Miljøministeriet
Miljøstyrelsen

# Miljøstyrelsens anbefaling om sikkerhed af tatoveringsfarver

**Titel:**

Miljøstyrelsens anbefaling om sikkerhed af tatoveringsfarver

**Udgiver:**

Miljøstyrelsen
Strandgade 29
1401 København K
www.mst.dk

**År:**

2014

**Redaktion:**

Sie Woldum Tordrup

**Illustration:**

Sie Woldum Tordrup

**ISBN nr.**

[xxxxxx]

**Ansvarsfraskrivelse:**

Miljøstyrelsen vil, når lejligheden gives, offentliggøre rapporter og indlæg vedrørende forsknings- og udviklingsprojekter inden for miljøsektoren, finansieret af Miljøstyrelsens undersøgelsesbevilling. Det skal bemærkes, at en sådan offentliggørelse ikke nødvendigvis betyder, at det pågældende indlæg giver udtryk for Miljøstyrelsens synspunkter. Offentliggørelsen betyder imidlertid, at Miljøstyrelsen finder, at indholdet udgør et væsentligt indlæg i debatten omkring den danske miljøpolitik.

Må citeres med kildeangivelse.

# Indhold

# Forord

Denne anbefaling er udarbejdet af Sie Woldum Tordrup, Teknologisk Institut for Miljøstyrelsen i perioden september 2013 til maj 2014.

I forbindelse med udarbejdelse af anbefalingen er der indhentet kommentarer til udformningen hos producenter og brugere af tatoveringsfarver samt konsulenter, som anses for kvalificerede til at udføre sikkerhedsvurdering af tatoveringsfarver.

# Sammenfatning

### De anbefalede krav til tatoveringsfarver

Tatoveringsfarver, der anvendes som tilsigtet, bør ikke udgøre en fare for sikkerhed og sundhed for den tatoverede. For at reducere de sundhedsmæssige risici, der er forbundet med at få en tatovering, har den danske Miljøstyrelse udarbejdet en række anbefalinger vedrørende sikkerheden ved tatoveringsfarver. Anbefalingerne kan opsummeres som følger:

- **Der bør udføres en sikkerhedsvurdering af tatoveringsfarven, for at sikre at den ikke udgør en risiko for menneskers sundhed, når den anvendes til tatovering.**

  Det betyder, at det kemiske indhold samt relevante egenskaber af tatoveringsfarven bør vurderes af en kompetent person med henblik på at sikre, at farven uden risiko kan anvendes til tatovering.

- **Tatoveringsfarve må under ingen omstændigheder indeholde ingredienser, der er klassificerede som kræftfremkaldende, mutagene eller reproduktionstoksiske.**

  Det betyder, at tatoveringsfarver ikke bør tilsættes ingredienser, der er klassificeret som kræftfremkaldende, mutagene eller reproduktionstoksiske (CMR-stoffer), selvom en sikkerhedsvurdering tyder på, at der ikke kan forventes at være en risiko for menneskers sundhed på grund af tilstedeværelsen af et CMR-stof.

- **Tatoveringsfarve må under ingen omstændigheder indeholde følgende stoffer i koncentrationer over den angivne grænseværdi:**
  - **Azofarver, der under nedbrydning vil afgive primære aromatiske aminer**
  - **Polycykliske aromatiske hydrocarboner (PAH), som kan findes som urenheder i fx carbon black, der anvendes i sorte farver**
  - **Bly.**

  Det betyder, at tatoveringsfarve ikke bør indeholde nogen af disse stoffer i koncentrationer over den grænseværdi, der er fastsat i denne anbefaling.

- **Tatoveringsfarver bør mærkes for at give kunden mulighed for at kontrollere indholdet i de enkelte farver.**

  En ingrediensliste bør være til rådighed for kunden. Listen skal indeholde enhver ingrediens, som indgår i farven i en mængde over 1 %. Uanset indholdet bør enhver ingrediens, der er klassificeret som et allergen, også være noteret på etiketten.

- **En tatoveringsfarve bør være steril, indtil den åbnes, for at reducere risikoen for infektioner og andre relaterede komplikationer i forbindelse med tatovering.**

  At få udført en tatovering er altid forbundet med en vis risiko for infektion. Det er vigtigt, at tatovøren arbejder så sterilt som muligt; og anvendelsen af en steril farve vil bidrage til at mindske risikoen for infektion.

- **Tatoveringsfarve skal være tydeligt mærket med en holdbarhedsdato, og produktet må kun sælges og anvendes inden denne dato.**

  Der bør fastsættes en holdbarhedsdato for tatoveringsfarve i henhold til den forventede stabilitet af produktet med hensyn til fx fysiske/kemiske egenskaber samt andre egenskaber relateret til sikker brug af farven. Denne dato skal fremgå klart og synligt på tatoveringsfarvens primære emballage for at gøre det nemt for såvel bruger som kunde at tjekke holdbarhedsdatoen, før farven anvendes til tatovering.

# 1. Baggrund

Miljøstyrelsen udførte i 2011 en undersøgelse af de 65 mest anvendte tatoveringsfarver på det danske marked. Undersøgelsen viste, at mange af farverne indeholdt kræftfremkaldende stoffer (Jacobsen et al, 2012). På baggrund af undersøgelsen foretog Miljøstyrelsen en risikovurdering, som viste, at koncentrationen af de kræftfremkaldende stoffer i nogle af tatoveringsfarverne var så høje, at de sandsynligvis ville udgøre en uacceptabel sundhedsrisiko for dem, som tatoveres med farven (Miljøstyrelsen, ikke dateret).

I et forsøg på at reducere de sundhedsmæssige risici forbundet med at få en tatovering har Miljøstyrelsen nu udarbejdet denne anbefaling vedrørende tatoveringsfarve.

## 1.1 Anbefalingens anvendelsesområde

En tatoveringsfarve defineres som ethvert stof eller enhver blanding, der anvendes til tatovering. Indenfor rammerne af anbefalingen dækker definitionen af en tatovering både indføring af tatoveringsfarve i læderhuden (dermis) og indføring af tatoveringsfarve under hornlaget (stratum corneum) i overhuden (epidermis). Det betyder, at også farve til permanent makeup er omfattet af anbefalingen.

## 1.2 Anbefalingens formål

Formålet med dette dokument er at liste og beskrive de tekniske elementer i kravene til tatoveringsfarve og permanent makeup, der i øjeblikket anbefales af Miljøstyrelsen.

Ud over beskrivelsen af de tekniske krav, der anbefales for tatoveringsfarve, er der udarbejdet detaljerede retningslinjer for sikkerhedsvurdering af tatoveringsfarve, der indgår som bilag til denne anbefaling. Endvidere angiver disse retningslinjer, hvor de nødvendige oplysninger til hver sektion af sikkerhedsvurderingen kan fremskaffes, og de illustrerer - ved hjælp af konkrete eksempler - hvordan man bruger oplysningerne til at dokumentere sikkerheden af tatoveringsfarve.

# 2. Anbefalede tekniske krav til tatoveringsfarve

## 2.1 Sikkerhedsvurdering

Tatoveringsfarver, der anvendes som tilsigtet, bør ikke udgøre en fare for sikkerhed og sundhed for den tatoverede. For at sikre en risikofri brug af tatoveringsfarve bør der foretages en sikkerhedsvurdering. Sikkerhedsvurderingen bør foretages i overensstemmelse med retningslinjerne i bilag 1, der sikrer, at den kemiske sammensætning af en given tatoveringsfarve ikke påvirker menneskers sundhed negativt, når den anvendes til tatovering.

Det anbefales, at der udarbejdes en sikkerhedsrapport på baggrund af sikkerhedsvurdering, som sammenfatter vurderingens resultater. Konklusionen af vurderingen bør klart fremgå. Hvis produktet er sikkert, anbefales det at bruge følgende formulering: "Tatoveringsfarven udgør ikke en risiko for menneskers sundhed ved tatovering". Hvis en sikker anvendelse ikke kan dokumenteres, bør tatoveringsfarven ikke anvendes til tatovering, og udarbejdelse af en rapport er ikke relevant.

## 2.2 CMR stoffer i tatoveringsfarve

En tatoveringsfarve er et stof eller en blanding, der anvendes til tatovering. En tatoveringsfarve indeholder typisk flere bestanddele, såsom pigmenter, opløsningsmidler, stabilisatorer, befugtningsmidler og fortykningsmiddel. En bestanddel af tatoverinsfarve er stoffer, der tilsættes tatoveringsfarven, uanset om de tilsættes som et enkelt stof eller som del af en blanding. Urenheder i råvarerne anses ikke for at være en bestanddel. Det samme gælder for tekniske hjælpestoffer, der anvendes til fremstilling af tatoveringsfarve, men som ikke er en del af det endelige produkt.

For at minimere den risiko, der er forbundet med at få udført en tatovering, anbefales det ikke at importere, sælge eller anvende tatoveringsfarve, der indeholder bestanddele, der er klassificeret som kræftfremkaldende, mutagene eller reproduktionstoksiske (CMR) i kategori 1A eller 1B i henhold til den europæiske forordning om klassificering, mærkning og emballering (CLP-forordningen, forordning (EF) nr. 1272/2008), eller som indeholder bestanddele, der klassificeres som kræftfremkaldende, mutagene eller reproduktionstoksiske i kategori 1 eller 2, i henhold til bekendtgørelse om klassificering, emballering, mærkning, salg og opbevaring af stoffer og blandinger.

### 2.2.1 Regulering af CMR-stoffer i forbrugerprodukter i REACH

Tatoveringsfarver anses som et forbrugerprodukt, da farven indføres i huden på den tatoverede og den tatoverede betragtes derfor som forbruger i denne sammenhæng (REACH forordning (EF) nr. 1907/2006).

Ifølge REACH (forordning (EF) nr. 1907/2006) skal koncentrationen af CMR-stoffer i en bestanddel, som anvendes i et forbrugerprodukt, være under de grænser, der er angivet i CLP-forordningen for klassificering (forordning (EF) nr. 1272/2008). Det betyder, at en bestanddel, der indeholder et stof, der er klassificeret som kræftfremkaldende eller mutagent i kategori 1A eller 1B, hvor ingen andre oplysninger er tilgængelige, maksimalt må indeholde 0,1 % af dette stof i henhold til CLP-forordningen (forordning (EF) nr. 1272 / 2008). For et stof klassificeret som reproduktionstoksisk i kategori 1A eller 1B, hvor ingen andre oplysninger er tilgængelige, er den

maksimale tilladte koncentration 0,3 % i henhold til CLP-forordningen (forordning (EF) nr. 1272/2008).

I retningslinjerne for sikkerhedsvurdering af tatoveringsfarve, punkt 4.1 i bilag 1 til denne anbefaling er CLP-forordningen beskrevet nærmere, og der er angivet links til relevante hjemmesider og databaser.

Hvis et CMR-stof er til stede som en urenhed under klassificeringsgrænserne beskrevet ovenfor, bør stoffet inkluderes i sikkerhedsvurderingen af tatoveringsfarven.

**Eksempel 1: Indhold**
Et indhold af 0,2 % cadmiumoxid (CAS-nr. 1306-19-0) er angivet på sikkerhedsdatabladet for en bestanddel af tatoveringsfarve. Cadmium-oxid er klassificeret som kræftfremkaldende i kategori 1B med H350: Kan fremkalde kræft (Den harmoniserede klassificering kan findes i det europæiske kemikalieagenturs database over klassificeringer og mærkninger på www.ECHA.com). For cadmiumoxid er grænseværdien 0,1 %, før bestanddelen skal klassificeres. Et indhold på 0,2 % medfører, at bestandelen skal klassificeres, og den er derfor ikke tilladt i forbrugerprodukter.
**Konklusion:** Bestanddelen er ikke tilladt at anvende i tatoveringsfarve.

## 2.3 Primære aromatiske aminer, PAH og bly i tatoveringsfarve

Nogle stoffer anses for at være særlig problematiske med hensyn anvendelse i tatoveringsfarve; primære aromatiske aminer, polyaromatiske kulbrinter (PAH) og bly. For at minimere den risiko, der er forbundet med at få en tatovering, anbefales det ikke at importere, sælge eller anvende tatoveringsfarver:

- som indeholder azofarvestoffer, som ved reduktiv spaltning af en eller flere azogrupper kan frigive en eller flere af de primære aromatiske aminer i tabel 1, nr. 1-9, der overskrider de angivede grænseværdier
- som indeholder stoffer - anført i tabel 1, nr. 10-12 - over de angivne grænseværdier.

Tatoveringsfarve bør ikke indeholde azofarvestoffer, som ved reduktiv spaltning af en eller flere azogrupper kan frigive enhver primær aromatisk amin anført i tabel 1, nr. 1-9, over grænseværdien. Otte af de ni primære aromatiske aminer er også inkluderet i Europarådets resolution om krav og kriterier for sikkerheden for tatoveringer og permanent makeup, ResAP (2008 )1 (Europarådet, 2008), men yderligere én primær aromatisk amin (anilin) er medtaget af Miljøstyrelsen i denne anbefaling. Indholdet af anilin i tatoveringsfarver på det danske marked blev bekræftet i undersøgelsen foretaget af Miljøstyrelsen (Jacobsen et al., 2012), og i nogle farver udgør stoffet en uacceptabel risiko for menneskers sundhed (Miljøstyrelsen, ikke dateret).

Andre stoffer, der anses for at være særlig problematiske, er polyaromatiske kulbrinter (PAH) og bly. PAH'er er kendt for deres kræftfremkaldende egenskaber, og bly betragtes som et neurotoksisk metal selv ved lave koncentrationer. Tatoveringsfarve bør derfor ikke indeholde PAH'er og bly, som anført i tabel 1, nr. 10-12, i en koncentration over den angivne grænseværdi.

For stofferne nummeret som 1-12 i tabel 1 er grænseværdierne meget lavere end den koncentration, som udløser krav om, at et CMR-stof i kategori 1A og 1B listes i et europæisk sikkerhedsdatablad (SDS). Derfor må oplysninger om indholdet af disse problematiske stoffer enten hentes fra producenten eller indhentes ved at udføre en analyse af indholdet i produktet.

Analytiske metoder, der er udviklet med henblik på kemisk at analysere for disse stoffer i tatoveringsfarver, er gengivet i kapitel 4 i Miljøstyrelsens undersøgelse om tatoveringsfarver udført i

2011 (Jacobsen et al., 2012). Relevante analytiske metoder er også angivet i ResAP (2008 )1, standarder for legetøj (EN 71-7:2002 ) og/eller tekstiler (EN 14362-1). For at metoderne kan anvendes til analyse af tatoveringsfarve, kan der være behov for mindre justeringer.

| Nr. | CAS-nr. | Navn | Grænseværdi (ppm) |
|---|---|---|---|
| **1** | 95-69-2 | 4-chlor-o-toluidin | 10 |
| **2** | 99-55-8 | 5-nitro-o-toluidin | 10 |
| **3** | 106-47-8 | 4-chloranilin | 10 |
| **4** | 615-05-4 | 4-methoxy-m-phenylendiamin | 10 |
| **5** | 91-94-1 | 3.3'-dichlorobenzidin | 10 |
| **6** | 95-53-4 | o-toluidin | 10 |
| **7** | 95-80-7 | 4-methyl-m-phenylendiamin | 10 |
| **8** | 90-04-0 | o-anisidin | 10 |
| **9** | 62-53-3 | Anilin | 5 |
| **10** | 50-32-8 | Benzo(a)pyren | 0.2 |
| **11** | 192-97-2, 56-55-3, 218-01-9, 205-99-2, 205-82-3, 297-08-9, 53-70-3 | Det samlede indhold af: benzo(e)pyren, benzo(a)anthracen, chrysen, benzo(b)fluoranthen, benzo(j)fluoranthen, benzo(k)fluoranthen og dibenzo(a,h)anthracen | 2 |
| **12** | 7439-92-1 | Bly | 10 |

**TABEL 1: ANBEFALEDE GRÆNSEVÆRDIER FOR SÆRLIGT PROBLEMATISKE STOFFER I TATOVERINGSFARVE**

**Eksempel 2: Indhold**
Et indhold af 5,0 µg/g benzo(a)pyren (CAS 50-32-8) findes analytisk i en tatoveringsfarve ved hjælp af GC/MS-analyse, som beskrevet af Jacobsen et al. (2012). Benzo(a)pyren er også klassificeret som kræftfremkaldende, kategorie 1B med H350: Kan fremkalde kræft (Den harmoniserede klassificering kan findes i det europæiske kemikalieagenturs database over klassificeringer og mærkninger på www.ECHA.com). Benzo(a)pyren er dog opført med en specifik grænseværdi på 0,2 ppm i tabel 1. 5,0 µg/g benzo(a)pyren svarer til 5 ppm benzo(a)pyren, som er over grænseværdien.

**Konklusion**: Med et indhold af benzo(a)pyren over grænseværdien anbefales tatoveringsfarven ikke til tatovering.

## 2.4 Mærkning

Det anbefales, at følgende oplysninger angives på tatoveringsfarvens primære emballage med uudslettelige, letlæselige og synlige bogstaver, så det kan læses af såvel brugeren som kunden:

- Fabrikantens virksomhedsnavn og adresse samt importørens virksomhedsnavn og adresse, hvis denne importerer til videresalg.
- Indholdets nominelle mængde (nominel masse eller nominelt volumen).
- Holdbarhedsdatoen. Foran holdbarhedsdatoen kan ordene »Må ikke anvendes efter …« fremgå, og datoen skal angives tydeligt og sammensættes i rækkefølge af enten måned/år eller af dag/måned/år. Om nødvendigt angives derudover de betingelser, på hvilke den anførte holdbarhed kan sikres.
- Fabrikationsseriens nummer eller referenceangivelse til identifikation af tatoveringsfarven.
- Liste over bestanddele. Listen indledes med udtrykket »ingredienser«. Listen over bestanddele opstilles i rækkefølge efter aftagende vægt på det tidspunkt, bestanddelene tilsættes i tatoveringsfarven. Bestanddele i en koncentration på under 1 % skal ikke nævnes, medmindre stoffet skal klassificeres som hudsensibiliserende. Angivelserne udtrykkes ved brug af internationalt anerkendt nomenklatur. Ved Internationalt anerkendt nomenklatur forstås stofnavne på fortegnelsen over kosmetiske ingredienser, INCI (International Nomenclature of Cosmetic Ingredients), navne i EINECS (europæisk fortegnelse over markedsførte kemiske stoffer) eller ELINCS (europæiske liste over anmeldte kemiske stoffer). Findes stoffet ikke på en af de ovennævnte lister, anvendes ISO- eller IUPAC-navne. Farvestoffer kan angives med deres registreringsnummer i Colour Index (CI).

For produkter, der importeres, sælges eller anvendes på det danske marked, skal mærkningen i overensstemmelse med ovenstående specifikationer være på dansk eller engelsk.

Hvis det ikke er praktisk muligt at angive de nødvendige oplysninger beskrevet ovenfor på selve den primære emballage, kan oplysningerne angives på en etiket eller lignende mærkat, som bør anbringes på tatveringsfarvens primære emballage.

Information om international nomenklatur for ingredienser kan findes i retningslinjerne for sikkerhedsvurdering af tatoveringsfarve, punkt 4.1 i bilag 1 til denne anbefaling, og yderligere oplysninger om, hvordan en holdbarhedsdato fastsættes, kan findes i afsnit 2.5.

## 2.5 Sterilitet

For at reducere komplikationer relateret til infektioner forårsaget af mikroorganismer stammende fra tatoveringsfarve anbefales det, at tatoveringsfarver er sterile i uåbnet tilstand. Dette kan opnås ved sterilisering af farven efter produktion. Sterilisering af tatoveringsfarve kan udføres ved anvendelse af en standardiseret fremgangsmåde, såsom ved anvendelse af ioniseret stråling efter ISO 11137.

Uåbnet tatoveringsfarve bør opfylde krav til sterilitet angivet i den europæiske farmakopé, kapitel 2.6.1. Steriliteten testes ved hjælp af en mikrobiologisk belastningstest (challenge test), hvor et vækstmedie indeholdende produktet inkuberes med en bestemt mængde og type af mikroorganismer, hvorefter væksten overvåges under bestemte vækstbetingelser. Hvis der ingen udvikling ses, kan produktet ikke opretholde mikrobiel vækst og overholder testen.

## 2.6 Holdbarhedsdato

For at sikre produktets kvalitet i hele holdbarhedsperioden bør en holdbarhedsdato fastsættes i henhold til den forventede stabilitet af tatoveringsfarven. Stabiliteten af tatoveringsfarve under

normale opbevaringsforhold kan vurderes ved hjælp af specifikt designede stabilitetstests. Inspiration kan findes i fx "Guidelines on stability testing of cosmetic products" (COLIPA , 2004), selvom justeringer kan være påkrævet i forhold til stabilitetstest af tatoveringsfarve. Testene skal sikre fysisk integritet af farven under passende opbevarings- og brugsbetingelser, kemisk stabilitet og mikrobiologisk stabilitet, og testene bør udføres i den beholder, som anvendes til det endelige produkt til salg for at sikre kompatibilitet mellem beholderen og dens indhold. Interaktion af stoffer samt den mulige nedbrydning af stoffer over tid kan føre til dannelsen af nye kemiske stoffer, der kan være af betydning fra et sundhedsmæssigt perspektiv. Derfor bør dannelse af nye stoffer samt deres forventede sundhedseffekter overvejes (fx dannelsen af primære aromatiske aminer ved spaltning af azofarvestoffer). Identifikation og kvantificering af kemiske stoffer i løbet af stabilitetstesten kan udføres ved hjælp af analytiske metoder, såsom HPLC, GC, AAS eller IR, hvis relevant. Udvælgelse af parametre til vurdering af produktets kvalitet (såsom viskositet, ændring i farve, sedimentering og kemisk sammensætning) bør udføres i henhold til erfaring, og stabilitet bør endvidere testes ved en eller flere temperaturer. Parametrene bør overvåges over tid for at sikre, at kvaliteten og sikkerheden af produktet, når det anvendes til tatovering, ikke kompromitteres indenfor holdbarheden af produktet.

Holdbarheden bør vurderes på grundlag af erfaringer samt udførte stabilitetstests, og en holdbarhedsdato bør beregnes for hvert parti af tatoveringsfarver. Datoen bør fremstå synligt på tatoveringsfarvebeholderen for at gøre det let for både brugeren og kunden at tjekke holdbarhedsdatoen, før der tatoveres med farven.

Holdbarhedsdatoen kan angives efter ordene »Må ikke anvendes efter …«, hvorefter datoen angives tydeligt og sammensættes i rækkefølge af enten en måned/år eller dag/måned/år. Om nødvendigt kan derudover angives de betingelser, hvorunder den anførte holdbarhed kan garanteres, fx kun i uåbnet emballage og/eller under opbevaring ved en bestemt temperatur.

# Bilag 1: Guidelines for safety assessment of tattoo ink

Tattoo ink should not endanger the health and safety of a person when applied and used as intended. To ensure safe use of tattoo ink a safety assessment should be carried out. It is recommended that the safety assessment is carried out in accordance with the requirements described in this appendix, ensuring that a specific chemical composition of a tattoo ink does not adversely affect human health when used for tattooing.

It is recommended that a safety report should be compiled based on the assessment, summarizing the results of the assessment. The conclusion of the assessment should be clearly stated. If the product is safe, it is recommended to use the following wording “the tattoo ink does not constitute a risk to human health when used for tattooing”. If a safe use cannot be documented, the tattoo ink should not be used for tattooing and compiling a report is not relevant.

A safety assessment of tattoo ink can follow existing guidelines for safety assessment such as described for cosmetics by the Scientific Committee on Consumer Safety (SCCS, 2012), for consumer products as described by Boyd and Larsen (2014) or in guidance documents published by the European chemicals agency (ECHA). This guide is built on the same principles. However issues not relevant for tattoos are omitted. Further, the available scientific data for tattoo ink is in some respects currently considered inadequate for some elements of the assessment following the existing guidelines, thus suggestions for a practical approach are provided here.

The safety assessment must be based on available and current knowledge and if new knowledge becomes available the safety report should be updated up to the expiry date of the tattoo ink. The report should include clear references to all sources of information used.

A safety assessment of tattoo ink should contain two subparts; A and B, see illustration in Figure 1.

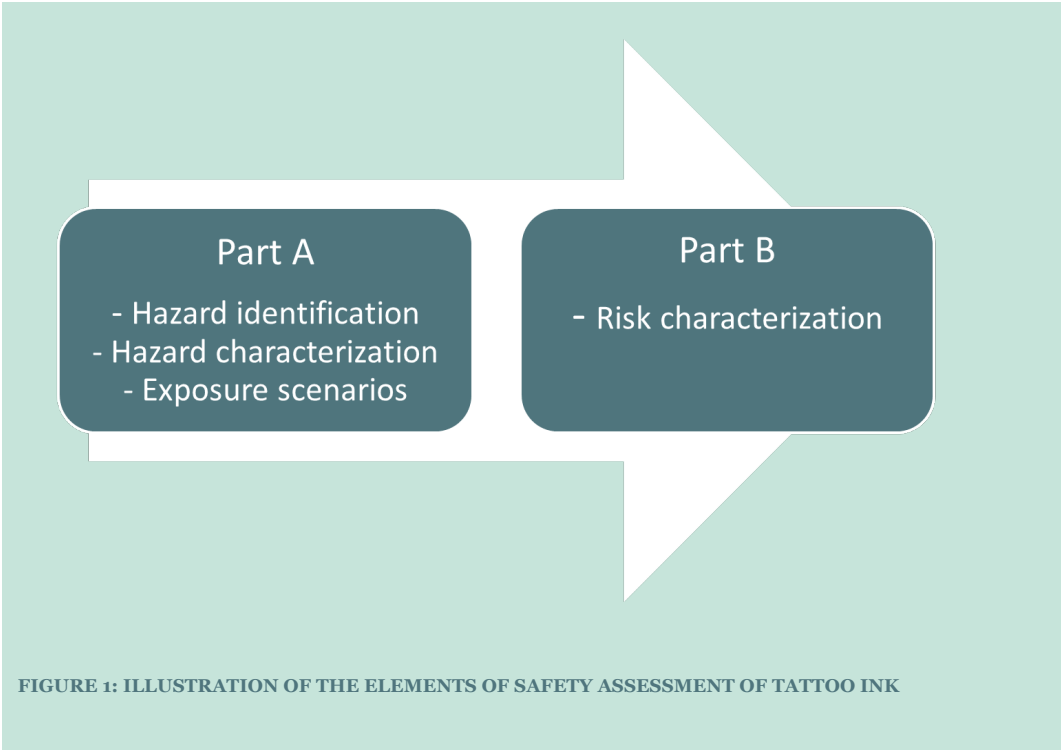


FIGURE 1: ILLUSTRATION OF THE ELEMENTS OF SAFETY ASSESSMENT OF TATTOO INK

Part A includes the compilation of all available data relevant for the safety of the tattoo ink and contains a hazard identification, hazard characterization and development of exposure scenarios.

Part B includes the assessment of the safety of the tattoo ink; the risk characterization, based on the data compiled in part A. The two parts will be explained in detail in the following paragraphs.

In order to further illustrate the practical approach described for the safety assessment a number of examples will also be given.

# 1. Available information

Manufacturers and importers of tattoo ink should base the safety assessment on all available information. It is not necessary to carry out a toxicological test in order to assure the safety of the inks. This further assures that the economic burden is kept at an acceptable level. It is acknowledged that the safety assessment might to some degree be compromised by this. The recommendation and suggested requirements for a safety assessment and a safety report should however assure that all available information is applied in the assessment of the tattoo inks. If no information is available or if the available information is of a poor quality, it should be clearly stated in the assessment report.

# 2. Sources of information

Information on the safety of the tattoo ink can be found through various sources. The safety datasheet (SDS) of the ingredients should be available from the manufacturer or importer of the substances or mixture of substances and should contain some of the information needed. Information might also be available from the supplier on request or may be found in the scientific literature. A number of databases containing references to toxicological information are also available. Experience gained with similar or other product categories (e.g., cosmetics or pharmaceuticals), available data on similar formulations, or computer models used to estimate, e.g.,

physico-chemical properties or toxicological effects of substances are also considered as valuable sources of information. Relevant sources of information will be referenced to in the following paragraphs and will be summarized in Tabel 2, at the end of this appendix.

# 3. Confidential information

Some information needed for the safety assessment as performed according to this guideline might be considered confidential information by the supplier of the ingredients used to manufacture tattoo ink. In that case, one possible solution is to hire a third party to perform the safety assessment and give the information from the supplier directly to the third party with no involvement of the tattoo ink manufacturer.
Another solution is to legally restrict the use of any confidential information supplied by the manufacturer of ingredients to the tattoo ink manufacturer during the preparation of the safety evaluation through a confidential disclosure agreement (CDA).

# 4. Part A – Information on the safety of tattoo ink

The first part of the safety assessment covers the requirements for data on substances in the tattoo ink. Information that should be compiled in part A is:

- Chemical identity of the tattoo ink – section 4.1
- Physico-chemical properties and stability of the tattoo ink – section 4.2
- Impurities of the tattoo ink and information on the tattoo ink container – section 4.3
- Toxicological profile of ingredients including any impurities – section 4.4
- Exposure to the tattoo ink, its ingredients and impurities – section 4.5
- Other relevant information – section 4.6

The following sections will specify the listed requirements.

## 4.1 Chemical identity of the tattoo ink

*For substances that are either a substance or a part of mixture in the tattoo ink the following should be stated, regardless of their concentration:*

- *The chemical name, using international nomenclature. 'International nomenclature' means substance names in the INCI (International Nomenclature of Cosmetic Ingredients), the EINECS (the European Inventory of Existing Commercial chemical Substances) or the ELINCS (the European List of Notified Chemical Substances). If the substance is not found on the aforementioned lists, then the ISO or IUPAC names must be used. Dyes can be stated using their Colour Index (CI) Constitution Numbers.*
- *Chemical formula (where possible).*
- *INCI name, CAS, EINECS and ELINCS numbers (where possible).*
- *The intended use (i.e. the function of the chemical).*

All substances in the tattoo ink formulation should be listed, including any known impurities (see section 4.3 below for details).

For information on the chemical identity and properties of substances and mixtures the SDS is an important source of knowledge. Chemical name and chemical formula could be found on the SDS if this is available. According to the European Chemical Agency (ECHA) the “safety data sheets are the main tool for ensuring that suppliers communicate enough information along the supply chain to allow safe use of their substances and mixtures” (ECHA, n.d.A), and they should therefore contain much of the information required here.

A manufacturer or importer is in many cases obliged to procure an SDS following European regulation requirements.

An SDS is required if:

1) a substance (and from 1 June 2015 a mixture) meets the criteria for classification as hazardous according to the Classification, Labelling and Packaging (CLP) regulation,
2) a mixture meets the criteria for classification as dangerous[1],
3) a substance is persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) according to the criteria given in Annex XIII of REACH, or
4) a substance is included in the candidate list for eventual authorization according to Article 59 (1) of REACH for any other reasons (ECHA, n.d.A).

The substance name can be specified according to INCI, EINICS or ELINCS. In the case of cosmetic substances and ingredients, the correct substance name according to INCI can be found using the European Commission Database, CosIng (CosIng, n.d.), e.g., from the CAS or EINECS/ELINCS number. CAS number, EINECS or ELINCS number can be found through the European chemical Substances Information System (ESIS, n.d.). International Union of Pure and Applied Chemistry (IUPAC) generated substance names using a defined set of rules in order to systematically name chemical compounds based on their chemical structure (IUPAC, n.d.). For pigments and dyes, the Colour Index (CI) constitution number is often used for identification. The CI numbers are assigned by Colour Index International and their database can be accessed on-line (a subscription is required) (Colour Index International, 2012). CI numbers of pigments and dyes allowed in cosmetics can also be found in Annex IV of the Cosmetics Regulation (EC) No 1223/2009. One or more of these names are also available from the SDS, if available.

The chemical formula, if not given on the SDS, can be found in several public databases, such as ChemSpider (ChemSpider, n.d.) and PubChem (PubChem, n.d.) by using, e.g., the CAS number or one of the chemical names.

The intended use of the ingredients should also be stated. An ingredient may typically function as, e.g., a pigment, solvent, binder, preservative, surfactant or a thickening agent but other intended uses may be stated as appropriate.

Concentrations of the substances in the tattoo ink are required in order to evaluate the exposure.

## 4.2 Physico-chemical properties and stability of the tattoo ink

*For substances which are either a single substance or a part of a mixture in the tattoo ink their physical and chemical properties should be listed.*

*For the tattoo ink, the stability under normal storage conditions as well as the shelf life when opened and unopened should be stated.*

Physical and chemical properties are considered important for the assessment of safety since they may be closely related to certain toxicological properties. Physical properties may include: form (liquid, solid, powder etc.), particle size, density, colour and smell (sharp, sweet etc.), vapour pressure, melting point, boiling point, refractive index, flash point and viscosity. Chemical properties may include: pH, reactivity and solubility.

[1] Dangerous Preparations Directive 1999/45/EC (DPD) (until 1 June 2015)

The physical and chemical properties for substances and mixtures are typically given on the SDS or may be found in on-line chemical databases, e.g., SciFinder (subscription necessary) (SciFinder, n.d.) or ChemSpider (ChemSpider, n.d.). Properties may also be found on ECHAs homepage for registered substances (ECHA, 2013A).

The stability of the tattoo ink under normal storage conditions should be evaluated in order to ensure that the quality and safety of the product when used for tattooing is not compromised within the shelf life of the product. Interaction of substances as well as the possible degradation of substances over time can lead to the formation of new chemical substances that could be of concern from a health perspective. Therefore, the potential formation of new substances as well as their expected health effect should be considered (e.g., like the formation of primary aromatic amines upon cleavage of azo dyes). Identification and quantification of chemical substances during stability testing can be done using analytical methods such as HPLC, GC, AAS or IR analysis, when relevant. See also section 2.6 for further details on stability testing.

## 4.3 Impurities of the tattoo ink and information about the tattoo ink container

- List the purity of the substances and mixtures in the tattoo ink
- List impurities in the tattoo ink
- Assess relevant properties of the tattoo ink container; particularly its purity and stability

The purity of the substance or mixtures used in the tattoo ink is typically given by the manufacturer either on the SDS, through specifications or on a technical datasheet.

All known impurities of substances or mixtures used as ingredients in the manufacturing of tattoo ink must be identified as part of the chemical composition of the tattoo ink (See section 3), since they may be relevant for the safe use of tattoo ink.

The chemical identity of any impurity of a substance or mixture which is it-self classified and contributes to the overall classification of the substance or mixture must be stated on the SDS. Information on these impurities should therefore be available on the SDS (ECHA, 2011).

If an impurity is not classified and therefore not stated on the SDS, the manufacturer of ingredients may be a valuable source of information regarding impurities. Information on impurities can be supplied through the supply chain either directly through inquiry to a supplier or manufacturer, through specifications/technical data sheets for each ingredient or obtained indirectly based on knowledge of the process for manufacturing the ingredient (origin of substance, production process, synthesis route, extraction process, solvent used, etc.).

The type of impurities will depend on the substance or mixture of substances and might include, e.g., primary aromatic amines, polyaromatic hydrocarbons (PAHs), residual organic solvents, residual monomers for polymeric substances, softeners like phthalates, heavy metals etc.

Known impurities emerging during the production of the ink, which are not removed or impurities that will be generated during the expected shelf life of the tattoo ink should also be listed.

For impurities stemming directly from the container, information on the material might be available from the supplier on request, from the literature or could perhaps be further assessed by someone skilled in the area of material science.

## 4.4 Toxicological profile of ingredients including any impurities

### 4.4.1 Information on toxicity of substances

The toxicological profile for substances which are either a substance or a part of a mixture in the tattoo ink should be determined and to do so the following should be stated:

- information on whether they are carcinogenic, mutagenic, toxic to reproduction, corrosive, irritating to the skin or eyes, skin sensitizers, show signs of UV photo-induced toxicity, genotoxicity or systemic toxicity
- effects on the toxicological profile due to particle size, including nanomaterials and chemical and physical reactions
- any read-across shall be documented and justified
- the source of information shall be clearly identified

The health risk associated with the use of tattoo ink will be determined by the substances contained in the tattoo ink, possible interactions between substances and degradation where new substances of health concern are formed. Therefore, information on toxicological effects of the substances or mixture of substances contained in the tattoo ink must be compiled in order to assess the safety of the formulation. This process is typically referred to as the hazard identification.

The CLP regulation (Regulation (EC) No 1272/2008) ensures that hazards presented by chemicals are clearly communicated through standard statements and pictograms to workers and consumers in the European Union. The classification system is based on the United Nations' Globally Harmonised System (GHS). The CLP database accessible through ECHA's homepage (ECHA, 2013B) contains information on substances notified under Regulation (EC) No 1272/2008 and registered under Regulation (EC) No 1907/2006 (the REACH Regulation) by manufacturers and importers. It also contains the list of legally binding harmonized classifications (Annex VI to the CLP Regulation) as well as self-classifications reported by manufacturers and importers. The database states the hazard class(es) (whether they are carcinogenic, mutagenic, toxic to reproduction, corrosive, irritating to the skin or eyes, skin sensitizers, genotoxic or show systemic toxicity) for each substance and can be searched using the chemical name or CAS number. More information on the registered substances (10.655 unique substances by November 28th 2013) can be accessed through "Chemical Substances Search" on ECHA's homepage (ECHA, 2013A).

The toxicological effect of a chemical substance can vary from mild skin irritation to more severe effects such as development of allergies or even cancer. After the hazard identification a hazard characterization is needed. In the characterization the toxicological effects of all substances should be evaluated and the critical effect of each substance be determined. The critical effects are the toxicological effects considered as the most essential for the risk assessment. The critical effects will depend on the specific endpoints identified and must be considered on a case-by-case basis by a person skilled in the art. The severity with respect to human health of each of the identified effects is a factor in determining the critical effects. The expected exposure route for the product in question should also be considered with respect to the critical effects, e.g., if only endpoints for inhalation effects are identified for a substance used in tattoo inks they will most likely not be considered relevant.

The No Observed Adverse Effect Level (NOAEL) of a substance is a threshold value, below which no adverse effects can be expected. NOAEL is the highest concentration or level of exposure to a substance where there is no biologically or statistically significant increase in the frequency of observed adverse toxicological effects seen in the exposed population when compared to a control population. Toxicological tests can be performed on a number of different species and the relevance of the conclusion with respect to expected effects on exposure to humans should be discussed and evaluated.

A threshold value is not seen for all toxicological effects and the exposure of substances with this type of effect will be associated with a risk of adverse effects regardless of the concentration, such as for some carcinogenic substances. Instead of a NOAEL, a Bench Mark Dose ($BMDL_{10}$ or $T_{25}$) is often established and used in place of the NOAEL to evaluate the risk of adverse effects.

A good strategy for gathering information on health hazards for a specific chemical is to search for safe doses derived internationally by authoritative bodies, and compare doses to more recent data to consider whether modification is necessary. If you need to characterize the hazard of a chemical substance, for which no specialist assessments are available, you might consider consulting an experienced toxicological risk assessor.

Studies on toxicological effects of substances are typically found in the scientific literature and critical dose levels may be found based on data on experience in humans or more often based on data from experimental animal testing. Searches for relevant scientific literature on the toxicological effect of substances can be carried out on-line, e.g., at the toxicology data network (TOXNET, n.d.) or PubMed (PubMed, n.d.). Toxicological data and safety assessments of substances used in cosmetics can also be found in opinions published by scientific committees, e.g., the Scientific Committee on Consumer Safety (SCCS) or the former Scientific Committee on Cosmetic products and non-food products intended for consumers (SCCNFP) (European Commission, n.d.). Also The Cosmetic Ingredient Review (CIR) reviews and assesses the safety of individual chemical compounds for cosmetics and publishes them on their homepage as well as in peer-reviewed scientific literature (CIR, n.d.).
Data from studies performed according to internationally recognized test methods (such as OECD Guidelines (OECD, n.d.)) should be preferred. The assessment should ideally be based on studies performed with the exact substances used in the tattoo ink, e.g. substances with the same chemical and physical characteristic such as particle size distribution.

Guidance on the assessment of toxicological data can be found in a number of guidance documents available from ECHA (ECHA, n.d.B): Quantitative Structure-Activity Relationships (QSARs) and read-across can be used between structurally related chemicals if no available or reliable information is found for a specific substance in cases where knowledge on similar substances exists. Such modelling and read-across can give valuable information in cases where no information is available through animal or human studies. Modelling and the resulting data are, however, associated with some uncertainty and must be carried out and evaluated by a trained toxicologist and always used with caution. Software for QSAR modelling is also available from OECD (QSAR Toolbox, n.d.).

Determining the NOAEL value (or benchmark dose) for toxicological effects should be carried out by careful evaluation of all available data and should only be carried out by a person skilled in the art as should the identification of the critical effects. It should be noted that the critical effect could be a local as well as a systemic effect. Also, it should be recognized that the critical effect is not necessarily the most severe effect of the chemical substance. In general safety assessments should be carried out by careful evaluation of all available data and requires the judgment of professionals suitably qualified and experienced in toxicology and chemical risk assessment.

### 4.4.2 The chemical composition and the production of tattoo ink

The assessment of the toxicological profile of a mixture, e.g., such as tattoo ink, is usually based on the knowledge of the toxicological profile of each single substance in the mixture. Therefore, the concentration of each substance in the tattoo ink must be known to evaluate the overall expected toxicological effect of the tattoo ink. Changes in the chemical composition during the production process should be accounted for, if at all possible, e.g., evaporation of solvent added or degradation of substances as a result of processing.

### 4.4.3 Effects of substance properties on toxicological profile

Some properties of the substances in the tattoo ink may impact the toxicological profile of the mixture and need to be addressed. Particular consideration shall be given to parameters including, but not limited to:

- Particle size, specifically with attention to substances (e.g. pigments) that fall under the category nanomaterials, as defined by the European Commission (European Union, 2011).
- Chemical and physical reactions: Substances known to interact upon mixing or degrade under production or normal storage conditions.

## 4.5 Exposure to the tattoo ink, its ingredients and impurities

To evaluate safety of tattoo ink exposure scenarios must be developed. Since tattoo inks are introduced into the skin, a parameter such as absorption is expected to affect exposure differently from a situation when the chemical substance is applied on the skin as is the case for e.g. cosmetics. In order to assess the tattoo inks according to the recommended requirements some assumptions may be made regarding exposure. The assumptions currently considered necessary and acceptable will be explained below.

### 4.5.1 Normal and foreseeable use

The normal and foreseeable use of the tattoo ink, including the expected use thereof per $cm^2$, as well as precautions when mixing and diluting should be described.

The normal and foreseeable use of the tattoo ink is for introduction directly into the skin without dilution of the ink. One study indicates that a normal concentration of pigment used for tattooing may be in the range of 0.6-9.4 $mg/cm^2$ with an average of 2.5 $mg/cm^2$ (Engel et al, 2008). This concentration is based on pigment alone and compensation for the remaining components in the tattoo ink is therefore necessary. According to the previous survey done for the Danish EPA, the dry matter content (pigment) of a tattoo ink is typically 30-60% (Jacobsen et al, 2012). Other available data may be used if source of information is clearly stated.

Sometimes mixing or diluting colours is desired by tattooists in order to get the exact shade wanted by the customer. Mixing and dilution can have a negative effect on the stability and integrity (e.g. hydrolysis) of the tattoo ink. Any details regarding relevant precautions when mixing which might affect the safe use of the tattoo ink should be addressed. Thus, if possible, e.g., recommendations on solvents for dilution or specific inks identified and tested as compatible on mixing of different coloured inks.

### 4.5.2 Exposure of tattoo ink

Exposure to tattoo ink should be estimated in relation to:

- the surface area(s) of application. If no other information is available, an area of 30 x 30 cm shall be used (equivalent to a large tattoo)
- the duration and frequency of exposure. If no other information is available, it is assumed that the chemical substances are absorbed over a 6-week period
- potential exposure of particular surface areas of the body
- potential exposure of a specific population group

To aid in the calculation of exposure, a range of assumptions on exposure to tattoo ink are given in the above. The assumptions are based on the presently available knowledge and should be updated as new, more relevant and valid data emerges. Other assumption might also be made for specific products where significantly different exposures are to be expected, e.g. for permanent make-up.

The exposure of tattoo ink from a newly made tattoo may be calculated using the information on normal and foreseeable use, and if no other information is available a surface area of application of 30 x 30 cm (900 $cm^2$) and assuming an absorbance of chemical substances over 6 weeks.

Very few scientific studies are available on absorption of tattoo ink and therefore only a few substances have been examined. The assumption of an absorbance of the chemical substances at a constant rate over a 6 week period after the tattoo ink is introduced into the skin is based on the results of a study performed on mice (Engel et al, 2008). The particle size is expected to have an effect on absorption. Smaller particles are expected to be absorbed easier and faster into the system than larger particles of the same chemical substance (e.g., for titanium dioxide (Wu et al, 2009)). If substances used in the tattoo ink are of a significantly smaller particle size than the pigments tested in the study, then the uptake might be faster and the systemic exposure limited to a shorter time and therefore a higher daily dose.

Considerations regarding the area of skin expected to be tattooed under normal foreseeable use could also affect the absorption time, e.g., for tattoos under the arms or other areas where the skin is thin.

Using the above, an expected systemic exposure can be calculated, e.g., in amount of tattoo ink/kg bodyweight/day. A default human bodyweight (BW) of 60 (SCCS, 2012) or 70 (ECHA, 2012; EFSA, 2012) kg is suggested for this calculation.

### 4.5.3 Exposure of ingredients and impurities

For evaluation of exposure to substances and mixtures, including impurities present in tattoo inks the level of exposure to substances with identified critical toxicological effects should be calculated based on:

- Normal and foreseeable use
- Estimated exposure of tattoo ink
- Concentration of substance in the tattoo ink
- Normal and foreseeable absorption. If no other information is available, it is assumed that 100% of the absorbed substances and mixtures, and two-thirds of the suspended particles, are absorbed systemically
- Effects on exposure due to particle size

The next step is developing exposure scenarios further and calculating the exposure to substances with a critical toxicological effect. Again, impurities present in the tattoo ink should be included if relevant.

The exposure is calculated using the exposure of tattoo ink (mg ink per kg body weight per day) and:

- Multiplying with the concentrations of each substance in the tattoo ink for which a critical toxicological effect has been identified (e.g. in μg/g ink).
- If no other information is available, it may be assumed that 100% of the absorbed substances and mixtures and two-thirds of the suspended particles are absorbed systemically.

As mentioned earlier particle size can be expected to have some effect on absorption and should, if possible, be considered when setting parameters for absorption in the exposure scenarios.

The calculations will give a unique systemic exposure dosage (SED) for each substance included in the assessment which should be compare to relevant toxicological threshold values, e.g., NOAEL, in the risk characterization in part B.

**Example A: Calculation of systemic exposure dosage (SED):**

In Jacobsen et al (2012) a tattoo ink with a concentration of 5.3 μg/g benzo(a)pyrene was found. To illustrate the calculation, the systemic exposure (SED) of that ink will be calculated here using the following assumptions:

Body weight (BW) = 70 kg
Area=900 cm²
Period = 42 days
Ink use =2.5 mg/cm²

Furthermore, it is assumed that all of the substance is absorbed since no other information is available for the calculation.

$$SED = \frac{C_{substance} \cdot Ink \cdot Area \cdot Absorption}{BW \cdot Period} = \frac{0.0053\mu g/mg \cdot 2.5mg/cm^2 \cdot 900cm^2 \cdot 100\%}{70kg \cdot 42d} = 0.004\mu g/kg/d$$

**Example B: Calculation of systemic exposure dosage (SED):**

In Jacobsen et al (2012) the measured content of phthalocyanine blue ranged from 46.000-189.000 μg/g. One sample had a content of 112.000 μg/g. Calculation of a systemic exposure (SED) of that ink can be carried out using the following assumptions:

BW = 70 kg
Area =900 cm²
Period = 42 days
Ink use= 2.5 mg/cm²

Furthermore it is assumed that 2/3 of the substance is absorbed since this is considered suspended particles (low water solubility) and no other information is available for the calculation.

$$SED = \frac{C_{substance} \cdot Ink \cdot Area \cdot Absorption}{BW \cdot Period} = \frac{112\mu g/mg \cdot 2.5mg/cm^2 \cdot 900cm^2 \cdot 67\%}{70kg \cdot 42d} = 57.4\mu g/kg/d$$

### 4.5.4 Margin of Safety (MoS)

Calculation of margins of safety (MoS) based on a no observed adverse effects level (NOAEL) are made and discussed if possible.

The final step of the safety assessment is to make a risk characterization. Here the probability that a substance under assessment causes damage to human health and the level of risk, are evaluated. The purpose of a risk characterization is to provide a quantitative statement about the risk by comparing the estimated exposure to an appropriate threshold value, if such a value is identified during the safety assessment.

Calculation of MoS should be included in the safety assessment of tattoo ink if possible with respect to the available toxicological data. The MoS should be based on the lowest NOAEL and the expected systemic exposure. It is calculated as (SCCS, 2012):

$$MoS = \frac{NOAEL}{SED}$$

SED being the systemic exposure dosage calculated based on exposure scenarios. If relevant, MoS for substances is calculated and assessed further in Part B. A high MoS represents a low risk of adverse effects occurring as a consequence of the examined use situation. A detailed description of the calculation of MoS can be found in "the SCCS's notes of guidance for the testing of cosmetic substances and their safety evaluation" (SCCS, 2012).

Other terms than MoS are often used as a mean to quantify the risk in safety assessments. The term used by ECHA is the Risk Characterization Ratio (RCR) which is the ratio of exposure to the derived no effect level (DNEL). MoE – margin of exposure is another term used for risk quantification which is very similar to MoS. For non-threshold effects a risk level may be calculated as an alternative to the MoS (Boyd and Larsen, 2014).

**Example C - Calculation of Margin of Safety (MoS)**

For phthalocyanine blue, Jacobsen et al (2012) identified a NOAEL of 200 mg/kg/d. The critical effect was a reduced number of red blood cells which was observed after oral administration of the pigment by gavage. The NOAEL is based on a 28 day rat study. Using this NOAEL, the MoS can be calculated (see Example A for data input to the formula):

$$MoS = \frac{NOAEL}{SED} = \frac{200 mg/kg/d}{0.0574 mg/kg/d} = 3484$$

## 4.6 Other relevant information

Any other known information considered to be of significance with regard to the risk to human health when tattooing with the tattoo ink currently being assessed should be included, e.g., sterility of the tattoo ink, see section 2.5 of *Recommendation from the Danish Environmental Protection Agency on Tattoo Ink*.

# 5. Part B – Assessment of safety

## 5.1 Assessment of safety

The safe use of a tattoo ink should be scientifically justified through the safety assessment and the safe use should be documented using the information in Part A with a clear account for the relevance of the toxicological profiles and how the conclusion is reached.

The scientific justification for the conclusion of the assessment should be given in part B of the safety assessment. The justification of the safe use of the tattoo ink shall be based on the information in Part A and must describe how the compiled toxicological information is relevant for exposure when the ink is used for tattooing and how it is used.

The assessor shall take all the compiled information on substances and mixture of substances used in the tattoo ink into consideration when evaluating the safety of the tattoo ink. Substances and their toxicological profiles, their chemical and physical properties and the conditions under which they are used should be assessed.

If a MoS can be calculated based on the available information this value should be assessed to determine if it reflects a safe use of the tattoo ink. Several aspects are involved in the extrapolation of experimental data to the exposure situation in humans, such as the variability in the experimental data and from intra- and inter-species variation, the nature and severity of the effect, length of the study and the sensitivity of the human (sub-) population. The calculated MoS should therefore be discussed in order to justify that the MoS is adequate and represents a safe use of the tattoo ink.

MoS must account for safety factors in extrapolation of a toxicological effect seen e.g. in a group of test animals to an average human being, and subsequently from average human beings to sensitive subpopulations. Generally a MoS of 100 is considered acceptable for a conclusion of safe use (SCCS, 2012). But depending on the factors such as the quality of data and the severity of the criticaleffect a higher margin could be considered appropriate. Guidelines for safety factors (or assessment factors; Boyd and Larsen, 2014) for some common extrapolations can be found in ECHA guidance documents. An example of a choice of adequate safety factors as well as calculation and assessment of MoS is given in example D below.

**Example D: Evaluation of MoS calculations:**
Any calculated MoS should be assessed to determine if it is sufficient for demonstrating a safe use of the tattoo ink. Assessment factors depending on the quality of the used NOAEL value are here used to estimate an acceptable MoS.

The NOAEL used in example C for phthalocyanine blue was based on a 28 day rat study with oral administration. In order to estimate the long-term effect in humans several assessment factors will be considered. The product of these factors constitutes an acceptable MoS.

| | |
|---|---|
| Factor 1: 4 | due to differences between rats and humans (4 is the value given in REACH guidance documents for interspecies variation between rat and human, but a default value of 10 is often seen) |
| Factor 2: 10 | due to human variability (intraspecies) |
| Factor 3: 6 | to account for a 28 day study being used for assessing chronic effects. |

The product of factors being: 4 x 10 x 6 = **240**

The product is in this case much lower than the calculated MoS in example C and, under the assumptions made, indicates a safe use of this particular ink with respect to phthalocyanine blue.

Other factors may be applied to account for poor quality of data, e.g., if a LOAEL is used in place of a NOAEL. For detailed description and examples see "*Guidance on information requirements and chemical safety assessment Chapter R.8 (ECHA, 2012).*

## 5.2 Assessment of stability and reactivity

The safety of the tattoo ink should be assessed with respect to potential reactions between substances and mixtures, including impurities in the tattoo ink, and the possible effects of stability.

The information, from part A of the safety assessment, should be reviewed. The potential reactions between substances and mixtures, including impurities in the tattoo ink, how the chemical and/or physical stability possibly affects the safety of use of the tattoo ink should be discussed, if relevant.

## 5.3 Conclusion of the assessment

The conclusion of the safety assessment of tattoo ink should be that the tattoo ink does not present a risk to human health.

The recommendation is that a tattoo ink should not be sold or used if its safety has not been assessed and a safety report has not been compiled, concluding that the tattoo ink does not constitute a risk to human health when used in tattooing.

NOTE: Although a safe use can be confirmed by carrying out the safety evaluation, some restrictions regarding use of chemicals of particular concern are recommended for tattoo ink, see section 2.2.

TABEL 2: KEY SOURCES OF INFORMATION

| Links | Description |
|---|---|
| www.echa.europe.eu | **ECHA**, The European Chemicals Agency, provides data for a number of chemical substances registered under REACH. The data includes, e.g., toxicological data, physical properties and chemical properties. |
| http://www.ncbi.nlm.nih.gov/pubmed | **PUBMED** is a database of references and abstracts on biomedical literature from MEDLINE, life science journals and online books. The database is maintained by the US National Library of Medicine (NLM) at the National Institutes of Health. |
| http://toxnet.nlm.nih.gov/. | **TOXLINE** (TOXicology information onLINE): Databases on toxicology, hazardous chemicals, environmental health, and toxic releases under The US National Library of Medicine (NLM). Also containing the **HSDB** (Hazardous Substances Data Bank) |
| http://www.cas.org/ | **CAS,** Chemical Abstracts Service, is a division of the American Chemical Society. It is the world's authority for chemical information and the CAS registry contains information on, e.g., property data more than 74 million unique organic and inorganic chemical substances. |
| http://www.oecd.org/ | **OECD**, The Organisation for Economic Co-operation and Development publishes guidelines for the testing of chemicals. The guidelines are a collection of the most relevant internationally agreed testing methods used by governments, industry and independent laboratories to assess the safety of chemical products. |
| http://esis.jrc.ec.europa.eu/ | **ESIS**, European chemical Substances Information System, is a complex, heterogeneous information system which provides information on chemicals. It includes information on substances in EINICS (European Inventory of Existing Commercial chemical Substances) and ELINCS (European List of Notified Chemical Substances). |
| http://ec.europa.eu/health/scientific_committees/index_en.htm | The European Commission relies on a number of scientific committees when preparing its policy and proposals related to consumer safety, public health and the environment. The **Scientific Committees** work independently and provide the Commission with sound scientific advice. From time to time, the Scientific Committees will publish opinions on substances containing, e.g., review on toxicological information on the substance. |
| http://www.colour-index.com/ | **Colour Index** International is a database on colorants published on-line by the Society of Dyers and Colourists and the American Association of Textile Chemists and Colourists. Serves as an authoritative international reference work on colorant nomenclature (CI numbers), physical form, constitution and application. |
| http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32009R1223:EN:NOT | **EU regulation on cosmetic products**, REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 November 2009 on cosmetic products.<br>ANNEX IV lists COLORANTS ALLOWED IN COSMETIC PRODUCTS and corresponding CI index numbers, while Annex V lists preservatives allowed in cosmetic products. |
| http://www.who.int/ipcs/en/ | World Health Organisation- International Program on Chemical Safety- (**WHO/IPCS**) work to establish the scientific basis for the sound management of chemicals, and to strengthen national capabilities and capacities for chemical safety. Tools for safety assessment and other literature is published. |

| | |
|---|---|
| http://www.atsdr.cdc.gov/ | Agency for Toxic Substances and Disease Registry (**ATSDR**). |
| http://www.cir-safety.org/ | The **Cosmetic Ingredient Review** (CIR) reviews and assesses the safety of individual chemical compounds for cosmetics and publishes the results in peer-reviewed scientific literature. |

# Referencer


Boyd, H.B.; Larsen, P.B., 2014, *Guidance for risk assessment of chemicals in consumer articles and products*, Survey of chemical substances in consumer products No. 125, 2014, Danish Environmental Protection Agency ISBN 978-87-93178-21-2

ChemSpider, ikke dateret/n.d., *ChemSpider – Search and share chemistry*, Tilgængelig på: http://www.chemspider.com/, set 2013.10.28

CIR, ikke dateret/n.d., Cosmetic Ingredient Review - About CIR, Tilgængelig på: http://www.cir-safety.org, set 2013.12.02

COLIPA, 2004, *GUIDELINES ON STABILITY TESTING OF COSMETIC PRODUCTS*, Tilgængelig på: https://cosmeticseurope.eu/publications-cosmetics-europe-association/guidelines.html?view=item&id=20%3Aguidelines-on-stability-testing-of-cosmetics-colipactfa-2004&catid=46%3Aguidelines, Cosmetics Europe (tidligere COLIPA), marts 2004, set 2013.10.28.

Colour Index International, 2013, *Introduction to the Colour Index: Classification System and Terminology,* Tilgængelig på: http://www.colour-index.com/ - revised by GH, April 2013, set 2013.10.28

CosIng, ikke dateret/n.d., *Welcome to CosIng*, tilgængelig på: http://ec.europa.eu/consumers/cosmetics/cosing/, European Commission – Health and Consumers, set 2013.10.28

Council of Europe, 2008, *Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up (superseding Resolution ResAP(2003)2 on tattoos and permanent make-up)*, tilgængelig på: http://www.coe.int/t/e/social_cohesion/soc-sp/resap_2008_1%20e.pdf, Adopted by the Committee of Ministers on 20 February 2008, set 2013.12.02

Miljøstyrelsen, ikke dateret/n.d., *The Danish EPA's Risk Assessment of Hazardous Substances in Tattoo Inks based on the project, "Chemical Substances in Tattoo Ink"*. Tilgængelig på: http://www.mst.dk/NR/rdonlyres/10A88C86-7653-4383-840B-F50FD38363C9/0/TheDanishEPARAoftatooinks.pdf, set 2013.11.06

ECHA, ikke dateret/n.d. A, *Safety Data Sheets,* tilgængelig på: http://echa.europa.eu/web/guest/regulations/reach/safety-data-sheets, Det europæiske kemikalieagentur, set 2013.10.28

ECHA, ikke dateret/n.d. B, *Guidance on Information Requirements and Chemical Safety Assessment – Pathfinder*, tilgængelig på: http://echa.europa.eu/web/guest/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment, set 2013.12.03

ECHA, 2011, *Guidance on the compilation of safety data sheets*, tilgængelig på: http://echa.europa.eu/documents/10162/13643/sds_en.pdf, Version 1.1, december 2011, ECHA-2011-G-08.1-EN, set 2013.12.02

ECHA, 2012, *Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health*, tilgængelig på: http://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf, Version 2.1 november 2012, ECHA-2010-G-19-EN, set 2013.12.03.

ECHA, 2013A, *Registered substances – Chemical Substances Search,* European Chemical Agency, tilgængelig på: http://echa.europa.eu/information-on-chemicals/registered-substances, opdateret 2013.11.28, set 2013.12.02

ECHA, 2013B, *C&L Inventory database*, European Chemical Agency, tilgængelig på: http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database, opdateret 2013.11.01, set 2013.12.02

EFSA, 2012, *Scientific Opinion - Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data,* European Food Safety Authority, EFSA Journal 2012;10(3):2579, tilgængelig på: http://www.efsa.europa.eu/en/efsajournal/doc/2579.pdf, set 2013.11.07

Engel, E; Santarelli, F; Vasold, R; Maisch, T; Ulrich, H; Prantl, L; König, B; Landthaler, M; Bäumler, W, 2008, *Modern tattoos cause high concentrations of hazardous pigments in skin*, Contact dermatitis 2008;58;228-232.

ESIS, ikke dateret/n.d., *ESIS: European Chemical Substances Information System*, tilgængelig på: http://esis.jrc.ec.europa.eu/, European Commission – Joint Research Center – Institute for Health and Consumer Protection, set 2013.10.28

European Commission, ikke dateret/n.d., Scientific Committees – About, tilgængelig på: http://ec.europa.eu/health/scientific_committees/about/index_en.htm, European Commission – Health and Consumers – Scientific Committees, set 2013.12.03

Europæisk Farmakope, *Chapter 2.6.1: Sterility*, 2011.04, tilgængelig på: http://online.pheur.org/EN/entry.htm (abonnement krævet).

European Union, 2011, *RECOMMENDATIONS, COMMISSION RECOMMENDATION of 18 October 2011 on the definition of nanomaterial, 2011/696/EU*, tilgængelig på: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:275:0038:0040:EN:PDF, Official Journal of the European Union – 2011.10.20 - L275/38 EN, set 2013.12.03

IUPAC, ikke dateret/n.d., *Nomenclature and Terminology (including IUPAC color books),* tilgængelig på: http://www.iupac.org/, International Union of Pure and Applied Chemistry, set 2013.10.28

Jacobsen, Eva; Tønning, Kathe; Pedersen, Eva; Bernth, Nils; Serup,oxide Jørgen; Høgsberg, Trine; Nielsen, Elsa, 2012, *Chemical Substances in Tattoo Ink, Survey of chemical substances in consumer products, no. 116, 2012*, Danish Environmental Protection Agency, ISBN no. 978-87-92779-87-8

OECD, ikke dateret/n.d., *OECD Guidelines for the Testing of Chemicals*, tilgængelig på: http://www.oecd-ilibrary.org/content/package/chem_guide_pkg-en, set 2013.12.03

PubChem, ikke dateret/n.d., tilgængelig på: http://pubchem.ncbi.nlm.nih.gov/, set 2013.10.28

PubMed, ikke dateret/n.d., *PubMed*, tilgængelig på: http://www.ncbi.nlm.nih.gov/pubmed, US National Library of Medicine National Institutes of Health, set 2013.11.07

REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 November 2009 on cosmetic products, tilgængelig på: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009R1223&from=EN, set 2014.05.05

REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on classification, labeling and packaging of substances and mixtures, tilgængelig på: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF, set 2013.12.02

REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, tilgængelig på: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006R1907&qid=1399286418717&from=EN, set 2014.05.05

SCCS, 2012, THE SCCS'S NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC SUBSTANCES AND THEIR SAFETY EVALUATION - 8TH REVISION (adopted on December 11th 2012), Scientific Committee on Consumer Safety, SCCS/1501/12. Tilgængelig på: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf, set 2014.04.09

SciFinder, ikke dateret/n.d., *SciFinder – The choice for chemistry research*, tilgængelig på: https://www.cas.org/products/scifinder, CAS – A division of the American Chemical Society, set 2013.10.28.

TOXNET, ikke dateret/n.d., TOXNET – Toxicology Data Network, tilgængelig på: http://toxnet.nlm.nih.gov/, set 2013.11.07

Wu, J; Liu, W; Xue, C; Zhou, S; Lan, F; Bi, L; Xu, H; Yang, X; Zeng, FD, 2009, *Toxicity and penetration of TiO2 nanoparticles in hairless mice and porcine skin after subchronic dermal exposure*, Toxicology Letters, Volume 191, Issue 1, 1 December 2009, Pages 1–8.

# Vocabulary

| | |
|---|---|
| BMDL10: | Bench Mark Dose, the lower 95% confidence limit on the benchmark dose associated with an adverse toxicological effect in 10% of the tested population |
| BW: | Bodyweight |
| CI-number: | Colour Index Constitution Numbers |
| CLP: | Classification, labelling and packaging |
| CMR: | Carcinogenic, mutagenic and toxic to reproduction |
| DNEL: | Derived No Effect Level |
| ECHA: | European Chemicals Agency |
| EINECS: | the European Inventory of Existing Commercial chemical Substances |
| ELINCS: | the European List of Notified Chemical Substances |
| INCI: | International Nomenclature of Cosmetic Ingredients |
| Mixture: | A mixture or solution composed of two or more substances |
| MoS: | Margin of Safety |
| NOAEL: | No Observed Adverse Effect Level |
| QSAR: | Quantitative Structure-Activity Relationship, used for modeling of toxicological effect of a substance using knowledge of toxicological effect of a structurally similar chemical. |
| RCR: | Risk Characterization Ratio |
| SDS: | Safety Data Sheet |
| SCCS: | Scientific Committee on Consumer Safety |
| Substance: | A chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. |
| T25: | Dose or concentration, at which the adverse toxicological effect occurs in 25% of the tested population |

[¶ Tekst - **slet ikke næste linje da det indeholder et sektionsskifte - se linjer ved at slå Vis/skjul til**]

**Anbefaling fra Miljøstyrelsen om sikkerheden af tatoveringsfarver**

At få lavet en tatovering må ikke udgøre en risiko for sikkerhed og sundhed, når tatoveringsfarven anvendes som tilsigtet. For at reducere de sundhedsmæssige risici forbundet med at få en tatovering har Miljøstyrelsen udarbejdet en række anbefalinger vedrørende sikkerheden af tatoveringsfarver herunder retningslinjer for sikkedhedsvurdering af tatoveringsfarver.

Miljøministeriet
Miljøstyrelsen

Strandgade 29
1401 København K
Tlf.: (+45) 72 54 40 00

**www. mst.dk**