that influence breathing (the so-called asphyxants) and the highly irritant substances. In addition, there is a residual group with substances that have effects on the nervous system. Concerning carcinogenic substances, questions often arise after a one-off exposure. So this chapter also provides an explanation of this risk.

For the sake of completeness, the alarm values of the selected substances are included in Annex 6 for one-off exposure through inhalation. These values are taken into account when classifying the different hazard classes.

Effects on oxygen transport and/or cell respiration - Asphyxants

There are a number of substances that are directly and easily absorbed by the lungs in the body. Once taken up they have a direct effect on oxygen transport in the body and/or on the respiration of cells, making them extremely toxic. Bluacid is considered the substance with the greatest dangers. There is no accumulation of these substances in the body. An overview of the substances concerned is included in the table below.

Table 8: Effects on oxygen transport and/or cell respiration in one-off (high) exposure

<table>
<tr><th>Name</th><th>Inhalation - one-off exposure</th><th>Effects</th></tr>
<tr><td>CO - Carbon monoxide</td><td></td><td rowspan="2">Are absorbed by the lungs in the body. Carbon monoxide has an effect on oxygen transport and hydrogen cyanide has an effect on cellular respiration.

Both substances cause headaches at relatively low doses, and are lethal at higher concentrations. (Main effect with single high exposure: on cardiovascular system and nervous system)

HCN - Hydrogen cyanide (hydrocyanic acid) is also absorbed through the skin, this does not apply to carbon monoxide</td></tr>
<tr><td>HCN - Hydrogen cyanide (hydrocyanic acid)</td><td></td></tr>
</table>

Strong irritant/corrosive effects

Substances with a strong irritant/corrosive effect have a direct effect on the airways. The degree of solubility determines where the first damage occurs in the airways. With a one-off (high) exposure there is a risk of suffocation. This is possible because the upper airways swell, but also because damage occurs at the level of the alveoli (e.g. pulmonary oedema). The latter can also occur from a few hours up to a day after the exposure. The effect is that there is such an influence on the respiratory system that the effects can be large.

Of the 32 selected substances, the substances in Table 9 have a corrosive effect with single - high exposure. It should be noted here that the effect is ultimately determined by a combination of the dose (concentration in the air) and the toxicity.

In addition, a number of substances in smoke can cause asthma, even in a one-off (high) exposure. In the literature, cases are described in which persons contract permanent asthma due to one-off exposure to (highly) irritant substances (so-called RADS (Reactive Airways Dysfunction Syndrome)[24]. The table below contains an overview of the substances concerned.

Table 9: Effect of irritant/corrosive substances in a one-off (high) exposure

Name	Inhalation - one-off exposure	Effects
NO_2 - Nitrogen dioxide		Caustic effect on (especially low) respiratory tract, can cause severe lung damage with influence on breathing, also the risk of developing asthma after a one-off exposure (Reactive Airways Dysfunction Syndrome (RADS).) Can cause suffocation due to pulmonary oedema.
Phosgene		
Perfluoroisobutene (PFIB),		
SO_2 - Sulphur dioxide		Caustic effect especially on upper airways, can cause suffocation by swelling of, in particular, upper airways. *At high concentrations also a risk of pulmonary oedema.* Emergence of asthma after a one-off exposure (Reactive Airways Dysfunction Syndrome (RADS)[24]. High exposure to isocyanates can also cause pneumonia and generate an immunological occupational asthma in addition to RADS.
HCL - hydrochloric acid		
Acrolein		
Formaldehyde		
Acetaldehyde		
Phosphorous pentoxide		
TDI - 2,4-toluene diisocyanate		
Methyl isocyanate		
Phenyl isocyanate		
HF - Hydrogen fluoride		Corrosive effect on respiratory tract also affects blood calcium levels, may also cause asthmatic reaction (main effect in acute exposure: on respiratory tract, cardiovascular system and nervous system). Emergence of asthma after a one-off exposure (Reactive Airways Dysfunction Syndrome (RADS) [24,25]

One substance with a high hazard potential is HF - hydrogen fluoride. This substance not only affects the lungs, but is also absorbed into the body, where it affects the calcium metabolism. This effect is particularly seen when specific hydrogen fluoride is present in the site of the fire (for example, companies with hydrogen fluoride in storage).

<u>Effects on the nervous system</u>

There is another group of residues with substances that can affect the nervous system with a one-off (high) exposure. However, the effect of these substances is not expected to be central. These substances occur in fire smoke, especially in combination with the above highly irritant substances and/or asphyxants. These effects are therefore expected to be predominant.

This involves the following substances:

Table 10: Effects on the nervous system with a one-off (high) exposure

Name	**Inhalation - one-off exposure**
Styrene	
Phenol	
Furan	
(mono) Chlorobenzene	

<u>(Suspicion of) carcinogenic substances</u>

For a number of substances, a CRP (Cancer Risk Potency) value is known[20], which can be used to quantify the risk of carcinogens in one-off exposure. However, one-off exposure to carcinogens has little impact on the accepted risk*).

CRP values**) are known for:

- Benzene - 2800 mg/m^3
- Formaldehyde - 1752 mg/m^3
- Acetaldehyde- 9900 mg/m^3

For Formaldehyde and Acetaldehyde, the CRP value is far above the life-threatening value of respectively 69 mg/m^3 (1 hour) and 1500 mg/m^3 (1 hour).

For Benzene the CRP value is 2800 mg/m^3 (1 hour), almost equal to the alarm value (2600 mg/m^3), but it is below the life-threatening value of 13,000 mg/m^3 [20]. The probability that the CRP value is achieved with one-off exposure to benzene in fire smoke is very low. In the case of benzene, this substance also occurs in fire smoke, particularly in combination with highly irritant substances and/or asphyxants. These effects are therefore expected to be predominant.

* For most carcinogenic and mutagenic substances, a safe lower limit cannot be determined. For these substances, a limit value with a target risk of 4 x 10^{-5} was chosen for 40 years of occupational exposure and a prohibition risk that is a factor of 100 higher.

**) All used intervention values (CRP, ALV, LBW) are derived for a duration of exposure of one hour[20]

<u>(Suspicion of) reprotoxic substances</u>

There are three substances that affect fertility in general: Benzo[a]pyrene, Lead and Hexane. It has been estimated that a one-off exposure has no lasting effects on fertility. In addition, there are a number of substances that can have a negative influence on the development of the unborn child: Carbon monoxide, Styrene, Toluene, Methylisocyanate, Lead and Benzo[a]pyrene. The extent of this risk depends on the dose taken in the body and the developmental stage of the unborn child. This question is not answered within this study, but it is essential for a decision as to whether there is actual damage from a one-off exposure to these substances in fire smoke.

3.3.2 Through the skin

There are two substances that can pose a risk from a one-off exposure due to skin absorption, namely HCN (hydrocyanic acid) and phenol.

Table 11: Overview of substances that can cause effects through the skin on one-off (high) exposure

Name	**Inhalation - one-off exposure**	**H-notation**	**Skin absorption mentioned in literature**
HCN - Hydrogen cyanide (hydrocyanic acid)		Yes	Yes, very rapid skin absorption
Phenol		Yes	Yes, rapid absorption

Both substances are absorbed rapidly through the skin, including on exposure to smoke through fire. In Cheminfo[19] two cases were described of firefighters with symptoms of cyanide poisoning - even though respiratory protection was worn - with a presumption of exposure through the skin. In both cases it was a special situation, namely the release of cyanide gas. There is no information on skin absorption of HCN - hydrogen cyanide (hydrocyanic acid) in smoke from fire. For the description of the effects, reference is made to the description in §3.3.1 - Inhalation.

3.4 Repeated exposure

In the event of repeated exposure to substances in fire smoke, there are the following scenarios:

- A substance rapidly leaves the body, but repeated exposure increases the chance of certain effects such as cancer, asthma;
- A substance accumulates in the body and therefore creates an extra-long exposure. This effect occurs in a small number of substances (TCDD, lead and hydrogen fluoride).

Most substances in fire smoke disappear rapidly after exposure.

3.4.1 Through inhalation

In the event of repeated inhalation of smoke, exposure to substances can arise which, on the basis of their effect, can be classified in the following groups:

- (suspicion of) carcinogenic and mutagenic substances, directly in the lungs or elsewhere in the body;
- substances that can cause (chronic) airway symptoms such as asthma, higher sensitivity to pneumonias, hypersensitivity reactions;
- substances that are absorbed by the lungs and cause a toxic effect elsewhere in the body.

(Suspicion of) carcinogenic and mutagenic substances

There are several substances that increase the risk of cancer or cause genetic damage (mutagenic substances) with repeated exposure. Benzene[a]pyrene and formaldehyde are carcinogenic to humans (H340). Furan and Benzo[a]pyrene can cause genetic damage (H350 mutagen). It should be noted that Benzo[a]pyrene is part of the group of substances that is also referred to as polycyclic aromatic hydrocarbons (PAHs). This group contains, in addition to Benzo[a]pyrene, even more carcinogenic substances.

Table 12 provides an overview of the tested substances that have (suspected) carcinogenic properties or the ability to cause genetic damage.

Table 12: Overview of the most important carcinogenic and mutagenic substances in fire smoke

Name	**Inhalation - repeated exposure**	**Carcinogenic according to H-phrases**	**Mutagen, according to H-phrases**	**Register CMR Nederland 2016**
Benzene		May cause cancer	May cause genetic damage	Carcinogenic Mutagen
Formaldehyde		May cause cancer	Suspected of causing genetic damage	Carcinogenic
Acetaldehyde		Suspected of causing cancer	No	Carcinogenic
Phenol		No	Suspected of causing genetic damage	No
Furan		May cause cancer	Suspected of causing genetic damage	Carcinogenic
TCDD (2,3,7,8-Tetrachlorodibenzodioxin)		No	No	Carcinogenic, safe lower limit
TDI - 2,4-toluene diisocyanate		Suspected of causing cancer	No	No
Benzo[a]pyrene (PAH)		May cause cancer	May cause genetic damage	Carcinogenic Mutagen

TCDD (belonging to the group of dioxins) is carcinogenic, but unlike many other carcinogenic substances, TCDD has a safe lower limit.

Formaldehyde has a strengthening effect on the carcinogenicity of other substances[19].

(Suspicion of) reprotoxic substances

As already mentioned in §3.3.1 there are a number of substances that can influence the fertility and development of the unborn child (Lead, Benzo[a]pyrene and Hexane). These effects may occur with repeated exposure.

(Chronic) airway effects

There are several substances that may have an effect on airways with repeated exposure, especially on the development of asthma and increased sensitivity to pneumonitis. An overview of these substances is included in Table 13.

Table 13: Effects on airways with repeated exposure

Name	**Inhalation - repeated exposure**	**Effect**
NO_2 - Nitrogen dioxide		Inflammation and impaired lung function with prolonged exposure
SO_2 - Sulphur dioxide		Lung disease, asthma/COPD; not proven
Acrolein		Chance of mucous membranes of the upper respiratory tract, always first upper respiratory tract irritation
Formaldehyde		Asthma, upper respiratory tract irritation
TDI - 2,4-toluene diisocyanate		Asthma
Methyl isocyanate		Asthma
Phenyl isocyanate		Asthma, chronic inflammations from nose to lung, lung fibrosis
Phosgene		Increased susceptibility to pneumonia during prolonged exposure
Perfluoroisobutene (PFIB),		Increased susceptibility to pneumonia during prolonged exposure
HF - Hydrogen fluoride		Severe damage to airways
Ultrafine dust/nanoparticles		(Cardiovascular diseases and) lung diseases[26.27]
PM 2.5		(Cardiovascular diseases and) lung diseases[26]

Effects on the nervous system - solvents

The table below provides an overview of substances that can be absorbed into the body through the lungs and that have an effect on the nervous system.

Table 14: Substances that affect the nervous system with repeated exposure

Name	Inhalation repeated exposure	Effect nervous system
Benzene		Central nervous system
Styrene		Central nervous system
Xylene		Central nervous system
Toluene		Central nervous system
Phenol		Central nervous system, liver and kidneys
Hexane		Peripheral nervous system.

Other effects

The table below provides an overview of substances that are absorbed into the body through the lungs and can have other toxicological effects elsewhere.

Table 15: Substances that may have different effects on the body with repeated exposure

Name	Inhalation - repeated exposure	Effect
CO - Carbon monoxide		Asfyxiant (systemic), Parkinson-like symptoms, psychological problems
NO_2 - Nitrogen dioxide		Blood damage (methemoglobinaemia), with long-term exposure (e.g. air pollution)
HCN - Hydrogen cyanide (hydrocyanic acid)		Asfyxiant (systemic), anemia, thyroid dysfunction, and non-specific symptoms such as headaches
Ultrafine dust/nanoparticles		Effect on cardiovascular disease [26, 27, 28, 29, 30, 31]
PM2.5		Effect on cardiovascular disease [26]

Name	Inhalation - repeated exposure	Effect
> TCDD (2, 3, 7, 8-Tetrachlorodibenzodioxin)		Very toxic substance (caused by chloracne, etc.) TCDD is the most toxic substance in this group of dioxins*). TCDD seems to reach the body mainly through eating (hand-mouth contact). There are also no limit values for the air concentration.

*) Dioxin is a collective name for a number of chemically related compounds. There are 75 chlorinated dibenzo-p-dioxins (PCDDs) and 135 dibenzofurans (PCDFs). These 210 chlorinated related compounds are called congeners. Due to a long elimination half-life of these 210 chlorinated compounds, the concentrations of 2,3,7,8-chloro-substituted dioxins and -furans in mammals in the liver and adipose tissue are higher than in other organs and tissues. These 17 compounds have toxic effects at extremely low doses compared to the other dioxins and furans and are therefore called the toxic congeners. TCDD is the most toxic substance in this group.

3.4.2 Through the skin

Based on the Hazard-phrases (H phrases) and literature search, it was determined which of the 32 selected substances could be absorbed into the body through the skin. These are 22 substances. For these 22 substances with the help of IH SkinPerm, the extent to which skin absorption is an important factor in relation to inhalatory exposure has been determined. An overview of this is included in the table below.

Table 16: Classification of substances based on the ratio between absorption through the skin and absorption through respiration.

Dermal/respiratory recording ratio	Explanation	Classification of substances
> 2	Skin absorption is important or greatest factor with regard to inhalation	HCN - Hydrogen cyanide (hydrocyanic acid) Phenol
> 1-2	Skin absorption relevant factor with regard to inhalation, but not dominant	Phenyl isocyanate Pyrene Benzo[a]pyrene
> 0.1 - 1	Inhalation is the most important factor, skin absorption is small but present factor	Dibenzofuran TDI Styrene
> 0.01 - 0.1	Inhalation is the most important factor, skin absorption is a minor factor	Toluene Xylene Ethylbenzene Furan Benzene
≤ 0.01	Inhalation is the most important factor, skin absorption is very small/irrelevant	Acrolein Formaldehyde (value for liquid - not for gas) Methyl isocyanate Phosgene PFIB HF - Hydrogen fluoride TCDD (2,3,7,8-Tetrachlorodibenzodioxin) Hexane

The fact whether skin absorption is a relevant factor (relative to inhalation) and the potential to cause effects in the body has led to a further hazard classification of these 22 substances.

Table 17 provides an overview of substances that may be relevant in the event of repeated exposure to smoke from fire by skin absorption or causing skin allergy/skin cancer. Table 18 contains substances that are classified in the "green" category on the basis of their H-phrases and/or the literature. These substances are not considered to be relevant for skin absorption on exposure to smoke caused by fire.

Table 17: Hazard classification of substances based on hazardous properties and the extent to

which they can be absorbed through the skin.

Name	Skin - repeated exposure	H-notation	Skin absorption mentioned in literature	Importance of skin absorption with regard to inhalation (Skinperm)	Effect
HCN - Hydrogen cyanide (hydrocyanic acid)		Yes	Yes, very rapid skin absorption	Important	Asfyxiant (systemic), anemia, thyroid dysfunction, and non-specific symptoms such as headaches.
Benzene		Yes	Yes, but low skin absorption	Low factor	Carcinogenic and mutagenic
Phenol		Yes	Yes, rapid skin absorption	Important	Phenol can strengthen carcinogenic properties of other substances (such as Benzo (a) pyrene (PAH) - which causes skin cancer) (synergistic effect)
TDI - 2,4-toluene diisocyanate		No	No	Small, but present	Skin allergy
Methyl isocyanate		No	Yes, unknown	Very small/not relevant	Skin allergy
Phenyl isocyanate		No	No	Relevant, not dominant	Skin allergy
Benzo[a]pyrene (PAH)		No	Yes, very rapid skin absorption	Relevant, not dominant	Carcinogenic, both after absorption through the skin and also directly causes skin cancer
Furan		No	Yes, but little	Low factor	Carcinogenic

In the case of repeated exposure to substances in fire smoke, dust-like components in particular pose a potential hazard. Especially in Benzo[a]pyrene (PAH) there is a hazard of skin cancer. This substance is rapidly absorbed through the skin.

HCN - Hydrogen cyanide (Blue Acid) is also absorbed very rapidly through the skin. Depending on the dose, it can cause symptoms at various points in the body.

Benzene and Furan are potentially hazardous substances as they are carcinogenic and mutagenic respectively. Absorption through the skin is, however, low. Benzene does have a skin notation, but in the literature it is indicated that absorption through the skin is usually low due to the rapid evaporation of benzene[19, 16].

There is also a real chance that some substances that occur simultaneously in fire will reinforce each other's effect. Animal studies suggest that Formaldehyde enhances the effect of other carcinogens and promotes or enhances allergic inflammatory reactions to allergens[19]. Fenol also seems to be able to strengthen the carcinogenic properties of other substances. In addition, it can cause damage at various places in the body (including the liver and kidneys). Phenol is absorbed relatively rapidly through the skin.

Table 18: Substances that have an H-notation or where skin absorption is mentioned in the literature, but which are classified in the lowest hazard class.

Name	**Skin - repeated exposure**	**H-notation**	**Skin absorption mentioned in literature**	**Importance of skin absorption with regard to inhalation (SkinPerm)[16]**	**Note**
Styrene		No	Yes	Small, but present	Styrene is absorbed through the skin, but skin absorption is not seen as a relevant source for employees.
Xylene		Yes	Yes	Low factor	Xylene can be absorbed through the skin (both liquid and vapour), but not to such an extent as through inhalation (no significant effects are to be expected through this route).
Toluene		No	Yes	Low factor	However, rapid absorption, but only effects at high concentrations
Ethylbenzene		Yes	Yes	Low factor	Ethylbenzene is absorbed by the skin in relatively small amounts. No harmful effects are expected due to skin absorption.
Acrolein		No	Yes	Very small/not relevant	Direct effects (corrosive) will first occur. In Cheminfo no indications that skin absorption takes place[19]. In chemistry map book no description of systemic effects
Pyrene		No	Yes	Relevant, not dominant	No effects known

3.4.3 Through the mouth

Based on the literature, effects by mouth are not considered to be really possible with gases. In addition, there are many relatively low-toxic substances, assuming that there is only hand-to-mouth contact.

There are three potentially high-risk substances/groups of substances, two of which are based on their potential to cause cancer:

- A number of Polycyclic Aromatic Hydrocarbons (PAHs), with Benzo[a]pyrene as one of the most important;
- A number of dioxins; tCDD (2,3,7,8-Tetrachlorodibenzodioxin) is the most toxic, this substance causes chloracne and is also carcinogenic;
- Lead - mainly affects the fertility of humans.

4 Discussion and assessment

Smoke is combined exposure

Many different substances are released when there is a fire. Some of these substances have the same impact or effect on the body, as a result of which the effects of these substances have to be added up as it were (so-called additive effect). This applies, for example, to asphyxants and solvents. In the interpretation of the hazards of the different substances, the separate substances have been considered in this study and no account has been taken of combined exposure.

It is also possible that substances will reinforce each other's effect (so-called synergistic effect). Examples are phenol and formaldehyde. These substances may enhance carcinogenic properties of other substances (such as Benzo[a]pyrene (PAH)). However, the synergistic effect of different substances is often unknown. When interpreting the hazards of substances in this study, this effect was therefore not included, but at most added as a comment when specific synergy was mentioned in the literature.

Smoke and health effects in general

In this study the health effects of the individual substances in smoke have been examined from a theoretical context. However, it is already known from the literature that exposure to smoke can cause health problems. This is how F. Greven reported in 2011[6] an increase in respiratory complaints after an inhalation incident, but also an increase in the chance of respiratory complaints with an increase in the number of exposures. Effects are also greater in persons with a predisposition to asthmatic disorders (atopy) and research has shown that there is more asthma in the fire service than in the general population[6, 32].

These findings are in line with the results of this study. Specifically, a number of substances in smoke from fire can be identified which can cause chronic respiratory symptoms when inhaled (inhalation exposure). In addition, these findings also support the earlier observation of the incomplete functioning of the respiratory protection used.

Smoke and other sources in the environment

In firefighting, in addition to smoke, exposure can also occur to other combustion gases caused by aggregates, diesel vehicles and/or cigarette smoke. These other combustion gases partly contain the same harmful substances as also occur in fire smoke. Both diesel exhaust gases and cigarette smoke are proven to be carcinogenic and can also cause respiratory complaints.

These exposures to other sources cannot be separated from smoke exposure due to fire when it comes to hazard indication and risk assessment. These sources were not included in the research that has been carried out, but they could have an influence on performing risk analyses and taking measures.

Specific substances at companies

As mentioned earlier, specific hazards/risks can arise when fires have to be extinguished in situations where specific hazardous substances are present, such as for example in certain BRZO companies. These hazards/risks have not been included in this study and should be included within the emergency response plans of the companies concerned.

Because that is far from always the case in practice, this can be regarded as an additional and insufficiently controlled risk for the fire service.

5 Conclusions

A number of questions were formulated at the beginning of this report. They are answered in turn below.

What are the absorption routes of the most important toxic substances that occur in fire smoke?

<u>One-off exposure</u>

For one-off exposure, intake through inhalation is the most important route. The chance of effects that occur with one-off (high) exposure through the skin is regarded as small.

- Inhalation

  The greatest hazard with one-off exposure to smoke is a relatively large group of substances that have a direct negative effect on the airways and some substances that influence oxygen transport or cell respiration.

- Skin

  There are only a limited number of substances that can be absorbed through the skin and with a one-off (high) exposure have the potential to cause effects. This concerns in particular HCN - hydrogen cyanide (hydrocyanic acid). In the literature, however, no effects have been described by HCN skin absorption caused during regular fires, but only in situations where specific hydrocyanic acid was released.

<u>Repeated exposure</u>

Even with repeated exposure to substances in smoke from fire, inhalation is the most important absorption route for many substances. The absorption route through the skin is only of importance for a limited number of substances.

- Inhalation

  Multiple substances in smoke can cause asthma with repeated exposure. Previous research has shown that there is more asthma in the fire service than in the general population and that the chance increases with the number of exposures[4]. This indicates that there is indeed exposure through breathing, despite the use of respiratory protection.

  In addition, there are quite a few substances that can cause other health damage during intermittent exposure, such as cancer, cardiovascular diseases, effects on the nervous system and similar. Whether these effects actually occur depends on the degree of exposure to smoke (and possibly other sources in the environment such as cigarette smoke and diesel exhaust gases).

- Skin

  With repeated skin exposure to substances in fire smoke, specific components in dust are important. This mainly concerns Benzo[a]pyrene (PAH), which can cause skin cancer and is absorbed rapidly through the skin. Simultaneous exposure to Phenol accelerates the skin absorption of Benzo[a]pyrene (PAH) in the body and simultaneous exposure to formaldehyde may potentially enhance carcinogenic properties. In addition, Benzene and Furan are potentially hazardous substances, since benzene is proven to be carcinogenic to humans and furan has mutagenic properties. Absorption through the skin is, however, low in these substances.

HCN - hydrogen cyanide (hydrocyanic acid) is rapidly absorbed through the skin and can act in different parts of the body depending on the dose. Lastly, there are a number of substances in smoke that can cause skin allergies, such as isocyanates.

- Absorption by mouth

  Through hand-mouth contact, there are three substances that, based on their properties, can present a hazard, namely Benzo[a]pyrene (PAH) and TCDD (2,3,7,8-Tetrachlorodibenzodioxin) through carcinogenic properties and lead through reprotoxic properties (negative effect on male fertility).

Is skin absorption a real route when exposed to toxic substances that occur in fire smoke?

Skin absorption is a real route for a very limited number of substances. So skin exposure should certainly be included in future risk assessments.

How important is this absorption route in relation to other routes of absorption (through inhalation and through the mouth)?

As far as the relationship between inhalation and skin exposure hazards is concerned, the risk of inhalation through inhalation is the greatest hazard when exposed to smoke. The risk of inhalation is present when, for example, the mask is removed too soon, when the mask does not connect properly to the face and/or when an unprotected person is not at an adequate distance from the fire. It should be noted here that exposure can also take place through inhalation of other sources where combustion processes take place, such as cigarettes or combustion of diesel (particularly relevant to the pump operator).

What are the most critical substances for absorption through the skin?

The risk of skin absorption and skin effects is especially present with repeated exposure. The most critical substance for absorption through the skin is Benzo[a]pyrene (PAH). Simultaneous exposure to Phenol accelerates the skin absorption of Benzo[a]pyrene (PAH) in the body. PAH is an important component because it occurs in all fires.

Benzene and Furan are also critical substances, given their carcinogenic properties, but these substances are absorbed less rapidly than Benzo[a]pyrene.

6 Recommendations

Based on the results of the study, the following recommendations are made:

1. Inhalation of substances

   Because inhalation of substances is the greatest hazard, continuing attention to the prevention of inhalation of smoke is important.

   It is advisable to make even more sure that inhalation of smoke is prevented. This can be done by:

   - Carrying out further research to better map the times at which smoke can be inhaled, such as in the event of a too rapid removal of respiratory protection or unexpected changes of wind. Based on the findings, further measures may be taken to prevent unnecessary exposure.
   - Strengthen the fire service's awareness process when exposure to smoke can take place, for example by making the exposure to different working methods literally visible through visualisation methods (such as Pimex*). It is recommended to link this to a good information campaign.
   - Introducing the so-called "fitness test" for everyone wearing respiratory protection, so that the mask always fits well on the face.

   **) PIMEX, in full Picture Mix Exposure, is a method to measure the effect of working methods and workplace conditions on the exposure to hazardous substances, nanoparticles, physical exertion and noise, and simultaneously show them in one video screen.*

2. From hazard to risk

   This study has focused in particular on the hazards and hazard potential of the most important 32 substances in smoke. To find out more about the actual risk of these substances in fire smoke, further research is needed into the actual exposure and absorption in the body. The first step is to compare the available literature on the concentration ranges of these substances and the results of this study. In this way the most critical substances can be determined and statements can be made about the risk of health effects.

   On the basis of this, it can also be determined whether these critical substances are already being measured at this moment or whether adaptation is necessary.

3. Skin exposure and skin absorption

   As with inhalation, the skin needs to be mapped when there is skin exposure during repression and when skin absorption is possible.

   The results of this study do not stand alone and will have to be combined with the two studies on pollution, permeability and cleanability of protective fireman's clothing and skin stress. If it turns out that firefighting clothing allows certain substances to pass through, it is important to determine for the substances with skin absorption how much can actually be absorbed during repression.

If the packs are permeable, it is possible that substances can get trapped between the pack and the skin (occlusion). This factor influences the amount and characteristic of skin absorption and should be borne in mind in the assessment of skin absorption.

What further measures/studies are needed or what advice can be given is also related to the results of the other two studies.

4. Prevent hand-to-mouth contact and skin contact

It is recommended to reinforce the existing hygiene rules and agreements about eating/drinking/smoking during and after extinguishing work in order to prevent hand-to-mouth contact and skin contact. A further consideration would be to provide information on this with the support of visualisation methods.

5. Monitoring

It could be envisaged, after implementing measures, to monitor whether these measures are sufficient. The use of biological monitoring, which measures whether substances are actually being absorbed in the body, could be considered as an option for this.

6. Special substances

This report has only assessed substances that occur most often in fire smoke. When extinguishing fires at particular companies/transport vehicles, completely different substances might pose the greatest risk. It is advisable to make an assessment of this within the disaster control plans.

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Annex 1 Performance and meetings

The project was carried out in the period November 2016 - April 2017. It was implemented by:

- Jolanda Willems MBA*), certified toxicologist and occupational hygienist, Coöperatie PreventPartner - project leader;
- Dr Remko Houba*), occupational hygienist and researcher, IRAS, NKAL and Coöperatie PreventPartner;
- Dr. Frans Greven*), registered toxicologist-researcher, GAGS, GGD Groningen, with a specific focus area: selection of substances during fires and the relation smoke exposure - health effects;
- Dr. Ellen Wissink, certified occupational hygienist (Coöperatie PreventPartner), with specific focus: skin (models).

The following experts have been involved in this study (Expert group):

- Ronald Heus*), IFV - client;
- Ir. Peter Bos, RIVM, because of his specific knowledge about skin absorption; testing of control banding;
- Wouter Fransman, TNO, because of his specific knowledge about skin absorption;
- Dr. Koen Desmet, Captain Fire service centre, SCK-CEN Academy Ghent/Visiting Professor at the University of Antwerp - former researcher on substances in fire smoke;
- Dr Marcel Mennen, RIVM, knowledge about substances in smoke;

A project group has been set up for the project-based and substantive implementation of the research. The members of the project group are marked with *).

The following meetings were held for the study:

Table 19: Overview of study meetings

Type of meeting	**Attendees**	**Result of meeting**	**Date**
Start meeting	Project group	Detail design project, preparation of meetings	December 2016
Experiment session skin absorption	E. Wissink, P. Bos, J. Willems, W. Fransman, R. Heus	Determination of the applicable methodology for skin exposure/absorption and testing of control banding of substances that are most critical for health in fire smoke	18-1-2017
Experts session smoke	K. Desmet, M. Mennen, F. Greven + project group	Selection of the most critical substances in smoke caused by fire	19-1-2017
Inventory of exposure in a fire	Experiential experts from fire service + project group	First rough inventory made with various stakeholders in the field, through a one-off meeting, to chart worst case situations and the	

		average exposure for each fire	
Discussion of outcomes with safety committee fire service	J. Willems, F. Greven R. Heus	Discussion of recommendations from reporting	20-4-2017

Annex 2 Background information on hazards of substances and H-phrases

The development of effects by toxic substances differs from substance to substance. Important aspects of the toxic effect are:

- Immediate effects versus exiting effects - most substances produce an effect immediately after administration, while carcinogens only become apparent after a long latency period.
- Reversible (reversible) versus irreversible (irreversible) effects.
- Local effects versus systemic effects - local effects occur at the site of contact, such as skin, eyes or airways. Systemic effects occur somewhere in the body after transport of the substance. The place where the effect is revealed is the target organ ("target").

Another classification of toxic substances is according to the nature of symptoms and the place of effect. This concerns the following classical classification of toxic substances, which can be seen in the Hazard-phrases:

- Irritants and corrosive substances: Irritants are substances with a stimulating effect on mucous membranes of mainly eyes and airways. Corrosive substances have a stronger effect on mucous membranes and skin.
- Asphyxants (respiratory toxins): These are substances that reduce the availability of oxygen through interaction at different levels.
- Narcotics (intoxicating or sleep-inducing substances).
- Systemic toxic substances (organ toxicants, for example kidney toxic or neurotoxic).
- Other effects (carcinogen, reprotoxic, allergenic).

If a toxic effect has been established, it is important to look at the relationship between the dose (or concentration) and the effect. The dose-effect relationship indicates the link between the dose and the level of effect. The dose-response relationship indicates the relationship between the dose and the number of persons in a group that responds to it:

- Acute toxicity: the dose-response relationship has been established with short-term exposure (single dose)
- Chronic toxicity: effects occur after a long period of exposure to a substance

Substances are classified according to the so-called CLP guidelines. In addition to a hazard symbol, they also receive warning phrases, the so-called H-phrases. An overview of the relevant H-phrases (for this study) is given in Table 20 on the next page.

Table 20: Overview of relevant H-phrases

Code	Applies to	Text
H300	Acute oral toxicity, hazard categories 1 and 2	"Lethal if swallowed."
H301	Acute oral toxicity, hazard category 3	"Toxic if swallowed."
H302	Acute oral toxicity, hazard category 4	"Harmful if swallowed."
H304	Aspiration hazard, hazard category 1	"May be lethal if swallowed and enters airways."

H310	Acute dermal toxicity, hazard categories 1 and 2	"Lethal in contact with the skin."
H311	Acute dermal toxicity, hazard category 3	"Toxic in contact with skin."
H312	Acute dermal toxicity, hazard category 4	"Harmful in contact with skin."
H314	Skin corrosion/irritation, hazard category 1A, 1B and 1C	"Causes severe burns and eye damage."
H315	Skin corrosion/irritation, hazard category 2	"Causes skin irritation."
H317	Skin sensitization, hazard category 1	"May cause an allergic skin reaction."
H319	Causes serious eye irritation	
H330	Acute inhalation toxicity, hazard categories 1 and 2	"Lethal by inhalation."
H331	Acute inhalation toxicity, hazard category 3	"Toxic on inhalation."
H332	Acute inhalation toxicity, hazard category 4	"Harmful by inhalation."
H334	Respiratory sensitization, hazard category 1	"May cause allergy or asthma symptoms or breathing difficulties on inhalation."
H335	Specific target organ toxicity - one-off exposure, hazard category 3, respiratory tract irritation	"May cause respiratory irritation."
H336	Specific target organ toxicity - one-off exposure, hazard category 3, narcotic effects	"May cause drowsiness or dizziness."
H340	Germ cell mutagenicity, hazard category 1A and 1B	"May cause genetic damage <report route if it is conclusively proven that the hazard is not present on other routes of exposure>."
H341	Germ cell mutagenicity, hazard category 2	"Suspected of causing genetic damage. State <exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."
H350	Carcinogenicity, hazard category 1A and 1B	"May cause cancer <expose exposure route if it is conclusively proven that the hazard is not present on other routes of exposure>."
H351	Carcinogenicity, hazard category 2	"Suspected of causing cancer <exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."

Code	Applies to	Text
H360	Reproductive toxicity, hazard category 1A and 1B	"May damage the fertility or the unborn child report <specific effect if known><report exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."
H361	Reproductive toxicity, hazard category 2	"Suspected of damaging the fertility or the unborn child may report <specific effect if known> Report <exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."

H362	Reproductive toxicity, additional category, effects on and through lactation	"Can be harmful through breastfeeding."
H370	Specific target organ toxicity - one-off exposure, hazard category 1	"Causes damage to organs <or include all organs involved, if known, report ><exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."
H371	Specific target organ toxicity - one-off exposure, hazard category 2	"May report damage to organs <or all organs involved if known to cause > Report <exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."
H372	Specific target organ toxicity - repeated exposure, hazard category 1	"Causes damage to organs <or inform all organs involved, if known>, if long-term or repeated exposure reports <exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."
H373	Specific target organ toxicity - repeated exposure, hazard category 2	"May report damage to organs <or all organs involved, if known, cause > through prolonged or repeated exposure <report exposure route if it is conclusively proven that the hazard is not present on other exposure routes>."
EUH071		"Corrosive to the airways."

Annex 3 Control banding

Control banding provides a risk classification for each exposure route, with a distinction being drawn between one-off exposure and repeated exposure. The report includes the tables in which an overview is given of how substances are classified in hazard classes. A number of considerations were relevant to the classification. For completeness and transparency, these considerations are set out in this annex.

3.1 One-off exposure

In the classification of the one-off exposure, it was assumed that firefighters were clearly - highly - exposed to fire smoke.

The hazard classification is based on the H-phrases and/or the alarm limits (ALV), with an additional test for effects from the toxicological database Cheminfo. An Alarm Limit Value (ALV) is the air concentration above which irreparable or other serious health effects can occur, or where persons are less able to bring themselves to safety through exposure to the substance. An overview of the ALV of the assessed substances is included in Annex 6.

The study assumed that one-off exposure does not have a lasting effect on fertility.

Inhalation, effects of one-off exposure to smoke (local and systemic effects)

Explanation of choices made:

- Carcinogenicity and mutagenicity are not applicable for one-off exposure to substances in fire smoke. One-off exposure to CMR substances has little or no influence on the accepted excess.

Absorption through the skin, effects of one-off exposure to smoke (local and systemic effects)

Explanation of choices made:

- On exposure to smoke through fire, there is no direct contact of the skin with the pure substance, but with soot/dust particles/condensed particles (and thus always part of mixtures and therefore lower concentrations). For this reason, dust properties are classified one scale lower than the classification in hazard class of I-SZW (self-inspection tool I-SZW). Another argument is that the exposure at the fire service is intermittent and not continuous.
- Direct effects on the skin (such as corrosive effects) are not reported in the case of substances in fire smoke. For this reason, all substances with corrosive/irritant effects on the skin are classified in the lowest hazard class.
- Carcinogenicity and mutagenicity are not applicable for one-off exposure to substances in fire smoke. One-off exposure to CMR substances has little or no influence on the accepted excess.

3.2 Repeated exposure

Inhalation, effects on repeated exposure to smoke (local and systemic effects)

Explanation of choices made:

- The assessment of repeated exposure through inhalation assumes that firefighters are generally protected against smoke by means of respiratory protection. However, repeated exposure can occur (unnoticed), for example if the mask is removed prematurely, if the mask does not connect properly to the face and/or if an unprotected person is not at an adequate distance from the fire.
- The assessment has been corrected for wearing respiratory protection by dividing substances into one hazard class lower than is customary for the control banding models[25]. It is assumed that all these substances have a threshold value for these effects. This applies, for example, to H330 (very toxic through inhalation). This H-sentence is "red" for all control banding systems, but is classified as "orange" in this study. H261F is in "orange" for all control banding systems, but is classified as "yellow" in this study. An exception is made for carcinogenic and mutagenic substances, because as a rule these substances do not have a safe dose (so-called stochastic effect) and therefore they are counted with an accepted risk.
- For the allergenic substances there is usually no safe dose to be given. However, because the effects are less severe than in carcinogenic and mutagenic substances, the substances that can cause allergy (H334) are classified in the hazard class "orange".
- Reprotoxic substances that (could) affect the unborn child and substances that may be harmful during breast feeding (H362) are not included in the control banding (H360D/H361D/H362).

Absorption through the skin, effects on repeated exposure to smoke (local and systemic effects)

Explanation of choices made:

- On repeated exposure through the skin to substances in fire smoke, there is no direct contact of the skin with pure substance, but with soot/dust particles/condensed particles (and therefore always part of mixtures and therefore lower concentrations). In addition, the skin exposure on the fire service is intermittent and not continuous. As a result, dust properties are classified one scale lower in hazard than the classification in hazard class of I-SZW (self-inspection tool I-SZW, see Table 3 in this annex), with the exception of substances with stochastic effect (mutagenic and carcinogenic).
- Reprotoxic substances that (could) affect the unborn child and substances that may be harmful during breast feeding (H362) are not included in the control banding (H360D/H361D/H362).

Absorption by mouth, effects of repeated **exposure to smoke (local and systemic effects)**

Explanation of choices made:

- Given the relatively small amounts that can be absorbed by hand-to-mouth contact through exposure to substances in smoke caused by fire, effects such as chemical pneumonitis (by vomiting etc.) are classified in the hazard class "green".
- On exposure to substances in fire smoke, there is no question of "drinking liquids and/or eating substances". So the red hazard class is not applied on exposure to substances in fire smoke. It is possible that exposure through the mouth can occur because (especially after repression) eating, drinking and smoking occur in combination with poor hygiene. This involves the absorption of relatively small quantities of the substance.
- Reprotoxic substances that (could) affect the unborn child and substances that may be harmful

during breast feeding (H362) are not included in the control banding (H360D/H361D/H362).

Table 21 Self-inspection tool I-SZW, registration table[27]

Health-related H-phrases								Health risk (GR)					
Carcinogenic		**Harmful**		**Toxic (toxic)**		**Lethal (very toxic)**		**Irritant**		**Burns**			
351	H	332	M	331	H	330	HH	319	M	314	HH		
350	HH	312	M	311	H	310	HH	335	M				
350i	HH	302	M	301	M	300	H	315	M				
Mutagenic													
340	HH												
341	H											**Risk**	**Score**
												L = Low	**0**
Reprotoxic								**Others**					
360F	HH							EU071			H	**M = Medium**	**2**
360D	HH							370			HH		
361f	H							372			HH	**H = High**	**5**
361d	H							318			HH		
362	M							373			H	**HH = Very high**	**10**
								304			H		
								336			M		
Sensitising								371			H		
334	HH												
317	H												
								Other H-phrases or R-phrases			L		

Annex 4 Toxidromes

In order to rapidly recognise and classify acute effects of substances, in practice, so-called toxidromes (HAZMAT) are used. This approach has been used in the description of the acute effects.

Substances that can cause acute effects are broadly classified into five groups/toxidromes:

- Hydrocarbons and halogenated hydrocarbons;
- Aggressive substances;
- Choking/asphyxiantia;
- Cholinergic substances;
- Irritantia;

With regard to the irritants, water solubility is considered to estimate the effect (see Table 22).

Table 22: Explanation of the classification of irritant gases on the basis of solubility and the expected effects.

Description of type of substance	**Effects at high exposure**
I Good water solubility, effect in upper airways ***E.g. chlorine, hydrochloric acid, ammonia, sulphur dioxide***	Acute – the upper respiratory tract: coughing, sore throat, burning sensation behind the sternum, pain through sighing. At high exposure risk of swelling of the vocal cords and/or the trachea with acute choking hazard. Risk of suffocation due to deep lung damage (pulmonary oedema) several hours after exposure. – *eyes: tears burning painful eyes.*
II Moderate water solubility, effect in lower airways and alveoli ***E.g. Nitrogen oxides, phosgene, ozone, finely divided oil mist***	ARDS (acute respiratory distress syndrome) with severe residual damage to the lungs. Complaints become apparent with hours of delay. Tightness, cyanosis, disturbed gas exchange. No effects on circulation.
III Poor water solubility, no effect in the lungs but systemic effect after absorption ***For example carbon monoxide, cyanides, dichloromethane, organic solvents***	Serious various effects, depending on the substance.

Annex 5 Overview of relevant physical properties

Table 23: Overview of relevant physical properties

Name	**Formula**	**CAS number**	**All H-phrases**[8.9]	**LogKow**[27]	**Relative molecular mass (MW in g/mol)**[27]	**H-notation**	**Dermal/Respiratory absorption ratio***
CO - Carbon monoxide	CO	630-08-0	360D-331-372	1.78	28	No	Not calculated
NO_2 - Nitrogen dioxide	NO2	10102-44-0	330-314-EUH071	0.06	46	No	Not calculated
HCN - Hydrogen cyanide (hydrocyanic acid)	HCN	74-90-8	300-310-330 (20% in water)	-0.69	27	Yes	2.94
SO_2 - Sulphur dioxide	SO2	7446-09-5	331-314 (as pressure container)	-2.20	64	No	Not calculated
HCL - Hydrochloride (Hydrochloric acid)	H Cl	7647-01-0	314-335	0.54	36.5	No	0.00
Benzene	C6H6	71-43-2	350-340-372-304-319-315	1.99	78.1	Yes	0.08
Styrene	C8H8	100-42-5	361d-372-332-304-319-335-315	2.89	104.2	No	0.15
Xylene	C8H10	1330-20-7	312 332 304 373 319 335 315	3.09	106.1	Yes	0.06
Toluene	C7H8	108-88-3	361d, 304, 373, 319, 315, 336	2.54	92.1	No	0.07
Ethylbenzene	C8H10	100-41-4	332, 304, 373,	3.03	106.2	Yes	0.06
Acrolein	C3H4O	107-02-8	311-300-314-euh071	0.19	56.1	No	0.00
Formaldehyde (as gas)	CH2O	50-00-0	Liquid, gas is not labeled by EU 300-341-330-	0.35	30	No	0.00 Liquid

			311-314-335-317				
Acetaldehyde	C2H4O	75-07-0	319-335-351	-0.17	44.1	No	0.00
Phenol	C6H6O	108-95-2	341-301-311-331-373-314	1.51	94.1	Yes	2.07
Furan	C4H4O	110-00-9	302, 315, 332, 341, 350, 373	1.36	68.1	No	0.10
Dibenzofuran	C12H8O	132-64-9		4.05	168.2	No	0.53
TDI - 2,4-toluene diisocyanate	C9 H6 N2 O2	584-84-9	315-317-319-330-334-335-351	3.74	174.2	No	0.96
Methyl isocyanate	C2H3NO	624-83-9	301-311-315-318-317-330-335-334-361d	0.79	57.1	No	0.00
Phenyl isocyanate	C7H5NO	103-71-9	302-314-317-330-334	2.59	119.1	No	1.83
(mono) Chlorobenzene	C6 H5 Cl	108-90-7	332-315	2.64	112.6	No	Not calculated
Phosgene	COCl2	75-44-5	314-330	-0.71	98.9	No	0.00
Perfluoroisobutene (PFIB),	C4F8	382-21-8	330-370[9]	3.03	200	No	0.01
HF - Hydrogen fluoride	HF	7664-39-3	300-310-330-314	0.23	20.01	No	0.00
Ultrafine particles/nanoparticles (?)	n.v.t.	n.v.t.	n.v.t.	n.v.t.	n.v.t.	No	Not calculated
PM 2.5	n.v.t.	n.v.t.	n.v.t.	n.v.t.	n.v.t.	n.v.t.	Not calculated

Name	**Formula**	**CAS number**	**All H-phrases[8.9]**	**LogKow[27]**	**Relative molecular mass (MW in g/mol)[27]**	**H-notation**	**Dermal/Respiratory absorption ratio***
PM 10	n.v.t.	n.v.t.	n.v.t.	n.v.t.	n.v.t.	n.v.t.	Not calculated
Benzo[a]pyrene	C20 H12	50-32-8	317-340-350-360fd[9]	5.99	252.3	Yes	1.26
Pyrene	C16H10	129-00-0	No[9]	4.93	202.2	No	1.36
TCDD (2,3,7,8-	C 12 H 4 Cl 4 O	1746-01-6	300-319[9]	6.92	322	No	0.00

Tetrachlorodibenzodioxin)	2						
Lead	Pb	7439-92-1	360df (as powder) -372	0.73	207.2	No	Not calculated
Phosphorous pentoxide	P2O5	1314-56-3	314	-2.69	142	No	Not calculated
Hexane	C6H14	110-54-3	315-304-336-373- 361f	3.29	86.2	No	0.00

*) The calculation of the Dermal/Respiratory uptake ratio is performed in SkinPerm[26]. The same scenario was chosen for all substances and the same exposure parameters were introduced in order to make a good comparison between the substances. These input data are chosen in such a way that they are closest to the fire practice and are coordinated with the expert group. The following input data have been used:

Scenario: "Vapour to skin"

Timing parameters:

- Start of deposition: 0 hr
- Duration of deposition: 4 hr
- End time observation: 12 hr

Other parameters:

- Affected skin area: 15,000 cm^2
- Air concentration: 0.001 mg/m^3
- Thickness or stagnant air: 3 cm
- Calculation intervals/hour: 10,000
- Report intervals/hour: 10

Substances where skin absorption is excluded in the literature are not included in the calculation. Only for Acetaldehyde and HCL - 2 substances of which it has been found in the literature that there is no skin absorption[8] - have calculations been performed for checking.

Annex 6 Alarm limit values (ALV)

In the table below, the alarm limit values (ALV) are included for the most critical substances. This gives an impression of how the substances relate to each other in terms of the dose-effect relationship[18]:

Table 24 Overview of alarm limit values

Dust	**Intervention value ALV in mg/m^3 (1 hour)**
Asphyxants	
CO - Carbon monoxide	97
NO_2 - Nitrogen dioxide	24
HCN - Hydrogen cyanide (hydrocyanic acid)	6.7
Aggressive substances	
SO_2 - Sulphur dioxide	5
HCL - Hydrochloride (Hydrochloric acid)	50
Acrolein	0.23
Formaldehyde	17
Acetaldehyde	500
Phosgene	1,2
Perfluoroisobutene (PFIB),	not known
HF - Hydrogen fluoride	20
Others	
Benzene	2,600
Styrene	540
Xylene	3,900
Toluene	2,100
Ethylbenzene	4,900
Phenol	90
Furan	**88**
Dibenzofuran	not known
TDI - 2,4-toluene diisocyanate	0.6
Methyl isocyanate	0.48
Phenyl isocyanate	AEGL2 0.048
Chlorobenzene	1,000
Phosphorous pentoxide	10
Hexane	10,000