

Review

# Occurrence and Regulatory Evaluation of Contaminants in Tattoo Inks

Patricia Fels<sup>1,2</sup>, Dirk W. Lachenmeier<sup>2,\*</sup>, Pascal Hindelang<sup>2</sup>, Stephan G. Walch<sup>2</sup> and Birgit Gutsche<sup>2</sup>

<sup>1</sup> Department of Chemistry and Toxicology, Rhineland-Palatinate University of Technology Kaiserslautern-Landau, Erwin-Schrödinger-Straße 52, 67663 Kaiserslautern, Germany; fels@rptu.de

<sup>2</sup> Chemisches und Veterinäruntersuchungsamt (CVUA) Karlsruhe, Weissenburger Strasse 3, 76187 Karlsruhe, Germany; pascal.hindelang@cvuaka.bwl.de (P.H.); stephan.walch@cvuaka.bwl.de (S.G.W.); birgit.gutsche@cvuaka.bwl.de (B.G.)

\* Correspondence: lachenmeier@web.de; Tel.: +49-721-926-5434

**Abstract:** Tattooing has been an enduring form of body art since ancient times, but it carries inherent health risks, primarily due to the complex composition of tattoo inks. These inks consist of complex mixtures of various ingredients, including pigments, solvents, impurities and contaminants. This literature review aims to shed light on the organic and inorganic contaminants present in tattoo inks prior to the implementation of the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) regulation in 2022. This review shows that the most common contaminants are polycyclic aromatic hydrocarbons (PAHs), with a concentration range of 0.005–201 mg/kg, mainly detected in black tattoo inks, and primary aromatic amines (PAAs), with a concentration range of 0.5–1100 mg/kg, and heavy metals such as lead (0.01–14.0 mg/kg) and chromium(VI) (0.16–4.09 mg/kg) which are detected in almost all tattoo inks. When compared to the new concentration limits outlined in REACH, it is clear that a significant part of these contaminants would be considered non-compliant. However, the results of the review are limited due to the lack of quantitative data on contaminants in tattoo inks. In addition, the future implementation of REACH is expected to lead to changes in the composition of tattoo inks, which will affect the presence of contaminants.

**Keywords:** tattoos; contaminants; impurities; REACH; PAH; PAA; metals



**Citation:** Fels, P.; Lachenmeier, D.W.; Hindelang, P.; Walch, S.G.; Gutsche, B. Occurrence and Regulatory Evaluation of Contaminants in Tattoo Inks. *Cosmetics* **2023**, *10*, 141. <https://doi.org/10.3390/cosmetics10050141>

Academic Editor: Enzo Berardesca

Received: 10 August 2023

Revised: 14 September 2023

Accepted: 3 October 2023

Published: 10 October 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Tattooing is an art form that is almost as old as mankind [1]. In 2017, 24% of people in Germany reported having at least one tattoo. Another 21% are thinking about getting a tattoo [2]. Younger people (25–35 years old) are particularly interested in tattoos. Almost half of them have at least one tattoo [3]. It is clear that the importance of high-quality tattoo ink is growing.

Although newer and more advanced tattoo inks have been on the market for decades, resolutions on tattoo inks and their ingredients were only introduced in the European Union (EU) in 2003 [4] and then revised in 2008 [5]. These resolutions only covered a small number of chemicals, elements, pigments, etc., that were restricted in their concentration or banned from tattoo inks due to carcinogenic, mutagenic, reprotoxic or sensitizing properties (e.g., 4-chloroaniline, 3,3'-dimethylbenzidine, o-toluidine). Both resolutions were non-binding but were a suggestion for the implementation of legislation on tattoos and permanent makeup. However, only eight EU Member States (the Netherlands, Germany, Belgium, France, Norway, Spain, Slovenia and Sweden) and two European Free Trade Association (EFTA) countries (Switzerland and Liechtenstein) implemented national legislation on tattoo and permanent makeup products in line with the recommendations of the EU resolutions by 2015 [6–8]. On the other hand, six other EU Member States (Italy, Malta, Romania, Czechia, Finland and Slovakia) used these resolutions to regulate tattoo practices (safety, health and hygiene requirements) but did not implement them into national legislation.

Three EU Member States (Austria, Denmark and Latvia) notified draft national legislation in 2013 (Austria, Denmark) and 2014 (Latvia). However, these drafts were put on hold by the EU Commission because they conflicted with Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) provisions [6–8]. All other EU Member States did not have specific regulations on tattooing [8].

In many of the countries that have implemented the resolutions, risk management measures have been taken because several tattoo ink manufacturers were obviously not complying with these requirements; e.g., most of the products were imported into the EU, and the directives did not apply in their country of origin. To increase the safety of tattoo inks and to unify the regulations for tattoo inks within the EU, tattoo inks and pigments were regulated under REACH in 2022 [9]. This led to restrictions and bans on commonly used pigments and ingredients for tattoo inks such as Pigment Blue 15 and Pigment Green 7 [10].

The ban on certain ingredients and pigments in tattoo inks has been controversial within the tattoo community. Although professionals and scientists have been advocating for a unified regulation for decades, many consumers are attracted to colorful tattoo inks that are not REACH-compliant and can no longer be used [11]. It is also unknown whether the documented adverse effects after tattooing, such as allergic reactions, granulomas, lichenoid reactions or rashes [6,12–14], are due to the pigments themselves, to other ingredients in the tattoo ink mixtures, such as solvents, or to contaminants and impurities of either the pigments or other ingredients.

This review provides a summary of the contaminants and their concentrations in relation to the limits set by the European Parliament and Council in the context of REACH for tattoo and permanent makeup products (Regulation (EC) No. 2020/2081) [10].

## 2. Materials and Methods

The electronic databases Google Scholar and PubMed were searched for available literature on contaminants in tattoo inks as these databases contain the most relevant data in this area. References from relevant articles were also included. Searches for the occurrence of contaminants were conducted in May and June 2023.

A publication was included in this review if the contaminants were measured in the tattoo ink itself, i.e., before tattooing. Publications that measured contaminants or degradation products after tattooing or laser removal were not included. Another criterion for inclusion was the year of publication. Only publications published after 2000, but especially publications published after 2008, were considered to be suitable for this review. This was to ensure that the information in the selected publications remained relevant, as the formulation of tattoo inks and permanent makeup changes over time. Another reason for the selected time frame was that the Resolutions on Requirements and Criteria for the Safety of Tattoos and Permanent Make-up (ResAP2003 and ResAP2008) were introduced in Europe to regulate the safety of tattoos and permanent makeup for the first time. Publications should be published in English or German and preferably from Europe or North America.

Initially, only publications that measured contaminants quantitatively were selected for this review. However, after an initial literature review was performed, publications that measured contaminants qualitatively were also included, as these contaminants appeared to be quite different from those measured quantitatively.

The focus was on publications that quantified contaminants in tattoo inks, specifically the amount of polycyclic aromatic hydrocarbons (PAHs) and aromatic amines (mostly primary aromatic amines (PAAs)) in tattoo inks and the degradation products of pigments and other ingredients in tattoo inks after exposure to sunlight. Publications quantifying the amount of degradation products after laser treatment were not included.

Search terms included but were not limited to the following: tattoo, tattoo ink, contaminants, analytical analysis, tattoo pigments, impurities, ingredients, PAH, primary aromatic hydrocarbons, PAA and aromatic amines.

All 19 retrieved articles or hits were considered suitable for this work, based on the information provided in their abstracts, because they met the eligibility criteria established beforehand. These were then entered into bibliographic software and then processed individually in detail. As the literature search revealed a lack of data, suitable articles were included regardless of their publication date.

In the end, 12 papers with data for detected organic contaminants and 7 papers with data for inorganic contaminants were selected for this review.

### 3. Results

The initial aim of the review was to find contaminants associated with a specific pigment. However, because many studies either did not specify the tattoo inks they tested or the tattoo ink manufacturer did not specify the actual pigments used, it was decided to sort the contaminants by tattoo ink color.

The contaminants were also divided into organic and inorganic contaminants, as presented in the following subsections.

#### 3.1. Organic Contaminants

The organic contaminants detected by quantitative and qualitative measurements are listed by tattoo ink color in Table 1. The overall table with the percentage of occurrence in the samples (Supplementary Table S1), the possible adverse effects of the contaminants shown here (Supplementary Table S2) and the quantification methods and limits of detection/limits of quantification (Supplementary Table S3) can be found in the Supplementary Materials.

**Table 1.** Organic contaminants of tattoo inks, sorted by tattoo ink color. Substances within a substance class are sorted by the highest measured concentration [15–26].

Tattoo Ink Color	Substance Class	Substance	Concentration Range <sup>a,b</sup>
Black	PAH	PAH sum	0.14–201 mg/kg
		Naphthalene	0.005–81 mg/kg
		Phenanthrene	0.006–30.5 mg/kg
		Pyrene	0.055–28 mg/kg
		Acenaphthylene	0.005–20 mg/kg
		Benzo[b]fluoranthene	0.073–8.8 mg/kg
		Fluoranthene	0.16–8.19 mg/kg
		Benzo[ghi]perylene	0.09–5.6 mg/kg
		Benzo[a]pyrene	0.048–5.3 mg/kg
		Anthracene	0.001–4.1 mg/kg
		9-Fluorene	0.02–3.04 mg/kg
		Chrysene	0.006–2.5 mg/kg
		Benz[a]anthracene	0.005–1.8 mg/kg
		Acenaphthene	0.12–1.7 mg/kg
		Fluorene	0.006–1.2 mg/kg
		Ideno[1,2,3-cd]pyrene	0.17–1.1 mg/kg
		Benzo[k]fluoranthene	0.03–1.01 µ/g
		Dibenzo[a,h]anthracene	0.1–0.2 mg/kg
		1,2,3,4-Tetrahydro-1-phenyl-naphthalene	n/a
	Phthalates	Dibutyl phthalate	0.12–691.2 mg/kg
		Di-(2-ethylhexyl)phthalate	0.2–19.3 mg/kg

Table 1. Cont.

Tattoo Ink Color	Substance Class	Substance	Concentration Range <sup>a,b</sup>
Black	Aromatic Amines	Methenamine	0.08–21.64 mg/kg
		<i>o</i> -Anisidine	4.9 mg/kg
	Chlorinated Aliphatic Diene	Hexachloro-1,3-butaidine	0.08–4.52 mg/kg
	Phenols	Phenol	0.2–385 mg/kg
	Dibenzofurans	Dibenzofuran	0.02–1.62 mg/kg
	Ketones	Benzophenone	0.26–556.66 mg/kg
	Hydroxylated Alkynes	3,6-Dimethyl-1-heptyn-3-ol	n/a
	Polyhydric Alcohols	1,6-Hexandiole	n/a
	Carboxamide	Oleamide	n/a
	Lactones	7-Hexyl-2-oxepanone	n/a
	Polyvalent Alkanols	Propylene glycol	n/a
	Dipropylene Glycols	1,1'Oxybis-2-propanol	n/a
		2,2'Oxybis-1-propanol	n/a
	Glycolether	2-(2-Ethoxyethoxy)ethanol	n/a
	Green	PAH	Naphthalene
1-Methylnaphthalene			n/a
Styrene			n/a
PAA		<i>o</i> -Anisidine	5.5–1775 mg/kg
		<i>o</i> -Toluidine	2.6–133 mg/kg
		Pentachloroaniline	10–80 mg/kg
		4-Chloro-2,5-dimethoxyaniline	70 mg/kg
		3-Methoxyaniline	20 mg/kg
		Aniline	1.7 µ/g
Pentachloro aniline		n/a	
Organic Silicon Compounds		Octamethylcyclotetrasiloxane	n/a
Alcohols		2-Methyl-1-propanol	n/a
Alicyclic Diether		1,4-Dioxane	n/a
Cyclic Enones		3,3,5-Trimethyl-2-cyclohexen-1-one	n/a
Oxygen Heterocycles		1,3-Dioxolane	n/a
Crown Ether	12-Crown-4	n/a	
Dibenzofurans	4,5,6,7-Tetrachloro-1,3-isobenzofuranedione	n/a	
Phthalates	Dibutyl phthalate	n/a	
	Diisooctyl phthalate	n/a	
Blue	PAH	Naphthalene	1.9–2.8 mg/kg
		<i>m</i> -Isopropoxyaniline	20–500 mg/kg
	PAA	4-Chloro- <i>o</i> -toluidine	5.9–15 mg/kg
<i>o</i> -Anisidine		0.75–4.9 mg/kg	
Brown	PAA	Aniline	79–230 mg/kg
		4-Methyl- <i>m</i> -phenylenediamine	1.8–200 mg/kg
		<i>p</i> -Chloroaniline	2.1–72 mg/kg
		Dichloroaniline	60 mg/kg
		<i>o</i> -Toluidine	1.0–13 mg/kg
		2-Ethoxyaniline	7 mg/kg
4-chloro- <i>o</i> -toluidine	7 mg/kg		

Table 1. Cont.

Tattoo Ink Color	Substance Class	Substance	Concentration Range <sup>a,b</sup>
Brown		5-Nitro- <i>o</i> -toluidine	5.8 mg/kg
		3,3'-Dichloroaniline	4 mg/kg
		<i>o</i> -Anisidine	4 mg/kg
		2,4-Xylidine/2,6-Xylidine	0.4 mg/kg
Orange	PAH	Naphthalene	1.3 mg/kg
		Aniline	56–110 mg/kg
		<i>m</i> -Isopropoxyaniline	100 mg/kg
	PAA	4-Methyl- <i>m</i> -phenylenediamine	16 mg/kg
		2-Ethoxyaniline	16 mg/kg
		Dichloroaniline	6 mg/kg
		1-Amino-2-naphthol	6 mg/kg
		2-Naphthylamine	2.6 mg/kg
		<i>o</i> -Toluidine	1.3 mg/kg
		3,3'-Dichlorobenzidine	n/a
		3,3'-Dichlorodiphenyl	n/a
	Haloaromatic	3,3'-Dimethoxybiphenyl	n/a
	Heteroaromatic	Acetanilide	n/a
	Aromatic Amine	Formanilide	n/a
	Red	PAH	Naphthalene
Trichloroaniline			20–1100 mg/kg
<i>o</i> -Anisidine			0.55–424 mg/kg
PAA		4-Methyl- <i>m</i> -phenylenediamine	1.2–400 mg/kg
		Aniline	0.54–300 mg/kg
		2-Ethoxyaniline	8–250 mg/kg
		5-Chloro-2,4-dimethoxyaniline	240 mg/kg
		5-Nitro- <i>o</i> -toluidine	6.2–190 mg/kg
		2-Nitro- <i>p</i> -toluidine	170 mg/kg
		3-Methoxyaniline	12–140 mg/kg
		Dichloroaniline	130 mg/kg
		1-Amino-2-naphthol	10–110 mg/kg
		<i>p</i> -Chloroaniline	1.1–100 mg/kg
		4-Chloro-2,4-dimethoxyaniline	6–80 mg/kg
		4-Methoxy- <i>m</i> -phenylenediamine	40 mg/kg
		4-Methyl-1,2-benzendiamine	20 mg/kg
		<i>o</i> -Toluidine	1.1–20 mg/kg
		4-Chloro- <i>o</i> -toluidine	1.2–14 mg/kg
		3,3'-Dichlorobenzidine	3.7–6.2 mg/kg
		2-Nitro- <i>p</i> -anisidine	4 mg/kg
4-Aminobiphenyl		1.1 mg/kg	
2,4-Xylidine/2,6-Xylidine		0.68–0.75 mg/kg	
2-Amino-4-nitrotoluene		n/a	
4-Nitrotoluene	n/a		
4-Aminobenzamide	n/a		
2-Methyl-5-nitroaniline	n/a		

Table 1. Cont.

Tattoo Ink Color	Substance Class	Substance	Concentration Range <sup>a,b</sup>	
Red	Aromatic Amine	2-Methylformanilide	n/a	
	Carboxamide	Benzamide	n/a	
		4-Hydroxybenzamide	n/a	
Violet	PAA	5-Chloro- <i>o</i> -anisidine	150–340 mg/kg	
		<i>m</i> -Isopropoxyaniline	65 mg/kg	
		2-Ethoxyaniline	6–45 mg/kg	
		Dichloroaniline	15 mg/kg	
		Aniline	1.6–10 mg/kg	
		4-Chloro-2,5-dimethoxyaniline	5 mg/kg	
		<i>o</i> -Anisidine	0.35–4.2 mg/kg	
		<i>o</i> -Toluidine	0.85 mg/kg	
		4-Chloroaniline	n/a	
		<i>o</i> -Anisidine	4.6–1150 mg/kg	
		4-Chloro-2,5-dimethoxyaniline	170–180 mg/kg	
Yellow	PAA	3-Methoxyaniline	14 mg/kg	
		2-Nitro- <i>p</i> -anisidine	14 mg/kg	
		<i>m</i> -Isopropoxyaniline	10 mg/kg	
		5-Chloro-2,4-dimethoxyaniline	10 mg/kg	
		3,3'-Dichlorobenzidine	2.5 mg/kg	
		<i>o</i> -Toluidine	0.68 mg/kg	
		<i>o</i> -Acetoacetanilide	n/a	
		2-(Hydroxyimine)- <i>N</i> -(2-methoxyphenyl)-3-oxobutanamide	n/a	
		<i>N,N</i> O-Bis(2-methoxyphenyl)urea	n/a	
		2-Methoxyacetanilide	n/a	
		2-Methoxyformanilide	n/a	
Gray	PAH	3,3'-Dichlorodiphenyl	n/a	
		<i>N</i> -(2-Methoxyphenyl)-3-oxobutanamide	n/a	
		Haloaromatic	3,3'-Dichlorobenzidine	n/a
		PAH	Naphthalene	1.0 mg/kg
			Pyrene	0.52 mg/kg
			Sum PAH	0.5–52 mg/kg
		No color specification	PAH	Benzo[ <i>a</i> ]pyrene
$\beta$ -Naphthol-ethoxylate	n/a			
1-Naphthol	n/a			
Styrene	n/a			
<i>N</i> -Nitrosodiethanolamine	0.006–24 mg/kg			
Nitrosamines	<i>N</i> -Nitrosomorpholine		0.009–0.625 mg/kg	
	<i>N</i> -Nitrosodibutylamine		0.053–0.093 mg/kg	
	<i>N</i> -Nitrosodimethylamine		0.017 mg/kg	
	<i>o</i> -Toluidine		0.5–30 mg/kg	
	<i>o</i> -Anisidine		0.5–30 mg/kg	
PAA	Aniline	0.5–30 mg/kg		
	5-Nitro- <i>o</i> -toluidine	0.5–30 mg/kg		
	3,3'-Dichlorobenzidine	0.5–5 mg/kg		
	4-Chloroaniline	n/a		

Table 1. Cont.

Tattoo Ink Color	Substance Class	Substance	Concentration Range <sup>a,b</sup>
No color specification	PAA	4-Methyl- <i>m</i> -phenylenediamine	n/a
		3,4-Dichloroaniline	n/a
		2-Ethoxyaniline	n/a
		4-Ethoxyaniline	n/a
	Haloaromatic	3,3'-Dichlorobenzidine	n/a
	Aromatic Amine	<i>N</i> -Isopropyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine	n/a
	Aromatic Hydrocarbons	Biphenyl	n/a
	Phenols	Thymol	n/a
		2,4,5-Trichlorophenol	n/a
	Hydrocarbons	1,2-Dichlorobenzene	n/a
		3,4-Dichlorobenzene	n/a
		3-Butenylbenzene	n/a
	Alkylphenols	Nonylphenol ethoxylate	n/a
		Octylphenol ethoxylate	n/a

<sup>a</sup> Substances with only one concentration shown were observed in only one sample. <sup>b</sup> Substances with n/a could only be measured qualitatively. n/a—not available.

### 3.1.1. Black Tattoo Ink

The main contaminants in black tattoo inks are PAHs, for which the concentration can be as high as 201 mg/kg. PAHs found in high concentrations include naphthalene, phenanthrene, pyrene and acenaphthylene. All other PAHs have concentrations much lower than those of these four substances.

Other contaminants include phthalates, PAAs, phenol, dibenzofuran, benzophenone and hexachloro-1,3-butadiene. Concentrations range from a few milligrams per kilogram of tattoo ink to over 0.6 g/kg. This wide range is particularly evident for benzophenone, phenol and dibutyl phthalate.

Black tattoo ink contains many classes of substances that were detected qualitatively and were not detected in other inks, such as lactones, alkynes, carboxamides and glycols. However, there was also one PAH that could only be detected qualitatively, not quantitatively.

### 3.1.2. Green Tattoo Ink

All quantitatively detected organic contaminants in green tattoo inks are PAAs. With a maximum concentration of 1775 mg/kg, *o*-anisidine is the most concentrated contaminant in green tattoo inks. However, *o*-anisidine also has the widest concentration range out of all contaminants in green tattoo inks. Three of the contaminants in green tattoo ink were detected only once.

Organic contaminants detected only by qualitative measurements are more diverse than organic contaminants that could be detected by quantitative measurements. These measurements detected PAHs as well as phthalates and dibenzofurans, similar to the contaminants in black tattoo inks. The contaminants identified also included substances and classes of substances that are unique to green tattoo inks, e.g., octamethylcyclotetrasiloxane and crown ether, some of which are banned by Regulation (EC) No. 1223/2009 and limited in their concentrations in tattoos by REACH Regulation (EU) No. 2020/2081.

### 3.1.3. Blue Tattoo Ink

The organic contaminants detected in blue tattoo inks are one PAH and four PAAs. The only contaminant detected with a concentration above 100 mg/kg is *m*-isopropoxyaniline

with a concentration as high as 500 mg/kg. The maximum concentrations of all other contaminants were less than 20 mg/kg.

#### 3.1.4. Brown Tattoo Ink

The only organic contaminants identified in brown tattoo inks are PAAs. Aniline and 4-methyl-*m*-phenylenediamine have the highest concentrations at over 200 mg/kg. More than half of the detected contaminants have a concentration of less than 10 mg/kg and were identified only once in all samples.

#### 3.1.5. Orange Tattoo Ink

The dominant organic contaminants in orange tattoo inks are PAAs with some PAHs. The combination of these two substance groups is similar to red tattoo inks. With over 100 mg/kg, aniline and *m*-isopropoxyaniline have the highest concentrations of all contaminants in orange tattoo inks. In contrast, the only PAH, naphthalene, has the lowest concentration in orange tattoo inks.

Contaminants identified using qualitative measurements in orange tattoo ink include PAAs, aromatic amines, haloaromatics and heteroaromatics. Some of the substances are present in other tattoo ink colors, such as yellow, but others are exclusive to orange tattoo inks such as acetanilide.

#### 3.1.6. Red Tattoo Ink

Red tattoo ink, along with black tattoo ink, has the most quantitatively measured organic contaminants out of all tattoo ink colors. It also has the highest reported amount of PAA contaminants. In particular, the amount of PAAs at high concentrations, such as trichloroaniline, *o*-anisidine, 4-methyl-*m*-phenylenediamine, aniline, 2-ethoxybenzenamine and 5-chloro-2,4-dimethoxyaniline with wide concentration ranges, is comparable to that found for orange tattoo ink, but the concentration of *o*-toluidine is very different between these two types of tattoo ink.

Similar to orange tattoo inks, red tattoo inks also contain contaminants, which could only be measured qualitatively, from the substance class of aromatic amines and PAAs, as well as carboxamides. Most of these substances have the basic structure of benzamide and toluene.

#### 3.1.7. Violet Tattoo Ink

The only contaminants identified in violet tattoo inks were PAAs. A high concentration of 5-chloro-*o*-anisidine was measured in almost all violet tattoo inks. With a concentration of at least 150 mg/kg, its level is significantly higher than that of all other contaminants combined. The lowest concentration measured was 0.65 mg/kg of *o*-toluidine, comparable to the amount of *o*-toluidine in orange tattoo ink.

Only one contaminant was identified by qualitative measurements. This contaminant was a PAA, as were the other contaminants in violet tattoo ink which were detected by quantitative measurements.

#### 3.1.8. Yellow Tattoo Ink

All reported organic contaminants in yellow tattoo inks are from the PAA group. The concentration ranges vary greatly between the substances. *o*-Anisidine has the highest concentration of all measured contaminants with concentrations of up to 1000 mg/kg tattoo ink. 4-Chloro-2,5-dimethoxyaniline also has a higher concentration than the other contaminants in yellow tattoo ink, but with a concentration of 180 mg/kg, it is much less present in the ink than *o*-anisidine. The lowest concentration is *o*-toluidine at less than 1 mg/kg, which is comparable to the amount of *o*-toluidine in violet and orange tattoo inks.

The contaminants identified by qualitative measurements are mostly aromatic amines and one haloaromatic. In contrast, the contaminants identified by quantitative methods are all PAAs. Many of the contaminants are similar to those detected in orange tattoo inks.

### 3.1.9. Gray Tattoo Ink

The gray tattoo ink measured was reported to contain only PAHs as organic contaminants. This color is also the one with the fewest reported organic contaminations. This is probably due to the fact that only one sample was measured. However, it can be seen that the concentration of PAHs is low, as compared to other tattoo inks in the same color spectrum (e.g., black). The low concentrations are probably due to the dilution of black tattoo ink with white tattoo ink to obtain gray tattoo ink. Due to the dilution, the concentrations of contaminations became lower.

### 3.1.10. No Color Specifications

This group consists of data where the color was not specified. The contaminants in this group are PAHs, PAAs and nitrosamines. Nitrosamines were reported in only one study [20]. Each contaminant listed here is found in a maximum of 37% of the measured samples (see Supplementary Table S1). The amount of PAHs found in these samples is the highest of all contaminants. The amount of benzo[a]pyrene, the best-known carcinogen of the PAH group [27], was only a fraction of the total amount of PAHs.

Most of the nitrosamines have a concentration of less than 1 mg/kg, except for *N*-nitrosodiethanolamine, the concentrations of which can be as high as 24 mg/kg. All aromatic amine contaminants have a concentration range of up to 30 mg/kg, except for 3,3'-dichlorobenzidine, whose highest concentration was 5 mg/kg.

Qualitatively detected compounds include PAHs, alkylphenols, phenols, hydrocarbons, aromatic hydrocarbons, haloaromatics and aromatic amines.

## 3.2. Inorganic Contaminants

Contaminants in tattoo inks may also be inorganic. In this subsection, the occurrence of inorganic contaminants, e.g., metals and heavy metals, is presented in Table 2. More detailed information on inorganic contaminants can be found in the Supplementary Materials (see Supplementary Table S4).

**Table 2.** Inorganic contaminants with the concentration range detected in all measured tattoo inks sorted by tattoo ink color [27–33].

Tattoo Ink Color	Substance	Concentration Range <sup>a</sup>
Black	Cadmium	0.001–0.14 mg/kg
	Cobalt	0.01–0.07 mg/kg
	Chromium	0.87–3.06 mg/kg
	Chromium(VI)	1.19–1.25 mg/kg
	Mercury	0.01–0.20 mg/kg
	Manganese	0.08–1.04 mg/kg
	Nickel	0.07–9.50 mg/kg
	Lead	0.007–1.45 mg/kg
	Strontium	0.05–0.17 mg/kg
	Vanadium	0.006–0.15 mg/kg
Green	Cadmium	0.03–0.5 mg/kg
	Cobalt	0.02–0.1 mg/kg
	Chromium	0.10–22.00 mg/kg
	Chromium(VI)	0.42–1.15 mg/kg
	Mercury	0.01–0.2 mg/kg
	Manganese	0.47–1.8 mg/kg

Table 2. Cont.

Tattoo Ink Color	Substance	Concentration Range <sup>a</sup>
Green	Nickel	0.15–11.70 mg/kg
	Lead	0.07–0.80 mg/kg
	Strontium	0.04–0.67 mg/kg
	Vanadium	0.12–1.40 mg/kg
Blue	Cadmium	0.02–1.15 mg/kg
	Cobalt	0.01–0.18 mg/kg
	Chromium	0.52–3.34 mg/kg
	Chromium(VI)	0.16–0.60 mg/kg
	Mercury	0.01–0.14 mg/kg
	Manganese	0.17–1.45 mg/kg
	Nickel	0.27–2.27 mg/kg
	Lead	0.01–0.87 mg/kg
Brown	Strontium	0.06–2.26 mg/kg
	Vanadium	0.01–1.98 mg/kg
	Cadmium	0.008–0.35 mg/kg
	Cobalt	0.003–6.44 mg/kg
	Chromium	0.45–147.23 mg/kg
	Chromium(VI)	0.43–0.63 mg/kg
	Mercury	0.04–0.15 mg/kg
	Manganese	0.15–98.79 mg/kg
Orange	Nickel	0.07–9.59 mg/kg
	Lead	0.03–8.13 mg/kg
	Strontium	0.007–4.12 mg/kg
	Vanadium	0.006–11.05 mg/kg
	Cadmium	0.01–2.99 mg/kg
	Cobalt	0.02–0.13 mg/kg
	Chromium	0.43–4.72 mg/kg
	Chromium(VI)	2.94 mg/kg
Red	Mercury	0.02–0.15 mg/kg
	Manganese	0.08–0.58 mg/kg
	Nickel	0.06–0.81 mg/kg
	Lead	0.10–14.80 mg/kg
	Strontium	0.004–0.29 mg/kg
	Vanadium	0.06–1.51 mg/kg
	Cadmium	0.007–0.04 mg/kg
	Cobalt	0.009–0.03 mg/kg
Red	Chromium	1.07–4.67 mg/kg
	Chromium(VI)	0.40–4.09 mg/kg
	Mercury	0.007–0.17 mg/kg
	Manganese	0.27–0.62 mg/kg
	Nickel	0.04–0.64 mg/kg

Table 2. Cont.

Tattoo Ink Color	Substance	Concentration Range <sup>a</sup>
Red	Lead	0.05–0.42 mg/kg
	Strontium	0.009–0.06 mg/kg
	Vanadium	0.03–0.17 mg/kg
Violet	Cadmium	0.003–0.92 mg/kg
	Cobalt	0.01–0.04 mg/kg
	Chromium	0.50–4.99 mg/kg
	Chromium(VI)	0.65–3.91 mg/kg
	Mercury	0.02–0.07 mg/kg
	Manganese	0.16–1.27 mg/kg
	Nickel	0.26–1.11 mg/kg
	Lead	0.03–0.12 mg/kg
	Strontium	0.14–0.24 mg/kg
Yellow	Vanadium	0.68–2.52 mg/kg
	Cadmium	0.05–0.25 mg/kg
	Cobalt	0.003–0.02 mg/kg
	Chromium	0.36–1.90 mg/kg
	Mercury	0.01–0.13 mg/kg
	Manganese	0.08–1.40 mg/kg
	Nickel	0.04–0.43 mg/kg
White	Lead	0.02–0.11 mg/kg
	Strontium	0.01–0.11 mg/kg
	Vanadium	0.03–1.13 mg/kg
	Cadmium	0.47–0.56 mg/kg
	Cobalt	0.01–0.04 mg/kg
	Chromium	0.32–0.84 mg/kg
	Chromium(VI)	0.35 mg/kg
	Manganese	0.12–1.29 mg/kg
Gray	Nickel	0.20–0.60 mg/kg
	Lead	0.03–0.07 mg/kg
	Strontium	0.10–0.21 mg/kg
	Vanadium	1.42–1.59 mg/kg
	Cadmium	0.01–0.52 mg/kg
	Cobalt	0.02–0.04 mg/kg
	Chromium	0.37–2.05 mg/kg
	Chromium(VI)	0.67 mg/kg
Gray	Mercury	0.09–0.13 mg/kg
	Manganese	0.23–1.53 mg/kg
	Nickel	0.22–1.07 mg/kg
	Lead	0.06–0.50 mg/kg
	Strontium	0.02–0.58 mg/kg
	Vanadium	0.008–2.60 mg/kg

<sup>a</sup> Substances with only one concentration shown were observed in only one sample.

Because most of the inorganic contaminants are detected in all tattoo ink colors, the results of the literature review are sorted by inorganic contaminant rather than by color.

### 3.2.1. Cadmium

Cadmium was detected in all the samples measured. The highest concentration of 2.99 mg/kg was detected in orange tattoo ink, while the lowest concentration was detected in red tattoo ink with a maximum of 0.14 mg/kg. Cadmium concentrations decreased in the following order: orange > blue > violet > white > gray > green > brown > yellow > black > red (see Supplementary Table S4). Cadmium is known to be a skin sensitizer and can cause swelling and phototoxic reactions on the skin after tattooing, which is often seen in red tattoos [34–39].

### 3.2.2. Cobalt

Cobalt was present in all samples. The highest concentration of 6.44 mg/kg was detected in brown tattoo ink, and the lowest concentration was detected in yellow tattoo ink which amounted to a maximum concentration of 0.02 mg/kg. It should be noted that the concentration in brown tattoo ink is many times higher than that in all other tattoo ink colors. The concentrations of cobalt decreased in the following order: brown > blue > orange > green > black > gray > violet > white > red > yellow (see Supplementary Table S4). Cobalt is a known skin sensitizer and may also cause allergic reactions and granulomatous lesions [39–42].

### 3.2.3. Chromium

Chromium was identified in all samples measured and had the highest amount of inorganic contaminants measured. The highest concentration was detected in brown tattoo ink at 147.23 mg/kg, while the lowest concentration was found in white tattoo ink at 0.84 mg/kg. All inks had a chromium concentration above 1 mg/kg except for white tattoo inks. Chromium concentration decreased in the following order: brown > green > violet > orange > red > blue > black > yellow > white (see Supplementary Table S4).

Acute adverse effects of chromium after tattooing may be allergic reactions. Chromium is also a known skin sensitizer [42–44].

### 3.2.4. Chromium(VI)

Chromium(VI) was detected in nine of the ten mentioned tattoo ink colors; no information was found on the content of chromium(VI) in yellow tattoo inks. For the remaining tattoo ink colors, chromium(VI) was identified in all of them, with the highest concentration at 4.09 mg/kg in red tattoo inks. The maximum concentration of chromium(VI) is significantly lower than the concentration of total chromium (see Section 3.2.3 and Supplementary Table S3). The lowest maximum concentration of chromium(VI) was detected in white tattoo ink with an amount of 0.35 mg/kg. Chromium(VI) concentrations decreased in the following order: red > violet > orange > black > green > gray > brown > blue > white (see Supplementary Table S4).

The acute adverse effects of chromium(VI) are the same as those of chromium, as seen in Section 3.2.3. However, chromium(VI) may additionally cause the following chronic effects: eczema and contact dermatitis [28,39,42,45].

### 3.2.5. Mercury

Mercury was detected in approximately 67% of the tattoo inks. The highest concentration was detected in green tattoo ink with 0.20 mg/kg, and the lowest observed concentration was found in yellow tattoo inks with a maximum concentration of 0.07 mg/kg. It should be noted that all maximum concentrations are close to each other. Concentrations of mercury decreased in the following order: green > black > red > brown > orange > blue > gray > yellow > violet > white (see Supplementary Table S4).

The only acute adverse effects seen after tattooing due to mercury are allergic reactions. However, due to the small amount of mercury in the tattoo inks, these adverse effects are quite rare [37,39,42,46,47].

### 3.2.6. Manganese

Manganese was detected in all samples measured. The highest concentration was found in brown tattoo inks at 98.79 mg/kg, and the lowest maximum concentration was found in orange tattoo inks at 0.58 mg/kg. Except for three tattoo inks, all maximum concentrations were below 5 mg/kg. Manganese concentrations decreased in the following order: brown > green > gray > blue > yellow > white > violet > black > red > orange (see Supplementary Table S4).

Adverse reactions to manganese after tattooing are mostly acute, such as swelling and itching. Chronic skin disorders such as erythema and scaling of the skin are quite rare [38,39,48].

### 3.2.7. Nickel

Nickel was detected in all samples measured. The highest concentration was found in green tattoo inks at 11.70 mg/kg, and the lowest maximum concentration was found in yellow tattoo inks at 0.43 mg/kg. More than half of the maximum concentrations were above 1 mg/kg. The maximum concentrations of nickel found decreased in the following order: green > brown > black > blue > violet > gray > orange > red > white > yellow (see Supplementary Table S4). Nickel is a known skin sensitizer and may also cause allergic reactions [39,49,50].

### 3.2.8. Lead

Lead was detected in all samples measured. The highest concentration was detected in orange tattoo inks with an amount of 14.80 mg/kg, and the lowest maximum concentration was detected in white tattoo inks which amounted to 0.07 mg/kg. The detected maximum concentrations of lead decreased in the following order: orange > brown > black > violet > blue > red > green > yellow > gray > white (see Supplementary Table S4). There are no known acute adverse effects of lead associated with tattooing.

### 3.2.9. Strontium

Strontium was detected in all measured samples. The highest concentration was 4.11 mg/kg detected in brown tattoo inks. On the other hand, the lowest maximum concentration was 0.06 mg/kg, which was detected in red tattoo inks. Only two tattoo ink colors (brown and blue) had a maximum concentration above 1 mg/kg. The maximum concentrations of strontium decreased in the following order: brown > blue > green > gray > orange > violet > white > black > yellow > red (see Supplementary Table S4). There are no known acute adverse effects of strontium associated with tattooing.

### 3.2.10. Vanadium

Vanadium was detected in all samples measured. The highest detected concentration was in brown tattoo inks with an amount of 11.05 mg/kg, while the lowest maximum concentration was detected in a black tattoo ink with an amount of 0.15 mg/kg. All of the maximum concentrations were above 1 mg/kg except for black and red tattoo inks. The maximum concentrations of vanadium decreased in the following order: brown > gray > violet > blue > white > orange > green > yellow > red > black (see Supplementary Table S4). There are no known acute adverse effects of strontium associated with tattooing.

## 4. Discussion

There are several quantifiable contaminants that occur in tattoo inks in a wide range of concentrations. Aromatic amines and PAHs are common contaminants. PAHs are particularly prevalent in black and gray tattoo inks, while aromatic amines make up the

majority of contaminants in all other tattoo ink colors (see Table 1 and Supplementary Table S1).

Black tattoo inks show the widest concentration ranges. PAH concentrations range from a few  $\mu\text{g}/\text{kg}$  to more than 100  $\text{mg}/\text{kg}$ . Possible explanations for these observations may be that the concentration ranges shown here were compiled from about a decade of published papers. The measurements themselves may also explain this finding, as different laboratories use different extraction and quantification methods to detect and determine the amount of PAHs in tattoo inks (see Supplementary Table S3). Finally, differences in the production of black tattoo inks between manufacturers and the fact that there are two main ways to produce carbon black [51,52], which is the main pigment for black tattoo inks [17], offer an explanation for the highly variable concentrations. Due to the differences in production, there are a number of different carbon black products with different properties and varying levels of PAHs [53]. Due to the pre-REACH regulations on tattoo inks, which only limited the amount of total PAHs in tattoo inks, any type of carbon black could be used for black tattoo inks [54], which could explain the wide range of PAH levels in different studies.

Another possibly confounding factor is that carbon black adsorbs most of the contaminants. The analytically detected PAHs are probably only a small fraction of the total [54]. It is also unknown what happens to the adsorptively bound PAHs in carbon black after tattooing [55]. Since about 98% of the tattoo pigment particles disappear over the years [56], it is questionable whether the PAHs remain bound to the carbon black particles or whether part of the PAH content enters the skin and poses a risk to human health.

The size of tattoos, and therefore the amount of tattoo ink injected into human skin, can vary widely. A survey conducted in Germany, Austria and Switzerland in the years 2007–2008 examined the size of the most recent tattoo among consumers [57]. The average size was about  $400\text{ cm}^2$ . Combined with a pigment concentration of about  $2.53\text{ mg}/\text{cm}^2$  (range:  $0.6\text{--}9.4\text{ mg}/\text{cm}^2$ ) in a tattoo solution of about 25% (*v/v*) [58], the total PAH sum in a  $400\text{ cm}^2$  tattoo can be up to 813  $\mu\text{g}$ . For benzo[*a*]pyrene, the concentration would be in the range of  $0.2\text{--}21\text{ }\mu\text{g}$ . The most problematic toxic effects are chronic, non-reversible effects such as mutagenicity and carcinogenicity of PAHs and especially benzo[*a*]pyrene. Acute effects are rare and only seen at high concentrations of PAHs (up to several  $\text{mg}$  per  $\text{kg}$  body weight), which is not realistic for PAH exposure from tattooing [59]. There is a paucity of epidemiological research on the association between the lifestyle factor of tattooing and cancer. Only one study of skin cancer reported that the risk was low because there are only about 50 case reports of skin cancer associated with tattooing in the past 40 years, while millions of people are tattooed [60]. No evidence was available for other cancer sites associated with PAH exposure, such as the lung, and it remains doubtful that epidemiologic studies are sensitive enough to detect an increased cancer risk from tattooing (single exposure) when common lifestyle risk factors, such as tobacco smoke (which also contains PAHs) or UV light exposure, increase risk at the same cancer sites as contaminants in tattoo inks, and with daily lifelong exposure. An experimental study showed that black tattoo ink with a benzo[*a*]pyrene content of more than  $1\text{ mg}/\text{kg}$ , which is above the concentration limit laid down in REACH Regulation (EU) No. 2020/2081 (see Table 3), did not induce skin cancer in hairless mice, but actually protected against UVR-induced skin cancer [61].

Gray and black tattoo inks in particular have a wide range of PAH concentrations. As many PAHs are classified by the IARC as category 1, 2A or 2B carcinogens [62], the concentration limit for these substances is  $0.5\text{ mg}/\text{kg}$  and the concentration limit for benzo[*a*]pyrene is  $0.005\text{ mg}/\text{kg}$  according to REACH Regulation 2020/2081 Annex 13. Most of these contaminants have concentrations above  $0.5\text{ mg}/\text{kg}$ . As a result, most black inks containing these levels of PAHs are in violation of REACH and cannot be sold in the European Union. The amount of benzo[*a*]pyrene is of particular concern, as the concentration can be as high as  $5\text{ mg}/\text{kg}$ , which is 1000 times higher than the limit in the above-mentioned REACH Regulation 2020/2081.

Comparing the tested levels of contaminants in tattoo inks with the concentration limit of the REACH Regulation (Table 3) allows an assessment of whether these compounds pose a potential risk to the consumer.

**Table 3.** Concentration limits of substances set by the European Parliament and the Council in relation to REACH for substances in tattoo inks and permanent makeup in Regulation (EU) No. 2020/2081 [10].

Substances	Concentration Limit <sup>a</sup>
Classified as carcinogen or germ cell mutagen (group 1A, 1B or 2)	0.5 mg/kg
Classified as toxic to reproduction	10 mg/kg
Classified as skin sensitizers	10 mg/kg
Classified as skin corrosive or irritant or serious eye damaging/eye irritant	100 mg/kg
Prohibited for use in cosmetic products in Annex II of Regulation (EC) No. 1223/2009 [63] <sup>b</sup>	0.5 mg/kg
Prohibited for use in cosmetic products in Annex IV of Regulation (EC) 1223/2009, subject to any of the following conditions: rinse-off products, not to be used in products applied on mucous membranes, not to be used in eye products <sup>b</sup>	0.5 mg/kg
Listed in Appendix 13 of Regulation (EU) No. 2020/2081 [10]	Specific concentration limits
Mercury <sup>c</sup>	0.5 mg/kg
Nickel <sup>c</sup>	5.0 mg/kg
Cadmium <sup>c</sup>	0.5 mg/kg
Chromium <sup>c</sup>	0.5 mg/kg
Cobalt <sup>c</sup>	0.5 mg/kg
Lead <sup>c</sup>	0.7 mg/kg
Benzo[a]pyrene <sup>c</sup>	0.005 mg/kg
PAH (classified as carcinogen or germ cell mutagen (category 1A, 1B or 2)) <sup>c</sup>	0.5 mg/kg

<sup>a</sup> Concentration limits converted from % (*w/w*) to mg/kg. <sup>b</sup> REACH Regulation (EU) No. 2020/2081 [10] cross-references Cosmetics Regulation (EC) No. 1223/2009 [63] because the EU Commission considers that if a substance is restricted for use on the skin, it must also be restricted for use in products that penetrate the skin [64]. <sup>c</sup> The substances and concentration limits shown are taken from Annex 13 of REACH Regulation (EU) No. 2020/2081 [10].

Most of the PAAs detected are listed in Annex II of Regulation (EC) No. 1223/2009 [63] as prohibited substances for use in cosmetic products, as the ingredients of tattoo inks, in particular pigments, may either degrade to or contain residual PAAs that are classified as carcinogenic or mutagenic [10]. These substances, which are restricted for use in cosmetic products that are applied to the skin, are also restricted for products that penetrate the skin, such as tattoos and permanent makeup [64]. A cross-reference has been introduced between REACH Regulation (EU) No. 2020/2081 and Cosmetics Regulation (EC) No. 1223/2009, which allows lists of substances banned in Regulation (EC) No. 1223/2009 to be collectively restricted in Regulation (EU) No. 2020/2081 for tattoo inks [64]. This means that most of these substances could only be present in concentrations below 0.5 mg/kg to be acceptable in tattoo inks under REACH Regulation (EU) No. 2020/2081. An exception is made for substances that are listed in Annex 13 of REACH Regulation (EU) No. 2020/2081. The concentration limit of Annex 13 of REACH Regulation (EU) No. 2020/2081 applies to all compounds in tattoo inks listed in Annex 13, regardless of other regulations. However,

almost all of them have concentrations higher than 0.5 mg/kg and 5 mg/kg, which are the most used concentration limits in REACH Regulation (EU) No. 2020/2081. This means that most of them violate this regulation if they are present in tattoo inks. Almost every measurement showed at least one PAA contaminant. This could be because most of the pigments in the color spectrum are azo pigments, so it is expected that at least some of the contaminants in these colors will be aromatic amines or PAAs, as this chemical structure is part of the basic structure of azo pigments.

PAAs can be found in almost all tattoo inks, but the concentration and the specific PAAs vary between the different colors of the tattoo inks (see Table 1). The carcinogenicity of PAAs for oral and dermal exposure has been established for decades [65]. The carcinogenicity of PAA via intradermal exposure has not been studied as extensively as other exposure routes [66]. However, there is some evidence that PAAs are also carcinogenic when inserted under the skin [67], which would be the exposure route of PAAs through tattoos.

Inorganic contaminants such as cobalt, cadmium, chromium, mercury, nickel and lead have specific concentration limits for their occurrence in tattoo inks (see Table 3). Only the concentrations of mercury are within these limits, as all measured samples have a mercury content below 0.5 mg/kg. This is an acceptable level of contamination in tattoo inks under REACH Regulation (EU) No. 2020/2081. Cadmium, cobalt, chromium, nickel and lead do not always meet the concentration limits set by REACH Regulation (EU) No. 2020/2081. In particular, the highest measured concentrations of lead, nickel and chromium are well above the set criteria. This means that tattoo inks containing these levels of inorganic contaminants could not be sold in the European Union after the implementation of REACH Regulation (EU) 2020/2081 on 4 January 2022.

Nickel has a concentration limit of 5.0 mg/kg set by Annex 13 of REACH Regulation (EU) 2020/2081. The measured concentrations of nickel in different tattoo inks range from 0.038–11.70 mg/kg, with three of the measured inks having a nickel concentration above 5 mg/kg. This means that almost all of the measured inks are below the concentration limit and therefore REACH-compliant. For a 400 cm<sup>2</sup> tattoo with a nickel content of 11.70 mg/kg, the nickel content for the whole tattoo would be 47 µg or 0.12 µg/cm<sup>2</sup>. In a study comparing two types of patch tests on people with a nickel allergy, people began to react to nickel at a concentration of 0.5 µg/cm<sup>2</sup> [68]. This concentration is four times higher than the scenario of the maximum measured nickel content in tattoo inks. Since publications on intradermal testing for nickel allergy are quite rare, patch testing could be an indication of how much nickel should be tolerated in tattoo inks [49]. Another consideration for the concentration limit should be the type of nickel in the tattoo. Most nickel in tattoos is an impurity from iron oxide pigments and is not soluble [49,69]. Therefore, it is not known whether allergic reactions are caused only by soluble nickel or also by insoluble nickel [69]. Tattoo inks with a nickel concentration above the established concentration limit of 5.0 mg/kg in tattoo inks may not cause allergic reactions to nickel. However, to protect people with nickel allergies, the concentration limit should be strictly adhered to.

Adverse effects associated with chromium include contact dermatitis and skin irritation [70]. In particular, chromium(VI) is recognized as one of the most common sensitizers in humans, causing most of the observed adverse effects associated with chromium [70,71]. Studies have shown that there may be an elicitation threshold for chromium(VI), which would be the lowest concentration that elicits a positive response. This threshold would be 2 ppm or 0.02 µg/cm<sup>2</sup> [72,73]. With a maximum concentration of 4.1 mg/kg in tattoo ink (0.04 µg/cm<sup>2</sup> in a 400 cm<sup>2</sup> tattoo), this product could cause an allergic reaction. With a concentration limit of 0.5 mg/kg, the concentration in a 400 cm<sup>2</sup> tattoo would be 0.005 µg/cm<sup>2</sup>, which would be below the triggering threshold. Considering that this threshold was measured with a patch test and not intradermally, the concentration limit set by REACH Regulation (EU) No. 2020/2081 should be followed.

Cobalt is known to cause allergic reactions such as contact dermatitis [74]. There have been limited studies investigating the elicitation threshold of cobalt, such as the study of Fischer et al. [75]. One study determined the elicitation threshold of cobalt

using patch testing [75]. This study found the elicitation threshold to be 30.8–259 ppm or 0.07–2.0  $\mu\text{g}/\text{cm}^2$  [75]. The highest measured concentration of cobalt in tattoo inks was 6.4 mg/kg, so the concentration of a 400  $\text{cm}^2$  tattoo would be approximately 0.07  $\mu\text{g}/\text{cm}^2$ . This concentration reaches the determined lower elicitation threshold determined by Fischer et al. [75]. However, taking into account the different exposure between patch testing (dermal) and tattooing (intradermal), the concentration limit of 0.5 mg/kg in tattoo inks set by REACH Regulation (EU) No. 2020/2081 should be respected.

Cadmium has been shown to be carcinogenic when injected subcutaneously into rats at a concentration of 30  $\mu\text{mol}/\text{kg}$  [76,77] and is also classified as a Group 1 carcinogen by the IARC [78]. Therefore, the concentration of cadmium in tattoo inks should be as low as possible to minimize the risk of cadmium carcinogenicity.

The main adverse effects of lead are reproductive and neurotoxic effects [79]. Therefore, the concentration of lead should be as low as possible and comply with the concentration limit set by REACH.

REACH Regulation (EU) 2020/2081 does not specify a concentration limit for manganese, strontium and vanadium.

## 5. Conclusions

From this literature review, it is clear that contaminants in tattoo inks have not been adequately evaluated by tattoo ink manufacturers, because tattoo inks tend to contain large amounts and a large number of different types of contaminants. However, most of the findings are repetitive, because most of the quantitative measurements are repetitions or refinements of the same analyses using the same standard substances. This could be due to the focus on substances that are considered to be of concern for human health or suspected to be the cause of most adverse effects after tattooing. Another explanation could be that other qualitative substances found were not considered to be of as much concern to human health as these other substances. It could also be possible that other contaminants require a more specific and advanced chromatographic analysis to be detected.

Due to REACH Regulation 2020/2081, many tattoo inks could no longer be sold in the EU [11], some because of high levels of contaminants or other chemicals and others because of banned pigments. This meant that the market needed new REACH-compliant tattoo inks. It also meant that there was a need for new tattoo ink formulations and new pigments to replace the old ones. To date, there are many new tattoo inks, black, white and colored, that claim to be REACH-compliant [80,81].

The limitations of this literature review are that only retrospective data prior to the implementation of REACH Regulation 2020/2081 were considered and that only publicly available data were used. In the future, the specific contaminants and their concentration ranges for each tattoo ink color are likely to change due to new ingredients and new pigments of tattoo inks. But because of these changes, it is necessary to look beyond these known contaminants to better analyze the hazards of tattoo inks. Thus, this review can be used as a benchmark for comparison with future data to see what has changed in terms of contaminants in tattoo inks.

**Supplementary Materials:** The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/cosmetics10050141/s1>, Table S1: Overview of contaminants found in tattoo ink sorted by tattoo ink color with percentages of occurrence in tattoo inks; Table S2: Contaminants in tattoo inks with possible adverse effects; Table S3: Contaminants in tattoo inks with quantification method and limit of detection and limit of quantification if known; Table S4: Overview of inorganic contaminants in tattoo inks sorted by color.

**Author Contributions:** Conceptualization, D.W.L. and B.G.; methodology, P.F.; software, P.F.; validation, D.W.L. and B.G.; formal analysis, P.F.; investigation, P.F.; resources, P.F.; data curation, P.F.; writing—original draft preparation, P.F.; writing—review and editing, D.W.L., P.H., B.G. and S.G.W.; visualization, P.F.; supervision, S.G.W.; project administration, S.G.W.; funding acquisition, S.G.W. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** The data presented in this study are available in the Supplementary Materials.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Pesapane, F.; Nazzaro, G.; Gianotti, R.; Coggi, A. A Short History of Tattoo. *JAMA Dermatol.* **2014**, *150*, 145. [CrossRef] [PubMed]
2. Nier, H. Jeder Vierte Deutsche ist Tätowiert. Available online: <https://de.statista.com/infografik/10024/umfrage-taetowierungen-in-deutschland/> (accessed on 28 June 2023).
3. Borkenhagen, A.; Mirastschijski, U.; Petrowski, K.; Brähler, E. Tattoos in der deutschen Bevölkerung: Prävalenzen, Soziodemographie und Gesundheitsorientierung. *Bundesgesundheitsblatt* **2019**, *62*, 1077–1082. [CrossRef] [PubMed]
4. Council of Europe. Resolution ResAP(2003)2 on Tattoos and Permanent Make-Up: ResAP(2003)2. Available online: [https://search.coe.int/cm/Pages/result\\_details.aspx?ObjectId=09000016805df8e5](https://search.coe.int/cm/Pages/result_details.aspx?ObjectId=09000016805df8e5) (accessed on 7 June 2023).
5. Council of Europe. Resolution ResAP(2008)1 on Requirements and Criteria for the Safety of Tattoos and Permanent Make-Up: ResAP(2008)1. Available online: [https://search.coe.int/cm/Pages/result\\_details.aspx?ObjectId=09000016805d3dc4#globalcontainer](https://search.coe.int/cm/Pages/result_details.aspx?ObjectId=09000016805d3dc4#globalcontainer) (accessed on 7 June 2023).
6. Piccinini, P.; Pakalin, S.; Contor, L.; Bianchi, I. Safety of Tattoos and Permanent Make-Up: Adverse Health Effects and Experience with the Council of Europe Resolution (2008)1. Report on Work Package 3, Administrative Arrangement N. 2014-33617, Analysis Conducted on Behalf of DG JUST. 2016. Available online: <https://publications.jrc.ec.europa.eu/repository/handle/JRC99882> (accessed on 7 June 2023).
7. Michel, R. Manufacturing of Tattoo Ink Products Today and in Future: Europe. *Curr. Probl. Dermatol.* **2015**, *48*, 103–111. [CrossRef]
8. Piccinini, P.; Bianchi, I.; Pakalin, S.; Senaldi, C. Safety of Tattoos and Permanent Make-Up Compilation of Information on Legislative Framework and Analytical Methods: Report on Work Package 1 Administrative Arrangement N. 2014-33617 Analysis conducted on Behalf of DG JUST. JRC Reports, Luxembourg, 2015. Available online: <https://op.europa.eu/en/publication-detail/-/publication/b09316c7-7950-4f21-8a7b-f918e0113295> (accessed on 4 July 2023).
9. European Commission. Daily News 04/01/2022: Chemicals: New EU Rules for Safer Ink Tattoos Across the EU. Available online: [https://ec.europa.eu/commission/presscorner/detail/en/mex\\_22\\_41](https://ec.europa.eu/commission/presscorner/detail/en/mex_22_41) (accessed on 7 June 2023).
10. European Council. Commission Regulation (EU) 2020/2081 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards substances in tattoo inks or permanent make-up. *Off. J. Eur. Union* **2020**, *63*, 6–17.
11. Alcorn, T. Tattoo Artists Face a Grayer Palette in Europe. Available online: <https://www.nytimes.com/2022/06/19/health/tattoo-ink-europe.html> (accessed on 29 June 2023).
12. Serup, J.; Hutton Carlsen, K.; Sepehri, M. Tattoo complaints and complications: Diagnosis and clinical spectrum. *Curr. Probl. Dermatol.* **2015**, *48*, 48–60. [CrossRef]
13. Rogowska, P.; Sobjanes, M.; Sławińska, M.; Nowicki, R.J. Tattoo Dermatological Complications: Analysis of 53 Cases from Northern Poland. *Dermatology* **2022**, *238*, 799–806. [CrossRef]
14. Dybboe Bjerre, R.; Heede Ulrich, N.; Linneberg, A.; Johansen, J.D. Adverse reactions to tattoos in the general population of Denmark. *J. Am. Acad. Dermatol.* **2018**, *79*, 770–772. [CrossRef]
15. Neale, P.A.; Stalter, D.; Tang, J.Y.M.; Escher, B.I. Bioanalytical evidence that chemicals in tattoo ink can induce adaptive stress responses. *J. Hazard. Mater.* **2015**, *296*, 192–200. [CrossRef]
16. Regensburger, J.; Lehner, K.; Maisch, T.; Vasold, R.; Santarelli, F.; Engel, E.; Gollmer, A.; König, B.; Landthaler, M.; Bäumlner, W. Tattoo inks contain polycyclic aromatic hydrocarbons that additionally generate deleterious singlet oxygen. *Exp. Dermatol.* **2010**, *19*, e275–e281. [CrossRef]
17. Lehner, K.; Santarelli, F.; Vasold, R.; König, B.; Landthaler, M.; Bäumlner, W. Black tattoo inks are a source of problematic substance such as dibutyl phthalate. *Contact Dermat.* **2011**, *65*, 231–238. [CrossRef]
18. Høgsberg, T.; Jacobsen, N.R.; Clausen, P.A.; Serup, J. Black tattoo inks induce reactive oxygen species production correlating with aggregation of pigment nanoparticles and product brand but not with the polycyclic aromatic hydrocarbon content. *Exp. Dermatol.* **2013**, *22*, 464–469. [CrossRef] [PubMed]
19. Hauri, U. Inks for Tattoos and Permanent Make-Up: Preservatives, Colourants, Primary Aromatic Amines, poly-Aromatic Hydrocarbons and Nitrosamines. 2020. Available online: <https://www.kantonlabor.bs.ch/dam/jr:d71126f3-85c9-42fb-a16d-8d21f7fc5ee8/2020-TattooTinten.Englisch.pdf> (accessed on 10 May 2023).
20. Hauri, U. Pigments, Preservatives and Impurities in Tattoo Inks. Available online: <https://mobil.bfr.bund.de/cm/343/pigments-preservatives-and-impurities-in-tattoo-inks.pdf> (accessed on 13 June 2023).

21. Jacobsen, E.; Tønning, K.; Pedersen, E.; Bernth, N.; Serup, J.; Høgsberg, T.; Nielsen, E. Chemical Substances in Tattoo Ink: Survey of Chemical Substances in Consumer Products. 2012. Available online: <https://www2.mst.dk/udgiv/publications/2012/03/978-87-92779-87-8.pdf> (accessed on 29 June 2023).
22. Hauri, U.; Hohl, C. Photostability and Breakdown Products of Pigments Currently Used in Tattoo Inks. *Curr. Probl. Dermatol.* **2015**, *48*, 164–169. [[CrossRef](#)] [[PubMed](#)]
23. Cui, Y.; Spann, A.P.; Couch, L.H.; Gopee, N.V.; Evans, F.E.; Churchwell, M.I.; Williams, L.D.; Doerge, D.R.; Howard, P.C. Photodecomposition of Pigment Yellow 74, a Pigment Used in Tattoo Inks. *Photochem. Photobiol.* **2004**, *80*, 175–184. [[CrossRef](#)]
24. Engel, E.; Spannberger, A.; Vasold, R.; König, B.; Landthaler, M.; Bäuml, W. Photochemical cleavage of a tattoo pigment by UVB radiation or natural sunlight. *J. Ger. Soc. Dermatol.* **2007**, *5*, 583–589. [[CrossRef](#)] [[PubMed](#)]
25. Engel, E.; Vasold, R.; Bäuml, W. Tätowierungspigmente im Fokus der Forschung. *Nachr. Chem.* **2007**, *55*, 847–851. [[CrossRef](#)]
26. Bauer, E.M.; Cecchetti, D.; Guerriero, E.; Quaranta, S.; Ripanti, F.; Postorino, P.; Tagliatesta, P.; Carbone, M. For Asia Market Only: A Green Tattoo Ink between Safety and Regulations. *Molecules* **2022**, *27*, 3491. [[CrossRef](#)]
27. IARC. Some Non-heterocyclic Polycyclic Aromatic Hydrocarbons and Some Related Exposures; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans No. 92, Lyon. 2010. Available online: <https://monographs.iarc.who.int/wp-content/uploads/2018/06/mono92.pdf> (accessed on 29 June 2023).
28. Bocca, B.; Senofonte, O.; Petrucci, F. Hexavalent chromium in tattoo inks: Dermal exposure and systemic risk. *Contact Dermat.* **2018**, *79*, 218–225. [[CrossRef](#)]
29. Agnello, M.; Fontana, M. Survey of European Studies of the Chemical Characterisation of Tattoo Ink Products and the measurement of Potentially Harmful Ingredients. *Curr. Probl. Dermatol.* **2015**, *48*, 142–151. [[CrossRef](#)]
30. Forte, G.; Petrucci, F.; Cristaudo, A.; Bocca, B. Market survey on toxic metals contained in tattoo ink. *Sci. Total Environ.* **2009**, *407*, 5997–6002. [[CrossRef](#)]
31. Christaudo, A.; Forte, G.; Bocca, B.; Petrucci, F.; Muscardin, L.; Trento, E.; Di Carlo, A. Permanent tattoos: Evidence of pseudolymphoma in tree patients and metal composition of the dyes. *Eur. J. Dermatol.* **2012**, *22*, 776–780. [[CrossRef](#)]
32. Serup, J.; Hutton Carlsen, K.; Dommershausen, N.; Sepehri, M.; Hesse, B.; Seim, C.; Luch, A.; Schreiber, I. Identification of pigments related to allergic tattoo reactions in 104 human skin biopsies. *Contact Dermat.* **2020**, *82*, 73–82. [[CrossRef](#)] [[PubMed](#)]
33. Manso, M.; Pessanha, S.; Guerra, M.; Reinholz, U.; Afonso, C.; Radtke, M.; Lurenço, H.; Carvalho, M.L.; Buzanich, A.G. Assessment of Toxic Metals and Hazardous Substances in Tattoo Inks Using Sy-XRF, AAS and Raman Spectroscopy. *Biol. Trace Elem. Res.* **2019**, *187*, 596–601. [[CrossRef](#)] [[PubMed](#)]
34. Goldstein, N. Mercury-Cadmium Sensitivity in Tattoos: A Photoallergic Reaction in Red Pigment. *Ann. Intern. Med.* **1967**, *67*, 984–989. [[CrossRef](#)] [[PubMed](#)]
35. Yazdian-Tehrani, H.; Shibu, M.M.; Carver, N.C. Reaction in a red tattoo in the absence of mercury. *Br. J. Plast. Surg.* **2001**, *54*, 555–556. [[CrossRef](#)]
36. McGrouther, D.A.; Downie, P.A.; Thompson, W.D. Reactions to red tattoos. *Br. J. Plast. Surg.* **1977**, *30*, 84–85. [[CrossRef](#)]
37. Negi, S.; Bala, L.; Shukla, S.; Chopra, D. Tattoo inks are toxicological risks to human health: A systematic review of their ingredients, fate inside skin, toxicity due to polycyclic aromatic hydrocarbons, primary aromatic amines, metals, and overview of regulatory frameworks. *Toxicol. Ind. Health* **2022**, *38*, 417–434. [[CrossRef](#)]
38. Nguyen, L.Q.; Allen, H.B. Reactions to manganese and cadmium in tattoos. *Cutis* **1979**, *23*, 71–72.
39. Lim, D.S.; Roh, T.H.; Kim, M.K.; Kwon, Y.C.; Choi, S.M.; Kwack, S.J.; Kim, K.B.; Yoon, S.; Kim, H.S.; Lee, B.-M. Non-cancer, cancer and dermal sensitization risk assessment of heavy metals in cosmetics. *J. Toxicol. Environ. Health* **2018**, *81*, 432–452. [[CrossRef](#)]
40. Yoong, C.; Vun, Y.Y.; Spelman, L.; Muir, J. True blue football fan: Tattoo reaction confined to blue pigment. *Australas. J. Dermatol.* **2010**, *51*, 22–51. [[CrossRef](#)]
41. Tamarro, A.; Magri, F.; Chello, C.; Sernicola, A.; Luzi, F.; de Marco, G.; Raffa, S. A peculiar adverse reaction to blue pigment tattoo. *J. Cosmet. Dermatol.* **2020**, *19*, 2401–2403. [[CrossRef](#)]
42. Forte, G.; Petrucci, F.; Bocca, B. Metal Allergens of Growing Significance: Epidemiology, Immunotoxicology, Strategies for Testing and Prevention. *Recent Pat. Inflamm. Allergy Drug Discov.* **2008**, *7*, 154–162. [[CrossRef](#)] [[PubMed](#)]
43. Bregnbak, D.; Johansen, J.D.; Jellesen, M.S.; Zachariae, C.; Menné, T.; Thyssen, J.P. Chromium allergy and dermatitis: Prevalence and main findings. *Contact Dermat.* **2015**, *73*, 261–280. [[CrossRef](#)] [[PubMed](#)]
44. Tazelaar, D.J. Hypersensitivity to Chromium in a Light-blue Tattoo. *Dermatologica* **1970**, *141*, 282–287. [[CrossRef](#)]
45. Franchini, I.; Mutti, A. Selected toxicological aspects of chromium(VI) compounds. *Sci. Total Environ.* **1988**, *71*, 379–387. [[CrossRef](#)]
46. Taaffe, A.; Knight, A.G.; Marks, R. Lichenoid tattoo hypersensitivity. *BMJ* **1978**, *1*, 616–618. [[CrossRef](#)] [[PubMed](#)]
47. Prantsidis, A.; Raikos, N.; Pantelakis, I.; Spagou, K.; Tsoukali, E. Unusual mercury poisoning from tattoo dye. *Hippokratia* **2017**, *21*, 197–200.
48. Jungmann, S.; Laux, P.; Bauer, T.T.; Jungnickel, H.; Schönfeld, N.; Luch, A. From the Tattoo Studio to the Emergency Room. *Dtsch. Ärzteblatt Int.* **2016**, *113*, 672–675. [[CrossRef](#)]
49. Kluger, N. Nickel and tattoos: Where are we? *Contact Dermat.* **2021**, *85*, 136–140. [[CrossRef](#)] [[PubMed](#)]
50. Ahlström, M.G.; Thyssen, J.P.; Wennervaldt, M.; Menné, T.; Johansen, J.D. Nickel allergy and allergic contact dermatitis: A clinical review of immunology, epidemiology, exposure and treatment. *Contact Dermat.* **2019**, *81*, 227–241. [[CrossRef](#)] [[PubMed](#)]
51. US EPA. AP-42: Compilation of Air Emissions Factors: Carbon Black. Available online: <https://www3.epa.gov/ttnchie1/ap42/ch06/final/c06s01.pdf> (accessed on 29 June 2023).

52. ICBA. How is Carbon Black Produced?: Carbon Black Is Produced Using Two Carbon Black Manufacturing Processes (Furnace Black and Thermal Black). Available online: <https://www.carbon-black.org/is-carbon-black-safe> (accessed on 29 June 2023).
53. ECHA. Annex XV Investigation Report: Investigation of the Available Analytical Methods to Measure Content and Migration of Polycyclic Aromatic Hydrocarbons, Limit Values in Rubber and Plastic Articles in Paragraphs 5 and 6 of Entry 50 of Annex XVII to REACH, and Alternative Low-PAH Raw Materials. Available online: [https://echa.europa.eu/documents/10162/13641/rest\\_pah\\_investigation\\_en.pdf/53877b6e-239b-fcb8-6560-e86f5b27349b](https://echa.europa.eu/documents/10162/13641/rest_pah_investigation_en.pdf/53877b6e-239b-fcb8-6560-e86f5b27349b) (accessed on 30 June 2023).
54. Barrero-Moreno, J.; Senaldi, C.; Bianchi, I.; Geiss, O.; Tirendi, S.; Folgado de Lucena, A.; Barahona, F.; Mainardi, G.; Leva, P.; Aguilar-Fernandez, P. Migration of Polycyclic Aromatic Hydrocarbons (PAHs) from Plastic and Rubber Articles: Final Report on the Development of a Migration Measurement Method; JRC Technical Reports. 2018. Available online: <https://publications.jrc.ec.europa.eu/repository/bitstream/JRC111476/kjna29282enn.pdf> (accessed on 30 June 2023).
55. Gerde, P.; Muggenburg, B.A.; Lundborg, M.; Dahl, A.R. The rapid alveolar adsorption of diesel soot-adsorbed benzo[a]pyrene: Bioavailability, metabolism and dosimetry of an inhaled particle-borne carcinogen. *Carcinogenesis* **2001**, *22*, 741–749. [CrossRef]
56. Lehner, K.; Santarelli, F.; Penning, R.; Vasold, R.; Engel, E.; Maisch, T.; Gastl, K.; König, B.; Landthaler, M.; Bäuml, W. The decrease of pigment concentration in red tattooed skin years after tattooing. *J. Eur. Acad. Dermatol. Venereol.* **2011**, *25*, 1340–1345. [CrossRef] [PubMed]
57. Karger, S. Wie Groß ist Das Tattoo, Dass Sie sich Als Letztes Haben Stechen Lassen? Available online: <https://de.statista.com/statistik/daten/studie/160688/umfrage/taetowierte-groesse-letztes-tattoo/> (accessed on 9 July 2023).
58. Engel, E.; Santarelli, F.; Vasold, R.; Maisch, T.; Ulrich, H.; Prantl, L.; König, B.; Landthaler, M.; Bäuml, W. Modern tattoos cause high concentrations of hazardous pigments in skin. *Contact Dermat.* **2008**, *58*, 228–233. [CrossRef] [PubMed]
59. European Food Safety Authority. Scientific Opinion of the Panel on Contaminants in the Food Chain on a request from the European Commission on Polycyclic Aromatic Hydrocarbons in Food. *EFSA J.* **2008**, *724*, 1–114. [CrossRef]
60. Kluger, N.; Koljonen, V. Tattoos, inks, and cancer. *Lancet* **2012**, *13*, 161–168. [CrossRef] [PubMed]
61. Lerche, C.M.; Sepehri, M.; Serup, J.; Poulsen, T.; Wulf, H.C. Black tattoos protect against UVR-induced skin cancer in mice. *Photodermatol. Photoimmunol. Photomed.* **2015**, *31*, 261–268. [CrossRef] [PubMed]
62. Jameson, C.W. Polycyclic aromatic hydrocarbons and associated occupational exposures. In *Tumor Site Concordance and Mechanisms of Carcinogenesis*; Baan, R.A., Stewart, B.W., Straif, K., Eds.; IARC Scientific Publication: Lyon, France, 2019; pp. 59–63. ISBN 978-92-832-2217-0.
63. European Commission. Regulation (EC) No 1223/2009 of the European Parliament and of the Council. *Off. J. Eur. Union* **2009**, *52*, 59–209.
64. HSE. Agency Opinion on a Proposal for a Restriction: Substances in Tattoo Ink and Permanent Make-Up. Draft for Consultation. 2023. Available online: [https://consultations.hse.gov.uk/crd-reach/reach-restriction-tattoo-ink-pmu-substances/supporting\\_documents/Restriction%20opinion%20tattoo%20inks%20%20draft%20SEA.pdf](https://consultations.hse.gov.uk/crd-reach/reach-restriction-tattoo-ink-pmu-substances/supporting_documents/Restriction%20opinion%20tattoo%20inks%20%20draft%20SEA.pdf) (accessed on 4 July 2023).
65. Radomski, J.L. The primary aromatic amines: Their biological properties and structure-activity relationships. *Annu. Rev. Pharmacol. Toxicol.* **1979**, *19*, 129–157. [CrossRef]
66. Foerster, M.; Schreiver, I.; Luch, A.; Schütz, J. Tattoo inks and cancer. *Cancer Epidemiol.* **2020**, *65*, 101655. [CrossRef]
67. Hecht, S.S.; El-Bayoumy, K.; Rivenson, A.; Fiala, E. Comparative carcinogenicity of o-toluidine hydrochloride and o-nitrosotoluene in F-344 rats. *Cancer Lett.* **1982**, *16*, 103–108. [CrossRef]
68. Fischer, L.A.; Johansen, J.D.; Menné, T. Nickel allergy: Relationship between patch test and repeated open application test thresholds. *Br. J. Dermatol.* **2007**, *157*, 723–729. [CrossRef]
69. Prior, G. Tattoo Inks: Legislation, Pigments, Metals and Chemical Analysis. *Curr. Probl. Dermatol.* **2015**, *48*, 152–157. [CrossRef]
70. Jumina, J.; Harizal, H. Dermatologic Toxicities and Biological Activities of Chromium. In *Trace Metals in the Environment: New Approaches and Recent Advances*; Murillo-Tovar, M.A., Saeid, A., Saldarriaga Noreña, H.A., Eds.; Intech Open: London, UK, 2021; ISBN 978-1-83880-332-2.
71. Shelnutt, S.R.; Goad, P.; Belsito, D.V. Dermatological Toxicity of Hexavalent Chromium. *Crit. Rev. Toxicol.* **2007**, *37*, 375–387. [CrossRef] [PubMed]
72. Basketter, D.A.; Angelini, G.; Ingber, A.; Kern, P.S.; Menné, T. Nickel, chromium and cobalt in consumer products: Revisiting safe levels in the new millennium. *Contact Dermat.* **2003**, *49*, 1–7. [CrossRef] [PubMed]
73. Nethercott, J.; Paustenbach, D.; Adams, R.; Fowler, J.; Marks, J.; Morton, C.; Taylor, J.; Horowitz, S.; Finley, B. A study of chromium induced allergic contact dermatitis with 54 volunteers: Implications for environmental risk assessment. *Occup. Environ. Med.* **1994**, *51*, 371–380. [CrossRef] [PubMed]
74. Faroon, O.; Keith, S. Toxicological Profile for Cobalt. 2004. Available online: [https://stacks.cdc.gov/view/cdc/6548/cdc\\_6548\\_DS1.pdf](https://stacks.cdc.gov/view/cdc/6548/cdc_6548_DS1.pdf) (accessed on 10 July 2023).
75. Fischer, L.A.; Johansen, J.D.; Voelund, A.; Lidén, C.; Julander, A.; Midander, K.; Menné, T.; Thyssen, J.P. Elicitation threshold of cobalt chloride: Analysis of patch test dose-response studies. *Contact Dermat.* **2016**, *74*, 105–109. [CrossRef] [PubMed]
76. Lansdown, A.B.G. Physiological and Toxicological Changes in the Skin Resulting from the Action and Interaction of Metal Ions. *Crit. Rev. Toxicol.* **1995**, *25*, 397–462. [CrossRef] [PubMed]
77. Waalkes, M.P.; Rehm, S.; Sass, B.; Konishi, N.; Ward, J.M. Chronic Carcinogenic and Toxic Effects of a Single Subcutaneous Dose of Cadmium in the Male Fischer Rat. *Environ. Res.* **1991**, *55*, 40–50. [CrossRef] [PubMed]

78. IARC. Arsenic, Metals, Fibres, and Dusts; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 100C, Lyon. 2012. Available online: <https://publications.iarc.fr/120> (accessed on 10 July 2023).
79. Rusmadi, S.Z.; Syed Ismail, S.N.; Praveena, S.M. A case study of selected heavy metals (lead, cadmium, and nickel) in skin-lightening creams and dermal health risk in Malaysia. *Ann. Trop. Med. Public Health* **2017**, *10*, 95–100. [CrossRef]
80. Dynamic Color. Reach Compliant Ink. Available online: <https://dynamiccolor.com/en-de/collections/reach-compliant-ink> (accessed on 30 June 2023).
81. Starr Tattoo & Piercing Supplies. EU REACH Compliant Inks. Available online: <https://startattoo.com/tattoo-ink/eu-reach-compliant-inks.html> (accessed on 30 June 2023).

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.