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JRC SCIENCE FOR POLICY REPORT

# Safety of tattoos and permanent make-up
# Final report

*Administrative Arrangement N. 2014-33617*
*Analysis conducted on behalf of DG JUST*

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**Abstract**
**Safety of tattoos and permanent make-up (PMU)**

- 12% of Europeans have tattoos
- Tattoo/PMU ink contains chemicals which stay in the body for life
- Adverse health effects like infections and allergies are increasingly reported
- Little is known about the long-term effects of these chemicals

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## Acknowledgements

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## Executive summary

**Quick guide** Nowadays, tattoos are considered body art and are largely spread. They are applied by injecting coloured inks into the dermis and are meant to stay life long, thus resulting in long term exposure to the chemicals injected including their degradation products. Permanent Make-up (PMU) consists in (semi)permanent tattoos used to resemble make-up.

**Policy context** This report addresses the issue of the safety of tattoo/PMU products and practices with a view to contribute to consumers' health protection. It has been prepared on behalf of the Directorate General Justice and Consumers (DG JUST), however it might also be of interest to other stakeholders dealing with health, internal market and environment, as well as to the European Chemicals Agency (ECHA). The conclusions of this project aim to provide the European Commission (EC) with the scientific evidences needed to decide if European Union (EU) measures are necessary to ensure the safety of tattoo/PMU inks and processes. In fact, apart from the general safety requirements by the General Product Safety Directive (GPSD) currently there is no specific EU legislation on tattoos/PMU products. In particular with regards to chemical requirements, there are chemicals which are banned in consumer products that get into direct contact with the skin under different EU legislations, like the Cosmetic Product Regulation or REACH, but not in tattoo inks.

The report presents an updated review of the national legislative framework, ink ingredients in use and reported adverse health effects, as well as new data on analytical methods, statistics, market surveillance and RAPEX (Rapid alert system for non-food dangerous products) notifications, risk perception and communication and experience with the implementation of the Council of Europe (CoE) Resolutions (ResAP).

**Main findings** Specific legislation, based on the CoE ResAPs (either of 2003 or 2008), exists in 7 Member States (MS) and 3 EFTA (European Free Trade Association) countries. 3 MS notified their draft legal acts (currently on-hold).

Statistics show that 12% of Europeans and up to 24% of United States' citizens are estimated to be tattooed, including teenagers. Tattoo prevalence in young adults may represent more than the double and is sometimes higher in women than in men, in particular in young generations.

Tattoo/PMU inks contain several ingredients, plus impurities. More than 100 colorants and 100 additives are in use. Most tattoo inks on the EU market are imported from the US, while PMU inks are generally manufactured in Europe. The pigments used are not specifically produced for tattoo/PMU applications and generally show low purity. The majority of them is not authorised for the use in cosmetic products and several should not be present according to the CoE ResAP(2008)1. Over 80% of the colorants in use are organic and more than 60% of them are azo-pigments, some of which can release carcinogenic aromatic amines. This degradation may happen in the skin, particularly under solar/Ultra Violet radiation exposure or laser irradiation.

Harmonised analytical methods for the analysis of tattoo/PMU inks are missing and need to be developed. For market surveillance purposes test methods developed for other products are used with some modifications.

Tattoo/PMU products containing hazardous chemicals have been found on the European market. Polycyclic Aromatic Hydrocarbons (PAH) (43%), Primary Aromatic Amines (PAA) (14%), heavy metals (9%) and preservatives (6%), as well as microbiological contamination (11%) were detected in the indicated percentages of the analysed samples.

In the absence of systematic data gathering, the actual prevalence of tattoo complications (mainly of dermatological nature) is currently unknown. Most complaints are transient and inherent to the wound healing process, but in some cases, up to 5% of the tattooed persons, bacterial infections may occur, especially in unhygienic settings.

Acute allergy and delayed hypersensitivity prompted by i.e. the inks ingredients and tattoo/removal trauma represent the bulk of tattoo/PMU complications, affecting mostly the red or black parts of the tattoos. Such nonspecific reactions, frequently exacerbated by sun exposure, are unpredictable and may sometimes appear after a long latency (decades), giving rise to chronic sequels in connection with underlying auto-immune pathologies. Additional adverse health effects, like skin pigmentation disorders may be encountered in 5-15% of patients having laser therapy, which is not always effective in removing completely the undesired tattoos. (Skin) cancer risk from tattoo procedures has been neither proved nor excluded.

Based on the experience gained from implementing national laws and the CoE ResAPs, experts agreed that an update of the chemical and labelling requirements would be desirable.

Risk perception is mainly based on the information given by tattooists, parents or friends, or read in mass media and internet. Among students, awareness about infectious risks seems to be higher that on non-infectious ones, but that knowledge is often only superficial.

Many data gaps and research needs were identified.

**Key conclusions** This report provides an up-to-date snapshot of the tattoo/PMU phenomenon. Due to the wide variety of legislative frameworks across Member States, some products can be sold in some MSs but not in others, because of different chemical or authorisation requirements, thus resulting in a fragmentation of the internal market. This might also have an impact on the protection of consumers' health.

Tattooing is an increasing fashion phenomenon which already involves over 60 million Europeans. In parallel, removal procedures are becoming more frequent. Adverse health effects linked to the application and removal of tattoos are reported in the literature; in addition the potential long term effects of exposure to the chemicals in the inks are still unknown and might become critical with time due to the high number of tattooed people. To bring light into this unknown area, even if costly, epidemiological studies and research on the fate of ingredients in the whole body are needed. In particular, prospective cohort studies should be conducted to investigate the correlation between tattoos and possible carcinogenesis.

Good Manufacturing Practices for manufacturing tattoo/PMU inks, as well as guidelines for their risk assessment should be developed. A full risk assessment of the ingredients, in particular colorants, used in tattoo/PMU inks is needed, including their phototoxicity, absorption level, distribution, metabolism and excretion, as well as Derived No Effect Level (DNEL), data which are largely missing so far. Further to this, it needs to be assessed whether the risks arising from the use of certain chemicals in tattoo/PMU inks are adequately controlled or need to be addressed by an EU measure. In the absence of this risk assessment, for azo pigments a precautionary approach would consist in not using those that contain in their structure aromatic amines classified as Carcinogenic, Mutagenic or Reprotoxic (CMR).

Harmonised analytical methods should be developed to ensure reproducible results and allow a correct implementation of the chemical requirements of legislation in place. Market surveillance activities should be continued to identify hazardous products and be carried out also on products sold on-line.

Additional information campaigns on risks for potential clients, particular targeted to teenagers and young people should be undertaken, allowing an informed choice. The training of tattooists should be compulsory and cover at least some key topics. The preparation of harmonised hygiene guidelines is highly recommended and inspections of studios required. The phenomenon of clandestine backyard tattooing should be stopped.

**Related and future JRC work** Three detailed reports on specific part of this project were published in 2015 and 2016 [1-3].

# 1. Introduction

The growing popularity of tattoos and permanent make-up (PMU) over the last years, confirmed also by the large availability of products on-line, has given rise to increasing concerns about the safety of tattoo inks, which may entail infectious and non-infectious risks, since they might contain hazardous chemical ingredients and/or microbiological agents, or be applied under poor hygiene conditions.

Tattooing is as old as humanity, but has rarely been addressed by regulators in a comprehensive and coordinated way. Tattoos are applied by injecting coloured inks into the dermis, are meant to stay lifelong. There are different types of tattoos which are classified as amateur or professional, according to the practitioner, "home" tattooist, or registered and trained professional. Cosmetic tattoos, also known as PMU, are used to resemble make-up and, probably due to the different ingredients and to the exposure to sunlight, might fade over years. Iatrogenic or medical tattoos are mainly carried out by physicians for diagnosis or therapeutic purposes, such as in nipple reconstruction; in Italy they can also be carried out by experienced beautician and/or tattooist with advanced training [4]. Finally traumatic tattoos may be provoked by accidents and explosions, where exogenous elements enter the human skin and colour it in an indelible way.

There is no specific EU legislation on tattoos/PMU products. They fall, together with any other. consumer products, under Directive 2001/95/EC on General Product Safety (GPSD) [5] requiring that only safe products may be placed on the market. In 2003, the Directorate General Health and Consumers (DG SANCO) requested the DG Joint Research Centre (JRC) to collect and analyse all available relevant data needed for considering common EU initiative on tattoo/PMU inks. The outcome of that study was published in 2003 as "Recommendations for European Union (EU) regulatory action on the safety of tattoos, body piercing and related practices in the EU" [6]. That report pointed out the microbiological risk of tattooing, together with inks' toxic and allergenic properties, stressing that the colorants used for tattoo purposes were just the same as those utilised by industry for car painting, printing inks, plastics coloration, etc.

The Council of Europe (CoE) adopted, also in 2003, a non-binding Resolution (ResAP) on the safety of tattoos and PMU, recommending inter alia some chemical, labelling and hygienic requirements [7]. These criteria were subsequently imbedded by several European countries into their domestic legislative framework, banning so the use of certain chemicals in tattoos and PMU inks The 2003 Resolution was overhauled in 2008 [8] by a revised one.

More than ten years after the first JRC Report, updated information was requested in order to take stock of significant modification of the state of play.

- Candidates for tattoo/PMU applications and removals are ever more numerous, especially among the young generation, and products can be increasingly purchased online.
- Some EU/EFTA (European Free Trade Association) countries have taken regulatory action in line with the CoE ResAP recommendations of 2003 and 2008.
- EU itself has enlarged, from 15 Member States in 2003 to 28 in 2014, with a corresponding increase in the EU population.
- New medical data related to health complications from tattoo/PMU application and laser removal are available.
- New information is available on ink ingredients.

In addition, new aspects, such as analytical methods, statistics, market surveillance activities, experience with the CoE ResAPs, risk perception and communication and data gaps, needed to be taken into consideration to provide a comprehensive overview of the situation.

In order to explore the necessity of an EU harmonised approach on tattoos/PMU products, DG SANCO set up in June 2014 the Consumer Safety Network Subgroup on Tattoos and Permanent Make-up (CSN-STPM) which gathered representatives from EU/EFTA national authorities, and other stakeholders, such as the Council of Europe and associations of tattooists, ink manufacturers, consumers, dermatologists, etc.

At the end of September 2014, DG SANCO tasked DG JRC with a new project on "Tattoos - Permanent Make-up" aimed to provide regulators with the scientific and technical basis needed for deciding whether EU measures are needed to ensure tattoo/PMU inks' safety and protect consumers[1].

The present report endeavours to take account of this new state of play, with a focus on quantifying the extent of the phenomenon: number and characteristics of nowadays tattoo/PMU recipients and removal candidates, incidence of adverse health effects, etc. The scope of this work includes the following topics and activities:

- description of the present regulatory framework in European countries and beyond;
- latest statistics on tattoo prevalence, both for applications and removals, influence of age and gender, size, localisation, market;
- list the chemicals present in inks (ingredients and impurities), as well as the analytical methods to detect those mentioned in the CoE Resolutions;
- to assess the RAPEX (Rapid alert system for non-food dangerous products) notifications and market surveillance carried out by EU Competent Authorities;
- to analyse the experience gained from implementing the CoE Resolutions;
- to investigate medical complications from tattoos (including henna-based temporary tattoos), and from their removal by laser devices;
- to evaluate the public risk perception and how the risk is communicated by authorities;
- to identify remaining data gaps, and need for further research.

[1] Administrative Arrangement 33617 "Tattoos - Permanent Make-up", signed by DG JRC, Unit I.1 Chemical Assessment and Testing, and DG SANCO, Unit B.3 Product and Service Safety, as from 1st January 2015 DG Justice and Consumers (JUST), Unit E.3 Product and Service Safety.

# 2. Methodology

## 2.1. Work Programme

The objectives of this 18-month project are to determine the size of the tattoo and PMU applications phenomenon; to understand what the current problems are and their dimension; and how they can be addressed to improve the safety of tattoo/PMU inks and practices.

This project was divided into 4 work packages (Table 2.1):

1. preparatory work [1];
2. state of play [2];
3. assessment and update of the CoE ResAP(2008)1 [3];
4. conclusions (final report).

**Table 2.1:** Work plan and expected outputs of the Tattoo/PMU Project.

| Work Package | Objectives | Topics | Deliverables |
|---|---|---|---|
| **WP1** | Preparatory work | Regulatory framework<br>Analytical testing methods | 1) CSN-STPM meeting 11 Nov 2014<br>2) WP 1 report |
| **WP2** | State of play | Current trends in tattoo practices<br>Prevalence<br>Data on inks market and composition<br>Post marketing surveillance | 3) CSN-STPM meeting 20 Apr 2015<br>4) WP 2 report |
| **WP3** | Assessing & updating CoE ResAP (2008)1 | Adverse health effects<br>Lists of hazardous chemicals<br>Impurities limits<br>Risk perception and communication<br>Data gaps and research needs | 5) CSN-STPM meeting 9 Nov 2015<br>6) WP 3 report |
| **WP4** | Conclusions | Identifying the elements to be addressed by any EU action on the safety of tattoos and PMU. | 7) CSN Plenary meeting with CSN-STPM 18 Mar 2016<br>8) Final report |

## 2.2. Sources of information

The information contained in this report was gathered as detailed below:

- international webinar on tattoos on 24th April 2014;
- CSN-STPM meetings;
- replies to questionnaires prepared by DG JRC;
- national legislative and guidelines texts;
- harmonised analytical methods;
- articles and books published in the literature;
- national studies and surveys;
- web search;
- RAPEX notifications;
- Presentations held at the meetings of the CSN-STPM.

### 2.2.1. International webinar

Representatives from the European Commission, the Organisation for Economic Co-operation and Development (OECD), Member States (Austria, Belgium, Denmark, Estonia, Finland, France, Germany, Hungary, Italy, Lithuania, Malta, The Netherlands), EFTA country (Norway) and other jurisdictions (Australia, Canada, Peru and the United States of America) took part in the webinar and exchanged information on safety issues related to tattoos.

### 2.2.2. CSN-STPM meetings

The CSN-STPM was set up in 2014 by DG SANCO. It was taken over by DG JRC in autumn 2014 when DG SANCO commissioned DG JRC to undertake this 18 month-project.

The members of the CSN-STPM included both experts from Competent Authorities and stakeholders, such as representatives from tattooists, ink manufacturers, dermatologists and consumers associations and the Council of Europe. Table 2.2 reports the list of participants in the CSN -STPM meetings. As much as 17 countries were represented by a total of 35 experts, plus 13 stakeholders. The meetings were held on:

- 23th June 2014
- 11th November 2014
- 20th April 2015
- 9th November 2015
- 18th March 2016

These meetings served to share the knowledge, discuss the data collected and propose recommendations. The minutes of those held in November 2014 and in April and November 2015 are collected in three JRC reports, respectively [1-3].

**Table 2.2:** Participants in CSN - STPM meetings.

| Country | Affiliation | National Expert |
|---|---|---|
| Austria | Austrian Agency for Health and Food Safety (AGES) | ÖZELT Gregor |
| | Federal ministry of labour, social affairs and consumer protection | MEWED Disa |
| Belgium | AZ Sint-Jan, Brugge - Ostende AV | De CUYPER Christa |
| Czech Republic | The ministry of health | KAPOUN Miroslav |
| Denmark | Danish Environmental Protection Agency (EPA) | BJERREGAARD LERCHE Dorte<br>DUDECK Camilla<br>PALUDAN Elisabeth<br>RASMUSSEN KOEFOED Julie |
| France | Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) | VERDIER Cécile |
| | Ministère des Affaires Sociales, de la Santé et des Droits des Femmes | MOKNI Walid |
| Germany | Bundesinstitut für Risikobewertung (BfR) | BLUME Annegret |
| | Federal Ministry of Food and Agriculture (BMEL) | MEISNER Anke |
| Hungary | National Institute of Chemical Safety (OKBI) | CSENGODY Krisztina<br>JALTAI Judit |
| Italy | Agenzia Regionale per la Protezione Ambientale Piemonte (ARPA) | AGNELLO Manuela<br>FONTANA Marco |
| | Istituto Superiore di Sanità (ISS) | ALIMONTI Alessandro<br>BOCCA Beatrice<br>RENZONI Alberto |
| Luxemburg | ILNAS - Surveillance du Marché | DA SILVA AREDE Luis |
| Netherlands | Ministry of Health Welfare and Sport (VWS) | HARTOG Peter<br>VAN GERWEN M. |
| | National Institute for Public Health and the Environment (RIVM) | JANSSEN Paul |
| | Netherlands Food and Consumer Product Safety Authority (NVWA) | De VRIES-HLAVACOVA Mariana<br>NIJBOER Lucas |
| Norway | Norwegian Food Safety Authority (Mattilsynet) | STAVENES ANDERSEN Ingrid |
| Slovakia | Public Health Authority of the Slovak Republic (UVZSR) | KISACOVA Janka |
| Slovenia | National laboratory of health- environment and food (NLZOH) | HRŽENJAK Vesna |
| Spain | Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) | VIDAL ARESES Maria |
| Sweden | Medical Products Agency (MPA) | CRONA Magnus<br>NOHRSTEDT Lena |
| | Swedish Chemicals Agency | SIMONSSON Elin |
| Switzerland | Kantonales Laboratorium Basel-Stadt | HOHL Christopher |
| United Kingdom | LGC LTD | AXFORD Ian |
| | Royal Borough of Greenwich | PINCHEN Robert |
| | **Affiliation** | **Stakeholders** |
| | Associazione tatuatori.it | GIUSEPPIN Eliseo<br>ZOPPETTI Marco |
| | European Society of Tattoo and Pigment Research (ESTP) | SERUP Jorgen |
| | Consumer Council at the Austrian Standards Institute (ANEC) | FIALA Franz<br>VUERICH Michela |
| | Council of Europe (CoE) | BAHRKE Susanne<br>SARACEVIC Amela |
| | H-A-N-Haus der Angewandten Naturwissenschaften-Gesellschaft mbH | DIRKS Michael<br>WERNER Alexander |
| | Sveriges Registrerade Tatuerare (SRT) | BERGSTROM Jens |
| | Tattoo Ink Manufacturers in Europe (TIME) | KEMNER Sina<br>MICHEL Ralf |
| | University of Regensburg | BAUMLER Wolfgang |

### 2.2.3. Questionnaires

Among the other sources of information, a number of questionnaires were prepared, distributed and analysed to extract data on the topics examined in this project.

The questionnaires were designed according to the topic requirements and also tailor-made according to the recipients. While the Member States were the principal audience, other input was sought according to the following mailing list distribution (Table 2.3):

- CSN members - 28 EU MS and 4 EFTA countries (Iceland, Lichtenstein, Norway and Switzerland);

- CSN- STPM members;
- other jurisdictions via the Organisation for Economic Co-operation and Development (OECD) secretariat;
- tattooists' and PMU professionals' associations;
- ink manufacturers/distributors/private labels;
- dermatologist associations.

**Table 2.3:** Questionnaires' mailing list.

| | Questionnaires | CSN members: • 28 EU MS • 4 EFTA countries (by DG JUST) | CSN-STPM members (by DG JRC) | Other non EU/EFTA countries (by the OECD Secretariat) | Others (by DG JRC) |
|---|---|---|---|---|---|
| 1 | **Regulatory framework** | X | X | | |
| 2 | **Analytical methods** | X | X | | |
| 3 | **Statistics** | X | X | X | 23 tattooists' and PMU professionals' associations<br>38 ink manufacturers/distributors/private labels. |
| 4 | **Ink ingredients** | X | X | X | 23 tattooists' and PMU professionals' associations<br>38 ink manufacturers/distributors/private labels. |
| 5 | **Health effects** | X (inviting them to distribute it to dermatologist associations, who had to further circulate it among their members) | | | 31 dermatologist associations (inviting them to share it with their members) |
| 6 | **Health effects CoE Res Risk communication and perception Data gaps** | X | X | | |

A more detailed description of the content of the questionnaires put forward is available in the Table 2.4:

1. regulatory framework (for Competent Authorities);
2. analytical methods (for Competent Authorities and stakeholders);
3. statistics (different questionnaires tailored for national authorities, for tattooist associations and for ink manufacturers);
4. ink ingredients (different questionnaires tailored for national authorities, for tattooist associations and for ink manufacturers);
5. health effects (for dermatologists);
6. health effects, CoE ResAP(2008)1, risk communication and data gaps identification (for Competent Authorities).

**Table 2.4:** Questionnaires' content.

| | Title | Questions | |
|---|---|---|---|
| 1 | **Regulatory framework** | a) Structured as the requirements of the CoE ResAP(2008)1<br>b) Chemical, hygienic, labelling, packaging and information requirements<br>c) Provisions on risk assessment, tattoo processes and studios<br>d) Details about national legislations, both in place or in draft<br>e) Guidelines applicable to tattooing practices and/or products | |
| 2 | **Analytical methods** | Analysis of substances listed in the CoE ResAP(2008)1 in tattoo/PMU products:<br>a) international (ISO and EN) standard methods<br>b) national standard methods<br>c) in-house validated methods<br>d) methods described in the literature | a) primary aromatic amines (PAA)<br>b) colorants<br>c) elements<br>d) polycyclic aromatic hydrocarbons (PAHs) |
| 3 | **Statistics** | **EU/EFTA countries:**<br>a) % of tattooed/PMU population<br>b) number of tattoos per person<br>c) % of regrets or removals/year<br>d) number registered/non-registered studios/artists<br>e) national tattooist/PMU associations, ink manufacturers/importers<br>f) origin of inks imported, volume of sales and purchases<br>g) main problems and comments | |
| | | **Tattooist and PMU professional associations :**<br>a) number of members<br>b) number of registered/non-registered tattoo/PMU studios/artists<br>c) suppliers of inks and yearly volume of purchased inks<br>d) existence of composition label on used products and type of container<br>e) suppliers of equipment and needles<br>f) main problems and comments | |
| | | **Ink manufacturers/distributors/private labels:**<br>a) origin of ingredients and raw materials<br>b) purity certificate for raw materials<br>c) volumes of tattoo/PMU ink produced per year<br>d) composition and other information on label and type of container<br>e) average sale price/ml of ink<br>f) Good Manufacturing Practices (GMP)<br>g) main problems and comments | |
| 4 | **Ink ingredients** | List of the ink composition:<br>a) Identified ingredients listed to complete<br>b) Open answer part to add | |
| 5 | **Health effects** | Complications following a tattoo/PMU application or removal:<br>a) skin and systemic symptoms and their frequency and severity<br>b) proportion of people with previous skin diseases, including allergy<br>c) allergic skin reactions<br>d) other inflammatory reactions<br>e) cutaneous/regional/systemic infections<br>f) tumours<br>g) correlations between health complications and certain tattoo characteristics/parameters (number of tattoos/patient, tattoo sizes, gender/age, colours, localisation) | |
| 6 | **Health effects CoE Res Data gaps** | a) Health effects:<br>frequency of different health issues amongst people having undertaken tattoos/PMU applications or removals and factors correlated to higher frequency of medical complications<br>b) Experience gained with the CoE ResAP(2008)1:<br>in terms of chemical, labelling, hygiene/sterility and other requirements<br>c) Risk communication and perception:<br>information campaigns, information on risk perceived by the general public, signature of a prior informed consent<br>d) Data gaps identification:<br>research or technical development to improve the safety of tattoo/PMU inks and practices | |

A total of 144 replies to questionnaires were received and analysed. The results are shown in Table 2.5 involving between 14 (the health effects questionnaire) - 28 (the regulatory framework questionnaire) country responses per questionnaire. Only 7 responses were received from manufacturers based in Germany and Italy (Table 2.6) and 10 from tattooist and PMU professional associations representing 7 countries (Table 2.7).

**Table 2.5:** Questionnaires' responses.

| Responses | Questionnaires | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | | | 4 | | | 5 | 6 |
| Countries | Regulatory framework | Analytical methods | Statistics | | | Ink ingredients | | | Health effects | Health effects CoE ResAP Risk perception/ communication Data gaps |
| **In Europe** | | | | | | | | | | |
| AT | X | X | X | | | | | | | |
| BE | X | | X | | | | | | 4 | X |
| BG | X | | X | | | X | | | | X |
| CH | X | X | X | 1 | | X | | | | |
| CY | X | | X | | | | | | | |
| CZ | X | | X | | | | | | | X |
| DE | X | | X | 2 | 4 | X | 2 | 4 | 5 | X |
| DK | X | X | X | 1 | | X | 1 | | 5 | X |
| EE | X | | | | | | | | | |
| EL | X | | | | | | | | | |
| ES | X | | X | 1 | | X | | | | X |
| FI | X | | X | | | | | | 1 | X |
| FR | X | X | X | | | X | | | | X |
| HR | X | | | | | | | | | |
| HU | | | X | | | | | | | |
| IE | X | | | | | | | | | |
| IS | | | X | | | | | | | |
| IT | X | X | X | 3 | 3 | X | 2 | 3 | | X |
| LI | X | | X | | | X | | | | |
| LT | | | | | | | | | | |
| LU | X | | X | | | X | | | | |
| LV | X | | | | | | | | | |
| MT | X | | | | | | | | | |
| NL | X | X | X | | | X | | | 3 | X |
| NO | X | | X | 1 | | X | 1 | | | |
| PL | X | | X | | | | | | | |
| PT | X | | | | | | | | | |
| RO | X | | X | | | | | | | X |
| SE | X | X | X | 1 | | X | 1 | | 1 | X |
| SI | X | X | X | | | X | | | | X |
| SK | X | X | X | | | | | | | X |
| UK | | X | X | | | | | | | |
| **Total** | **28 countries** | **10 countries** | **24 countries** | **10 associations** | **7* manufacturers** | **13 countries** | **6 associations** | **7* manufacturers** | **19 dermatologists** | **14 countries** |
| **Outside Europe** | | | | | | | | | | |
| CA | | | X | | | X | | | | |
| MX | | | X | | | | | | | |
| NZ | | | X | | | | | | | |
| US | | | X | | | X | | | | |
| **Total** | | | **4 countries** | | | **2 countries** | | | | |

* ink manufacturers/distributors/private labels

**Table 2.6:** List of ink manufacturers respondents.

| Country | Company |
|---|---|
| **IT** | ABC INK |
| **IT** | Biotek srl |
| **IT** | Clinita |
| **DE** | DC-TP Europe GmbH |
| **DE** | H-A-N Haus der Angewandten Naturwissenschaften-Gesellschaft GmbH |
| **DE** | MT DERM GmbH |
| **DE** | WEFA colors Jo Weinbach |

**Table 2.7:** List of tattooist and/or PMU professional associations respondents.

| Country | Tattooist and/or PMU professional associations | Acronym |
|---|---|---|
| **CH** | Verband Schweizerischer Berufstätowierer | VST |
| **DE** | Bundesverband Tattoo | BVT |
| **DE** | United European Tattoo Artists | UETA |
| **DK** | Dansk Tatovør Laug | DTL |
| **ES** | Spanish National Union of Professional Tattooists | UNTAP |
| **IT** | Associazionetatuatori.it | ART |
| **IT** | Confederazione Nazionale Artigianato | CNA |
| **IT** | Associazione Tatuaggio Estetico Correttivo | ATEC |
| **NO** | Norwegian Tattoo Union | NTU |
| **SE** | Sveriges Registrerade Tatuerare | SRT |

The response rate was very low in the case of the health effects questionnaires. Although 31 dermatologist associations in a representative sample of European countries were reached, only 19 dermatologists responded of which 15 reported less than 15 and 4 up to 150 patients/year showing tattoo complications. In addition, only 5 national authorities completed the questionnaire in the part related to health effects. By consequence, the chapter regarding adverse health effects is based on the literature review.

### 2.2.4. National legislative and guidelines texts

The regulatory review, updated until November 2014, was based on the analysis of 93 documents, including legislation in place and in draft, as well as guidelines. The list of the documents taken into consideration and a description of the main points addressed in each document is available in the JRC report on Wok Package 1 [1].

### 2.2.5. Harmonised analytical methods

The information regarding available analytical methods for the determination of hazardous substances in tattoo/PMU products and other matrices was collected through questionnaires, web search of standard methods in the ISO (International Organization for Standardization) and CEN (European Committee for Standardization) catalogues and analysis of Standard Operating Procedures (SOPs), as well as literature review.

### 2.2.6. Literature

Literature searches were carried out in PubMed and Scifinder data bases. The health effects chapter benefited from a review performed according to the guidelines named Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) [9].

Exclusion/inclusion criteria were applied to select the relevant articles (Figure 2.1):

- years included 2004-2015;
- key words present in abstract and title;
- removal of duplicates, patents, some languages, documents classified as historical, dissertation, biography, commentary and conference;
- priority given to 1) reviews, recent books and national reports; 2) clinical trials and 3) other papers;
- filtering for relevance to tattoos or PMU.

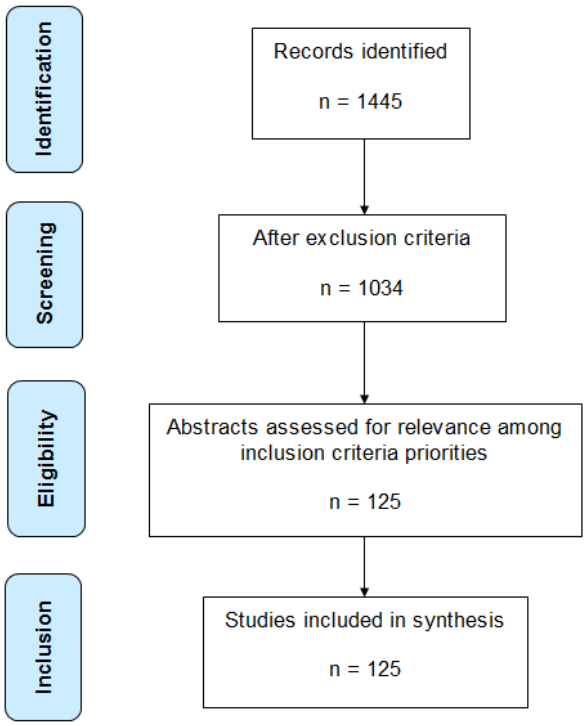



**Figure 2.1:** PRISMA flowchart on tattoo health effects.

The full list of references used for the elaboration of the reports in this project can be found in the reference chapter.

### 2.2.7. National studies and surveys

The complete list of national studies reviewed to elaborate this report is available in Table 2.8 where 7 countries have undertaken studies on tattoos and PMUs.

**Table 2.8:** List of national studies/reports/surveys considered in this report.

| Country | Year | Institution | Title |
|---|---|---|---|
| BE | 2015 | Conseil Superieur de la Santé (CSS) | 8893 Produits de tatouage et de maquillage permanent et semi-permanent - avis intermédiaire visant à limiter les complications et à accroître la sécurité des produits et techniques de tatouage et de maquillage permanent et semi-permanent en attendant une liste positive de produits pour ceux-ci |
| | 2011 | | 8631 Semi-permanent makeup and tattoo |
| CH | 2014 | Gesundheitsdepartement des Kantons Basel-Stadt/Kantonales Laboratorium | Tinten für Tattoos und Permanent Make-Up/Pigmente, Konservierungsstoffe, Aromatische Amine, Polyaromatische Kohlenwasserstoffe und Nitrosamine |
| DE | 2012 | Bundesinstitut für Risikobewertung (BfR) | Requirements for tattoo inks |
| | 2013 | Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL) | Berichte zur Lebensmittelsicherheit – Monitoring 2013 |
| | 2007 | | Berichte zur Lebensmittelsicherheit |
| DK | 2014 | Danish Ministry of the Environment Environmental Protection Agency (DK EPA) | Recommendation from the Danish Environmental Protection Agency on the safety of Tattoo Ink |
| | 2012 | | Chemical Substances in Tattoo Ink: Survey of chemical substances in consumer products |
| | 2012 | | Risk Assessment of Hazardous Substances in Tattoo Inks based on the project "Chemical Substances in Tattoo Inks" |
| | 2011 | | Table of banned tattoo colours |
| | 2002 | | Investigation of pigments in tattoo colours |
| NL | 2015 | Nederlandse Voedsel en waren autoriteit (NVWA) | Polycyclische aromatische koolwaterstoffen (PAK's) in tatoeagekleurstoffen |
| | 2014 | | Resultaten onderzoek van kleurstoffen voor tatoeages en permanente make-up in de periode 2008 – 2013 |
| | 2008 | | Nalevingsmonitor tatoeage en permanente make-up kleurstoffen (overzicht 2004 – 2007) |
| SE | 2015 | Medical Products Agency (MPA) | Control of tattoo inks for tattoo and permanent makeup |
| | 2012 | Swedish Chemical Agency (KEMI) | Analysis of tattoo inks |
| | 2010 | | Hazardous substances in tattoo inks |
| | 2010 | | Analysis of tattoo inks |
| UK | 2013 | Public Health England | Literature review on the epidemiology of tattooing and its complications |
| CA | 2011 | Health Canada | Market survey of tattoo dyes: heavy metal testing |
| | 2011 | | Market survey of tattoo dyes: microbial testing |
| NZ | 2013 | Ministry of Health | Survey of selected samples of tattoo inks for the presence of heavy metals |
| US | 2012 | Centers for Disease Control and Prevention (CDC) | Tattoo-associated nontuberculous mycobacterial skin infections--multiple states, 2011-2012 |
| | 2006 | | Methicillin-resistant Staphylococcus aureus skin infections among tattoo recipients |
| | 2010 | Pew Research Center | A portrait of generation next: confident. Connected. Open to change |
| | 2007 | | How Young People View Their Lives, Futures and Politics – A portait of "Generation Next" |
| | 2014 | Harris Poll Global Omnibus | Los Angeles is America's "Most Inked Market" |
| | 2013 | | A867 – Tattoos, October 2013 |
| | 2012 | | One in Five U.S. Adults Now Has a Tattoo |
| | 2008 | | Three in ten americans with a tattoo say having one makes them feel sexier |
| | 2003 | | A Third of Americans With Tattoos Say They Make Them Feel More Sexy, October 8 |

[10-38]

### 2.2.8. Web search

To complete the findings, a web-based research was carried out on:

- legislative framework in some countries;
- analytical methods available at International Organization for Standardization (ISO) and Comité Européen de Normalisation (European Committee for Standardization – CEN) level;
- tattoo/PMU market situation in terms of brands, suppliers and products sold online;
- market share;
- manufacturers/importers/suppliers/distributors;
- inks ingredients.

### 2.2.9. RAPEX notifications

Since 2001, the Rapid Alert System for non-food dangerous products (RAPEX) shares information among 31 European countries and the European Commission regarding products presenting a serious health risk to consumers and measures taken. RAPEX notifications are published every week. The RAPEX database[2] was searched in the years 2005-2015 (until week 15) and data retrieved as described in Table 2.9.

**Table 2.9:** RAPEX data base search and data.

| | |
|---|---|
| **Key word** | Tattoo |
| **Years** | 2005-2015 |
| **Risk types** | Chemical<br>Microbiological |
| **Product category** | Chemical products |
| **Results** | **126 entries** |
| **Data** | Production country |
| | Chemicals and the microbiological agents involved |
| | Geographical production area |
| | Brand name and type of product |
| | Year and week of the notification |
| | Legal basis according to which the product was considered to pose an identified risk |
| | Action taken by national authorities or 'voluntarily' by producers and distributors. |

RAPEX notifications related to tattoo and PMU inks were identified and the risks linked to chemical and microbiological content evaluated.

### 2.2.10. Presentations held at the meetings of the CSN-STPM

Data presented in the meetings of the CSN-STPM held in Ispra were also taken into consideration, when adequate to complete the data.

[2] http://ec.europa.eu/consumers/safety/rapex/alerts/main/index.cfm?event=main.search

# 3. Council of Europe Resolutions

The Council of Europe[3] is an international organisation which comprises 47 European countries, among which the 28 members of the European Union. It was set up to promote democracy and protect human rights and the rule of law in Europe. Its activities were then expanded to include among others also the health protection of consumers and the integration of people with disabilities into the community. In the CoE, the European Directorate for the Quality of Medicines and Health Care (EDQM) has been established to contribute to the basic human right of access to good quality medicines and healthcare and to promote and protect human and animal health.

## 3.1. CoE ResAP(2003)2

In 2003 the CoE published a ResAP on *tattoos and permanent make-up* [7] whose purpose was to contribute to the harmonisation of legislation in the public health field and to the preservation of consumer health through the insurance of tattoo and PMU products' safety. It took into account:

1) the increasing popularity of tattoos and PMU;
2) their possible resulting health risks (due to microbiological contamination, presence of hazardous chemicals in inks or weak hygiene habits);
3) the importance of risk assessment for decision-making;
4) the lack of national legislation in most member countries and of EC regulation;
5) the advantage of regulation harmonisation at European level.

This resolution makes recommendations to CoE member state governments to include its principles in their legislations on tattoos and permanent make-up. The overarching principle is that tattoo and PMU products should not endanger the health and or safety of persons or the environment. Therefore, a risk evaluation should be performed and products should comply with the following chemical, labelling, packaging, hygienic and information provisions.

### Risk evaluation

The manufacturers or importers/distributors have to perform a risk evaluation based on recent toxicological data, and sent out this evaluation in a dossier available to the Competent Authorities before putting the product on the market.

### Chemical requirements

The ResAp recommends that certain chemicals should not be present (or released, in the case of aromatic amines) in tattoo and PMU inks. The following negative lists are mentioned in the CoE ResAP(2003)2:

1. Table 1 includes 26 aromatic amines, classified as carcinogenic substances with only two exceptions;
2. Table 2 contains a non-exhaustive list of 35 pigments with carcinogenic, mutagenic, reprotoxic or sensitising properties;
3. all ingredients listed in Annex II of the Cosmetics Directive 76/768/EEC (now substituted by EC Regulation 1223/2009, the Cosmetics Regulation) [39];

[3] http://www.coe.int/aboutCoe

4. all colorant specified in Annex IV, with restrictions in columns 2 to 4 of Directive 76/768/EEC (now substituted by EC Regulation 1223/2009, Annex IV, column g) [39];
5. carcinogenic, mutagenic and reprotoxic (CMR) substances of categories 1, 2 or 3 that are classified under Directive 67/548/EEC (now substituted by EC Regulation 1272/2008 on Classification, Labelling and Packaging (CLP), Table 3.1 in part 3 of Annex VI, categories 1A, 1B and 2) [40].

In addition, preservatives should not be present in tattoo/PMU inks.

In the future, the CoE aims to establish positive lists of substances.

### Labelling requirements

Tattoo and PMU products' packaging should contain the following information:

- name and address of the manufacturer or the person responsible for placing the product on the market;
- minimum date of durability;
- conditions of use and warnings;
- batch n° used by the manufacturer for batch identification;
- list of ingredients according to their International Union of Pure and Applied Chemistry (IUPAC) name , CAS number (Chemical Abstract Service of the American Chemical Society) or Colour Index (CI) number;
- guarantee of sterility of the contents.

### Hygienic and packaging requirements

Tattoo and PMU products must be supplied in a container that maintains the sterility of the product until application. The packaging size should be supplied for single use on an individual consumer.

Tattoo and PMU application and activities, including sterilisation and disinfection of the instruments, must be carried out by the tattooist in conformity with the hygiene regulations laid down by national public health services.

### Information requirements

The public should be informed about the risks of tattooing by all appropriate means, such as mass information campaigns or via the Internet. Complete, reliable and comprehensible information to the consumer is mandatory for tattooists about the risks entailed by those practices, including the potential occurrence of sensitisation.

## 3.2. CoE ResAP(2008)1

On 20 February 2008, the CoE adopted a revised ResAP(2008)1 superseding the previous Resolution from 2003. The main differences are listed hereunder and summarised in Table 3.1.

- Table 1 of CoE ResAP(2008)1 contains 27 aromatic amines, (compared to 26 in the previous version), paraphenylenediamine was added. These aromatic amines should not be present or released in concentrations that are technically avoidable according to Good Manufacturing Practices (GMP); their presence or release

should be determined by using appropriate test methods which should be harmonised across the member states.

- Two analytical methods which could serve as models for harmonising test methods for the analysis of aromatic amines were added.
- A new table was added listing the maximum concentrations of impurities.
- Tattoo and PMU inks should also comply with the minimum requirements for further organic impurities for colorants used in foodstuffs and cosmetic products as set out in Directive 95/45/EEC [41].
- Preservatives can be used only after a safety assessment and in the lowest effective concentration to avoid the product contamination after opening and by no means to compensate for poor microbiologic quality during the manufacturing process or for questionable hygiene conditions while performing the tattoo/PMU application.
- Single use packaging is preferred. In case of multi-use containers, their design should ensure that the contents will not be contaminated during the period of use.
- Tattooists should duly inform the customer about care following the application of a tattoo, reversibility and removal of tattoos, and the advice of consulting a physician in case of medical complications.
- The Competent Authorities should evaluate the specific safety data of ink ingredients (e.g physico-chemical properties and toxicological data), starting with colorants, in order to exclude the use of harmful substances by progressively establishing a positive list of safe substances in tattoos and PMU.

**Table 3.1**: Main differences between CoE Resolutions (2003)2 and (2008)1.

| | | CoE ResAP(2003)2 | CoE ResAP(2008)1 |
|---|---|---|---|
| **1) Risk evaluation** | Safety assessment | Done by manufacturers or importers/distributors | Manufacturers: Provide composition of products and toxicology of substances (using existing guidelines if any)<br>Authorities: Take steps to replace negative lists with positive lists of safe substances |
| **2) Chemical requirements** | Aromatic amines negative list | 26 aromatic amines in Table 1 | Paraphenylenediamine added to Table 1 |
| | | | Concentrations should be lower than those technically avoidable and should be determined by test methods to be harmonised |
| | Purity criteria | none | Maximum allowed concentrations of metal and polycyclic aromatic hydrocarbon (PAH) impurities (Table 3) |
| | | | Minimum requirements of organic colorant impurities for colorants used in foodstuffs and cosmetic products [Directive 95/45/EEC] |
| | Preservatives | should not be used | Only to ensure preservation after opening, not as purity correction nor inadequate hygiene |
| | | | Only after safety assessment and in the lowest effective concentration |
| **3) Hygienic and packaging requirements** | Container size | Single use recommended | If multi-use containers, designed to avoid contamination during use |
| **4) Public information** | Risks | risks including potential sensitisation | Added:<br>aftercare<br>removals<br>physician consultation if medical complications |

[Directive 95/45/EEC] [41]

# 4. Legislative framework in the EU/EFTA countries and other jurisdictions

The regulatory review of different EU (and beyond) national legislation and guidelines on tattoo/PMU prepared by DG JRC in 2003 [6] needed an update due to changes in the legislative framework of some countries, following the adoption of the two CoE Resolutions, and to the enlargement of the European Union (since 2004 13 new MS joined). Taking stock of these new developments, DG JRC collected in 2014 data on the regulatory framework of each EU and EFTA (Iceland, Liechtenstein, Norway and Switzerland) countries[4], plus other jurisdictions. The findings, as of November 2014, are presented hereunder. More details are available in the JRC report on Work Package 1 [1].

## 4.1. EU/EFTA countries

The situation varies widely across Europe, as many countries have endorsed and, except in 3 MS, also enforced national legislation on tattoo/PMU products in line with the recommendations of the CoE ResAPs of 2003 and 2008, while some others do implement the chemicals legislation (CLP and REACH) [40, 42] and the general safety requirements of the GPSD [5] without referring specifically to tattoo/PMU products.

According to the degree of development of ad hoc policy on tattoo/PMU products and practices, the various countries can be divided in four different groups (See Figure 4.1):

1. **Belgium, France, Germany, Norway** and **The Netherlands** adopted regulatory provisions in line with CoE ResAP(2003)2, while **Slovenia, Spain, Sweden** and **Switzerland** (plus **Liechtenstein**, which follows the Swiss legislation) enforced the CoE ResAP(2008)1 recommendations. (see Table 4.1 of this document).
2. **Austria, Denmark** and **Latvia** have notified national legislation based on the CoE ResAP(2008)1, but they have been kept on hold so far.[5]
3. **Czech Republic, Finland, Italy, Malta, Romania** and **Slovakia** have taken health and safety measures regulating tattooing activities, including hygiene requirements of tattoo parlours. In addition, in the context of RAPEX notifications Italian and Slovakian health authorities carry out market surveillance activities on tattoo/PMU inks referring to the CoE ResAP(2008)1 lists of hazardous chemicals [43, 44].
4. **Bulgaria, Croatia, Cyprus, Estonia, Greece, Ireland, Luxembourg, Poland** and **Portugal** have not yet put in place any specific tattoo/PMU regulatory framework, though they are supposed to implement, as all other MS, general safety provisions regarding consumer products (GPSD), and follow up the chemicals legislation (REACH and CLP).

The main elements of the regulatory framework existing in the various countries that have embodied the ResAP's recommendations can be summarised as follows.

[4] Hungary, Iceland, Lithuania and the United Kingdom did not reply to the enquiry.
[5] Denmark and Austria in 2013, and Latvia in 2014 have notified draft national legislation on tattooing products and services. The proposed drafts are currently put on hold by the European Commission as they are in conflict with REACH provisions.

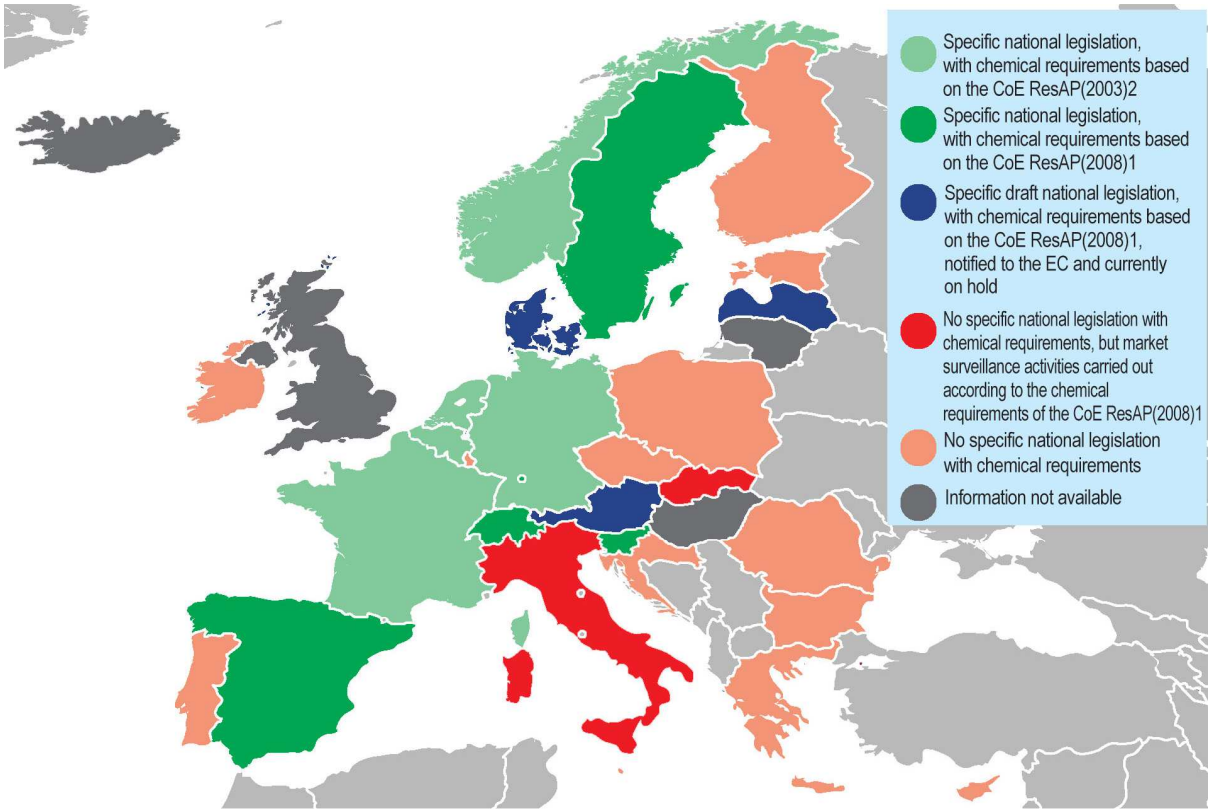



**Figure 4.1:** Legislative framework on tattoo/PMU products in the EU/EFTA countries.

### 4.1.1. Chemical requirements

There are currently no EU harmonised legal requirements for chemicals in tattoo/PMU inks. A number of chemicals present in inks, either as ingredients or as impurities, are however banned in consumer products that get into direct contact with the skin under different legislative frameworks, like in cosmetics (Cosmetic Product Regulation) or in textiles (e.g. REACH restriction for aromatic amines).

Table 4.1 reports an overview of the chemical recommendations mentioned in the CoE ResAPs (in columns) with the indication if they are included into the legislations in place in Belgium, France, Germany, Liechtenstein, Norway, Slovenia, Spain, Sweden, Switzerland and The Netherlands. Even though these legal acts are all based on the ResAPs from 2003 or 2008, differences are present among them either due to dissimilarities in the ResAPs or to deviations from them.

For instance, even if the French and German national legislations are based on CoE ResAP(2003)2, the negative list for PAAs mentioned inhere includes also p-phenylenediamine which is mentioned in the CoE ResAP (2008)1. Moreover, although the CoE ResAP(2003)2 does not allow the use of preservatives, the French and German legislations do not give any specific indication about this issue, while the Norwegian one includes a positive list with restrictions.

Another example is the Swiss legislation that foresees a limit of 30 mg/kg for the total content of forbidden PAA in tattoo/PMU products, even if the CoE ResAP (2008)1 does not indicate specific thresholds for this class of compounds.

Remarkably, the national legislations in place forbid all substances classified as CMR in categories 1A, 1B and 2 under the CLP Regulation (the only exception is Germany), as well as those listed in Annex II and Annex IV (with restrictions in column g) of the Cosmetics Regulation in tattoo/PMU products. Actually, the German act bans the substances classified as CMR before 2010 as they are included in Annex II of the Cosmetics Regulation.

It has to be noted that France and Switzerland have some additional requirements. The French regulation also forbids: 1) sensitising substances category 1 as defined in EC Regulation 1272/2008 [40]; 2) sensitising substances in hair dyes identified by opinions of the Scientific Committee on Consumer Safety (SCCS) and 3) CMRs and sensitising substances as specified in the Commission decision 2002/371/CE [45] establishing the ecological criteria for the award of the EU Ecolabel for textile products (now substituted by the Commission decision 2014/350/EU [46]). The Swiss law additionally bans fragrances and flavouring agents in tattoo/PMU inks.

**Table 4.1**: Chemical requirements in the national legislations in place.

| Country | National legislation based on the CoE ResAP | Negative list for PAAs | Negative list for colorants | Impurity limits | Preservatives | Negative list for substances EC Reg 1223/2009 Annex II | Negative list for colorants EC Reg 1223/2009 Annex IV (column g) | Negative list for CMRs EC Reg 1272/2008 Table 3.1 | Dir 95/45/E EC |
|---|---|---|---|---|---|---|---|---|---|
| **BE** | (2003)2 | 26 | 35 | no | banned | yes | yes | yes | yes |
| **DE** | (2003)2 | 27 (26 + paraphenylene diamine) | 36 (35+ solvent yellow 14) | no | no special provisions | yes | yes | no, however Annex II of EC Reg 1223/2009 contains the substances classified as CMRs before 2010 | no |
| **FR** | (2003)2 | 27 (26 + paraphenylene | 35 | no | no special provisions | yes | yes | yes, plus sensitisers cat. 1 | no |
| **NL** | (2003)2 | 22 | 36 | no | banned | yes | yes | yes | |
| **NO** | (2003)2 | 26 | 35 | no | positive list with several restrictions* | yes | yes | yes | |
| **CH, LI** | (2008)1 | 27 (CH - with specific limit for the sum, 30 mg/kg) | 35 | yes (except for nickel and antimony) | positive list of 26 allowed for prolonged contact with the skin (leave-on cosmetics) | yes, referring to the corresponding national legislation | yes, referring to the corresponding national legislation | yes, referring to the corresponding national legislation | no |
| **ES, SE, SI** | (2008)1 | 27 | 35 | yes (15 impurities) | tolerated under certain conditions** | yes | yes | yes | yes (SE) |

*e.g. max concentrations and labelling

** e.g. only after risk assessment and in the lowest effective concentration

### 4.1.2. Packaging requirements

Along the lines of the CoE Resolutions, Belgium, France, Liechtenstein, Norway, Slovenia, Spain, Sweden, Switzerland, The Netherlands, together with Italy, Malta and Romania, impose appropriate packaging ensuring sterility of tattoo inks before use. Single use containers are encouraged by authorities, who made it already mandatory in Malta and Spain, but not favoured by tattooists associations, who argue that such packaging make inks getting dry. They rather support multiple use containers provided that other sterility measures are taken, e.g., sterile water for diluting inks instead of tap water, plus low sensitisation preservatives.

### 4.1.3. Labelling requirements

Almost all current legislative frameworks for tattoo and PMU inks contain labelling requirements, in conformity with the CoE ResAP(2008)1. Besides, the period after opening (PAO), where inks are still safe, is indicated in Germany, Spain, Sweden and Norway. The latter applies similar standards as for cosmetic products.

### 4.1.4. Hygienic requirements

Most of national laws/guidelines contain general provisions regulating cleaning of tattoo premises, sterility of tools (such as single use of needles) and hygiene of staff (e.g. skin disinfection).

### 4.1.5. Requirements for risk assessment

In some countries (such as Czech Republic, France, Norway, Slovenia or Spain) the manufacturer/importer has to submit to the Competent Authorities a safety assessment dossier of the tattoo/PMU product before placing it on the market, while in some other Member States the safety assessment file needs to be handed to Competent Authorities only if required. This dossier contains inks' composition, physical-chemical and toxicological properties, health risk assessment, data on microbiological status, together with details on manufacturing conditions and quality check. However, France and Norway forbid any animal testing for tattoo toxicological and risk assessment purposes. The tattooists operating in Romania and Spain, have to carry out an allergy test for the dye to be used prior to the tattoo application.

In Sweden, data on potential adverse health effects of tattoo inks, including the preservatives contained in it, must be sent to the Medical Products Agency and to the Swedish Poisons Information Centre.

The Spanish Competent Authority[6] is the only one in the EU that established a positive list of tattoo and PMU inks allowed for use on the Spanish market.

### 4.1.6. Information requirements

Tattoo operators in France, Liechtenstein, Malta, Norway, Slovenia, Sweden, Switzerland and The Netherlands have to provide tattoo receivers before handling them, with complete, often written information, focusing on the potential risks of such application, on the aftercare treatment, on tattoo removal and emphasizing the necessity to consult a doctor should health complications arise. Many countries, like France, Italy, Norway, Switzerland or The Netherlands, impose a written consent from the customer, or from his legal guardian.

Norway and The Netherlands, for instance, have put in place public information campaigns targeting tattoo customers about the possible health risks of tattooing/PMU procedures. Besides, the website http://www.veiligtatoeerenenpiercen.nl/ lists all Dutch licensed parlours and indicates client's age limits, providing also data on risks of tattoos, aftercare instructions, etc. See more details in Chapter 11 (risk perception and communication).

### 4.1.7. Adverse health reactions notifications

In France the national vigilance system put in place allows the public to retrieve information on health risks related to tattoo inks. The Italian market monitoring Authority ensures tattoo inks comply with the CoE ResAP(2008)1 and other hygienic/sanitary guidelines, initiating otherwise a market withdrawal procedure under the RAPEX system. In Sweden the producer or importer reports to a national register, while in Germany market surveillance authorities and the Poison Centres are at regional level. A reporting system of adverse health effects from tattoo inks exists also in e.g. Austria, France, Norway, Romania, and The Netherlands. The Dutch monitoring system (CESES, Consumer Exposure Skin Effects and Surveillance) registers all complications

[6] (Agencia Española de Medicamentos y Productos Sanitarios, AEMPS)

including allergic reactions caused by cosmetics. Instead of cross references to other legislation Norway proposed market surveillance Authorities should use "supporting lists" for the identification of banned substances.

### 4.1.8. Requirements for processes and tattooists

In Belgium, Czech Republic, Italy, Liechtenstein, Malta, Romania, Slovenia, Slovakia, Switzerland and The Netherlands, a license is compulsory for opening a tattoo studio and carrying out tattoo-related activities, delivered sometimes upon due medical examination (Czech Republic) or vaccination against Hepatitis B (Malta and Switzerland). Luxembourg requires a diploma of hairdresser, beautician or manicurist in order to open such a parlour.

In Belgium, Czech Republic, France, Italy, Liechtenstein, Romania and Sweden, legal provisions specify which training courses tattooists must follow, e.g. on hygiene and health topics. Draft legislation in Austria, Denmark and Latvia also regulates access to the profession and ad hoc training for tattooists.

Tattooing is forbidden to minors without a parental approval, i.e. under 18-s, in Belgium, Denmark, Malta, Romania and Spain. However, the customer's minimum age limits can sometimes be as low as 15 years in Slovenia, or 16 years in The Netherlands (down to 12 years with parents' authorisation). Italy regulates such matters at regional level. Furthermore, according to the Danish Tattoo law some body parts, such as head, neck and hands may not be tattooed.

The Netherlands and Romania consider tattoo removal as a medical act; hence it may only be carried out by qualified medical staff within hospital premises.

## 4.2. Other jurisdictions

The information has been collected by searching published regulations and guidelines in the internet and through an international webinar, which took place in April 2014.

**New Zealand** is the only country outside Europe to expressively recommend tattoo/PMU guidelines based on the CoE ResAP(2008)1. Under the remit of the Environmental Protection Agency (NZ-EPA), a Tattoo and Permanent Make-up Substances Group Standard has been established to discuss the potential health risks provoked by the chemicals contained in those products. In line with the aforementioned Resolution, the NZ Authorities have established a list of 27 aromatic amines and 35 colorants that should not be present in tattoo inks, with the same limits for 15 impurities.

In **Australia**, the public health department of each jurisdiction (e.g. New South Wales, Queensland, Tasmania, etc.) regulates its own Body Art practices and standards, leading to a wide variety of procedures.

The Food and Drug Administration (FDA) of the **United States of America** has not yet developed legal scheme covering tattoo inks and parlours at federal level, though specific requirements do exist at state level, leading to a wide variety across the US. During the abovementioned webinar, the United States expressed their interest in envisaging further regulatory measures ensuring an improved safety of tattoo inks.

**Canada** has no specific legislation on tattooing at central level. However, every provincial authority (such as in British Columbia, Ontario, Québec, etc.) edicts health guidance governing Personal services establishments (PSEs), and ensures their enforcement.

In **Japan**, highly industrial chemicals entering in the composition of consumer products undergo strict marketing and use restrictions. However, to our knowledge, tattoo inks are not regulated as such, and tattoo studios are not covered by a specific legislative scheme.

To summarise, regulatory control of tattoo/PMU products and practices largely vary across the abovementioned developed countries (Australia, Canada, Japan, New Zealand and United States of America), but also inside each national jurisdiction.

The different rules and guidelines mainly lay down requirements for tattoo processes and hygiene standards, and less on chemical ingredients contained in tattoo and PMU inks.

# 5. Statistical data related to tattoo and PMU practices

In the 1950s and 1960s in the USA and in Europe, tattooing was a practice generally not well accepted by the middle classes and associated with certain groups of people, such as sailors, the military, criminals and prostitutes [47]. According to many experts, tattoo prevalence has increased over the years together with their acceptance by the society. Nowadays, tattoos are considered an artistic expression, referred to as body art, and getting tattoos has become more and more a fashion trend, in particular in the young generations. Popularity of tattooing has increased its visibility more recently, most likely through television and social media [47-49].

This chapter attempts to provide certain quantification to this evolution, despite all difficulties such as the fact that there is no official registration system whatsoever in the EU. It also provides information related to the tattoo market, in terms of studios, artists, associations, manufacturers, brand names, etc. As mentioned in chapter 2, data originates from replies to questionnaires, peer-reviewed literature, national reports and web searches. More details are available in the JRC report on Work Package 2 [2].

## 5.1. Prevalence

### 5.1.1. General population

Fig. 5.1 reports the available data on the tattoo prevalence in the general population in countries within and outside Europe. 13 Member States, plus Canada, New Zealand and the United States provided information through questionnaires. The uncertainties are unknown and, in many cases, also the sources. In the literature, data from Germany, Denmark, France, Sweden, United Kingdom, Australia and the United States were found [10, 13, 17, 34-38, 47, 48, 50-58]. They were generally in agreement with what reported in the questionnaires.

Based on the figures from 14 MS (questionnaires: AT, BG, CY, DE, DK, FI, FR, HU, IT, LU, NL, PL and SE; literature: UK) weighed by the population of each of them, it can be estimated that:

- **12%, of the whole European population has one tattoo or more**

This corresponds to more than 44 million tattooed people in the 14 considered countries and to more than 60 million people in the EU-28.[7]

Fig. 6.2 shows the prevalence data used for the estimation. The darker the violet colour, the higher the prevalence is. Member States for which no information was available are represented in dark grey and countries not belonging to the European Union are in light grey. The picture also shows the estimated number of tattooed people expressed in millions. National tattoo prevalence in Europe ranged between 7 and 19%, with the exception of Luxembourg (60%), Hungary (50%) and Cyprus (30%). These three high values do not significantly impact the estimate that would be decreased to 11.8% in case the Luxembourgian and Cypriot data would not be taken into account and to 10.7% if the Hungarian one would be taken out from the calculation.

The current estimate of 12% for the EU tattoo prevalence rates higher than the 5-10% reported for tattoos and piercing in a previous 2003 JRC report [6] and seems to indicate an increase over time. This can be supported particularly considering that: 1) only one decade have passed; 2) the prevalence in the general population is slowly influenced by changes in the prevalence of specific age groups (e.g. young people); 3) the estimate

[7] For the purpose of estimating the tattoo prevalence in Europe, the tattoo prevalence in each considered country has been multiplied by the number of people living there (including everyone, e.g. children), thus obtaining the number of tattooed people in that country. The total number of tattooed people in the 14 countries considered was then used to calculate the tattoo prevalence in the EU-28. This might have led to a slight overestimation of this parameter.

done in 2003 overestimated the tattoo prevalence as it included also people who had just piercing. If in the following years tattoos will continue to be "trendy", the impacts will accumulate and the general prevalence will continue to increase.

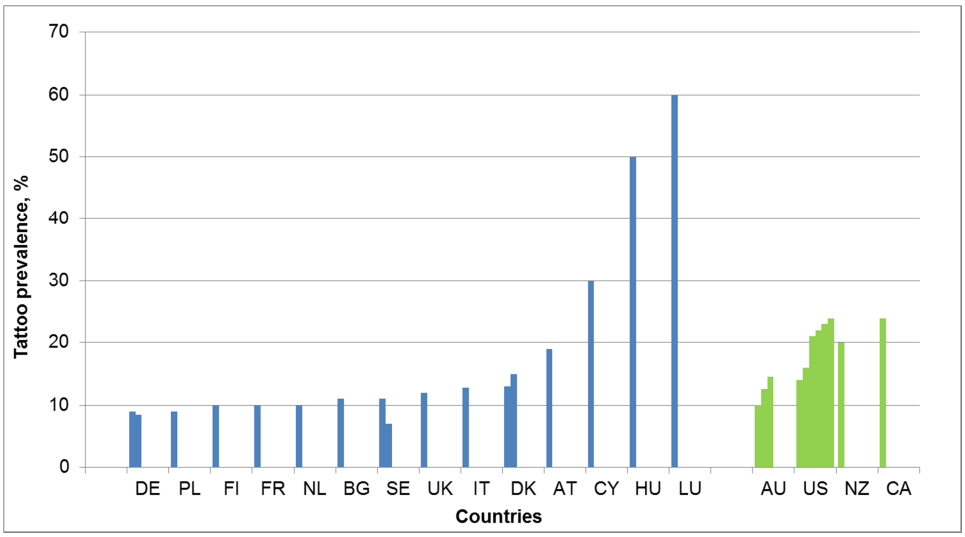



**Figure 5.1:** Tattoo prevalence in the general population in the world.

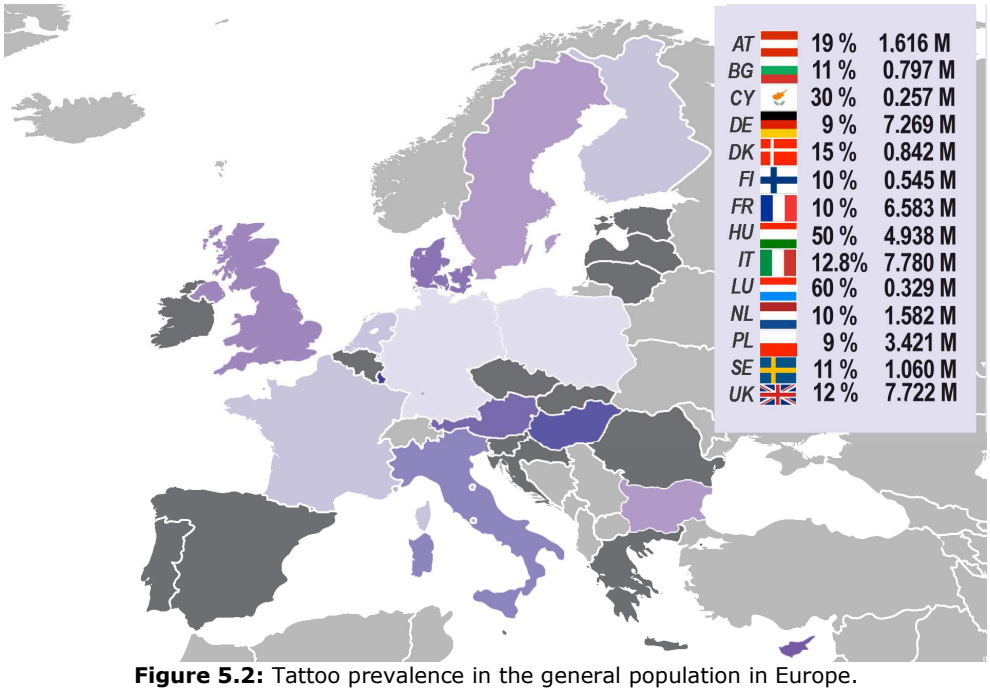



**Figure 5.2:** Tattoo prevalence in the general population in Europe.

The tattoo prevalence in the general population in Canada, New Zealand and the United States is higher than in Europe while in Australia is quite similar to Europe, as shown in Fig. 5.1 and Table 5.1.

Permanent make-up was seldom reported and data vary considerably in Europe (Table 5.2). No data were available for countries outside Europe.

**Table 5.1** Tattoo prevalence in the general population in the world.

| Countries | Prevalence (%) |
|---|---|
| **Europe** | 12 |
| **Australia** | 10-14.5 |
| **New Zealand** | 20 |
| **United States** | 21-24 |
| **Canada** | 24 |

**Table 5.2:** PMU prevalence in the general population in Europe.

| Countries | Prevalence (%) |
|---|---|
| **Italy** | 3 |
| **Bulgaria** | 8 |
| **Cyprus** | 20 |

### 5.1.2. Influence of age

Data on tattoo prevalence in various age ranges are available for some European countries (Austria, Denmark, Finland, France, Germany, Iceland, Italy, Norway and The Netherlands), plus Canada and the United States (questionnaires and [12, 34, 35, 38, 51, 52, 55-57, 59-69]). As example, Figure 5.3 reports the situation in France. The horizontal red line represents the tattoo prevalence in the general population in this country.

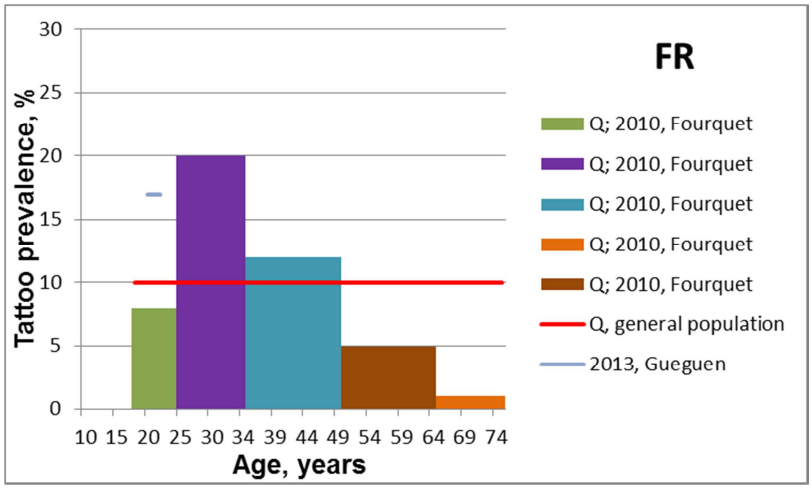



**Figure 5.3:** Tattoo prevalence in the various age ranges in France.

The influence of age on the tattoo prevalence is remarkable. As shown in Figure 5.4, teenagers between 12-19 years old, whether from Europe or North America, have tattoos with prevalence in the range 2-9%.

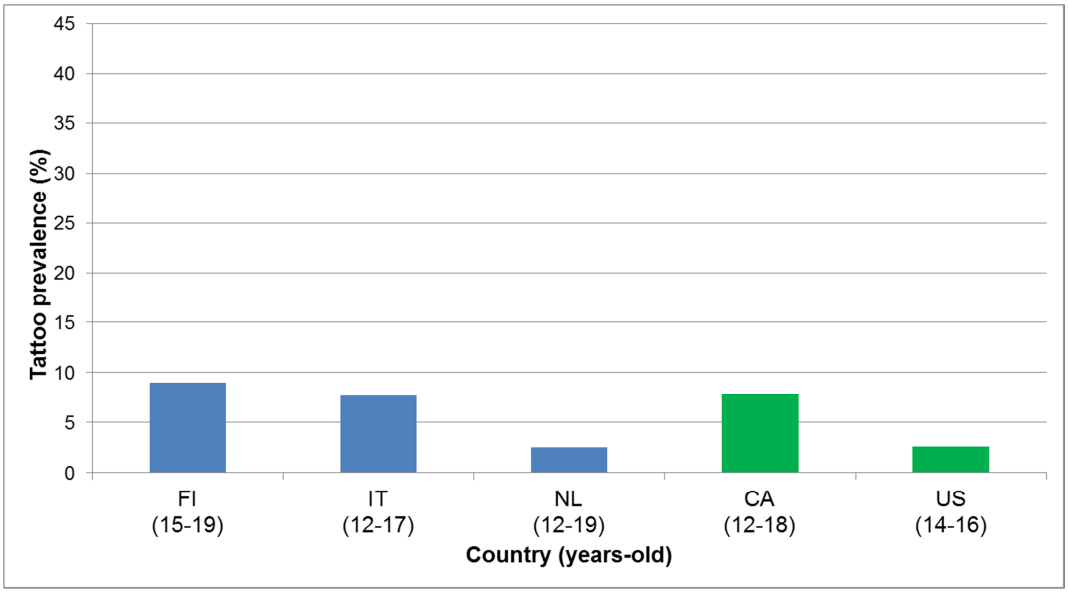



**Figure 5.4:** Tattoo prevalence in teenagers in and outside Europe.

Table 5.3 shows the prevalence of tattoos in the general population of some European and North America countries, as well as the ratio between the prevalence in certain age groups and the one in the general population of the considered country. Despite the difficulties of comparing data provided in different age ranges for various countries, common trends may be identified.

1) More in the young

The tattoo prevalence in the young generations is around 20-30% in Europe and up to almost 40% in the US (Figure 5.5). It is higher than in the general population in each country and can reach almost the double (Finland, France and Italy) and in some cases even more (Germany and The Netherlands). If this trend continues, the prevalence in the general population will increase in the next decades.

2) Less in the older

The tattoo prevalence significantly decreases for people over fifty and it is usually lower than 10%, with just few exceptions.

The information taken into consideration come from the questionnaires, as well as from the literature [12, 34, 35, 38, 51, 52, 55-57, 59-69].

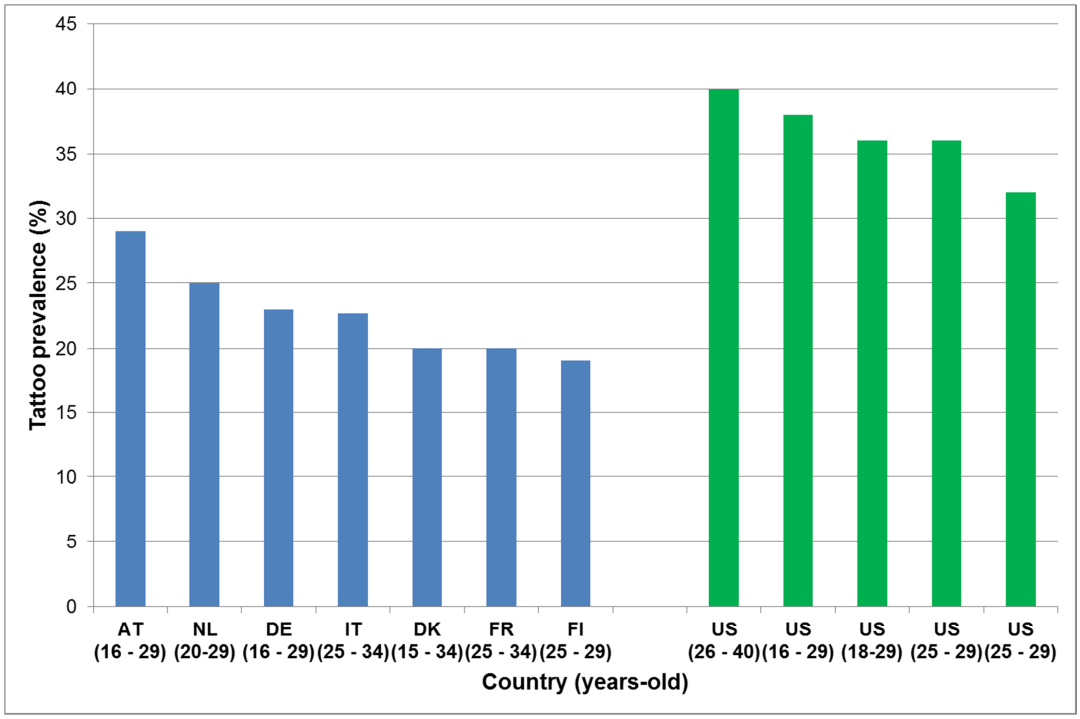



**Figure 5.5:** Tattoo prevalence in the young generations in and outside Europe.

**Table 5.3:** Influence of age on the tattoo prevalence in different age groups in and outside Europe.

| Country | general tattoo prevalence (%) | Age range (years) | tattoo prevalence ratio | Age range (years) | tattoo prevalence ratio | Age range (years) | tattoo prevalence ratio | Age range (years) | tattoo prevalence ratio | Age range (years) | tattoo prevalence ratio | Age range (years) | tattoo prevalence ratio |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| In Europe | | | | | | | | | | | | | |
| AT | 19 | | | | | 16 - 29 | 1.5 | 30 - 49 | 1.4 | 50+ | 0.4 | | |
| DE | 9 | | | | | 16 - 29 | 2.6 | 30 - 44 | 1.1 | 45 - 59 | 0.7 | 59+ | 0.2 |
| DK | 15 | | | | | 15 - 34 | 1.3 | 35 - 49 | 1.3 | 50 - 64 | 0.6 | 65 - 74 | 0.2 |
| FI | 10 | 15 - 19 | 0.9 | 20 - 24 | 1.2 | 25 - 29 | 1.9 | | | | | | |
| FR | 10 | | | 18 - 24 | 0.8 | 25 - 34 | 2.0 | 35 - 49 | 1.2 | 50 - 64 | 0.5 | 64+ | 0.1 |
| IT | 12.8 | 12 - 17 | 0.6 | 18 - 24 | 1.7 | 25 - 34 | 1.8 | 35 - 44 | 1.9 | 45 - 54 | 1.2 | 54+ | 0.2 |
| NL | 10 | 12 - 19 | 0.2 | | | 20 - 29 | 2.5 | 30 - 49 | 2.7 | 50 - 59 | 1.2 | 59+ | 1 |
| Outside Europe | | | | | | | | | | | | | |
| CA | 24 | 12 - 18 | 0.3 | | | | | | | | | | |
| US | 21 | | | 16 - 24 | 1.0 | 25 - 29 | 1.4 | 30 - 39 | 1.8 | 40 - 49 | 1.3 | 50 - 64 | 0.5 |
| | 23 | | | | | 16 - 29 | 1.6 | 30 - 45 | 1.4 | 46 - 64 | 0.6 | 64+ | 0.3 |
| | 14 | | | 18 - 24 | 0.6 | 25 - 29 | 2.3 | 30 - 39 | 1.8 | 40 - 49 | 0.9 | 50 - 64+ | 0.6 |
| | 24 | | | 18 - 25 | 1.5 | 26 - 40 | 1.7 | | | 41 - 64 | 0.4 | | |
| | 24 | | | | | 18 - 29 | 1.5 | 30 - 40 | 1.0 | 41 - 50 | 0.6 | | |
| | 16 | | | 18 - 24 | 0.8 | 25 - 29 | 2.2 | 30 - 39 | 1.7 | 40 - 49 | 0.9 | 50 - 64 | 0.6 |
| | 21 | 14 - 16 | 0.1 | 17 - 21 | 0.4 | | | | | | | | |

The first tattoo is very often got when people are young (less than 30 years old) or even adolescent. In Denmark 37% of the tattooed people got their first tattoo when they were less than 20 years old, this percentage becomes 44% and 18% (for teenagers less than 18 years old) in France and Germany, respectively. Table 5.4 reports the percentage of people who received their tattoo(s) before the age indicated in the first column. The information was retrieved from the questionnaires, as well as in the following publications [56, 68, 70, 71].

Only little information was collected with regards to the age of getting the first PMU; however, the trend seems to be that, in general, this age is higher than the one for the first tattoo.

**Table 5.4:** Age of first tattoo.

| Country | Age (Years) | Frequency (%) |
|---|---|---|
| In Europe | | |
| **Denmark** | <35 | 86 |
| **France** | <30 | 84,8 |
| **Germany** | <36 | 94,6 |
| Outside Europe | | |
| **Canada** | <43 | 60 |
| **United States** | <24 | 65 |

### 5.1.3. Influence of gender

While in the past women represented a minority of the tattooed population, nowadays this is not always the case. According to recent studies, women represent the majority of the tattooed population in Denmark, Italy and the United States. This new tendency seems to be more pronounced in adolescents and young generations in Europe, Australia and North America (questionnaires and [38, 50, 52-57, 63-69, 72-76]).

## 5.2. Exposure

The level of exposure to chemicals due to the presence of tattoos depends on several factors, among which the quantity of inks injected in the derma and the number and size of the tattoo(s).

The quantity of pigment used for performing a tattoo has been experimentally evaluated and described in the literature [77]. Just after the application, on average around 2.53 mg of pigment were present in 1 cm² of skin. This would mean that for a tattoo of about 400 cm², the skin contains a total amount of 1 g of pigment.

The size of a tattoo can greatly vary and in the literature different classifications exist and various units are used (Table 5.5) [10, 13, 16, 17, 56, 70, 71, 77-79]. The Belgian "Conseil Supérieur de la Santé" (CSS) reported that a tattoo covering one arm, the back or the entire body is about 800, 4500 and 16400 $cm^2$, respectively. Tattoos can broadly be divided into small, medium and large according to their area.

**Table 5.5:** Size of tattoo.

| Ranges | Surface (cm²) | Localisation | Surface (cm²) | Units |
|---|---|---|---|---|
| **Small** | ≤ 30 | **Arm** | 800 | % of body skin |
| **Medium** | 30 – 300 | **Back** | 4500 | Hand palm |
| **Large** | ≥ 300 | **Entire body** | 16400 | cm² |

An internet survey with 3411 participants [70] showed that most tattooed German people (61%) have tattoos bigger than 300 cm² (16% even larger than 900 $cm^2$), while in Denmark and the United States tattoos are smaller than 182 cm² in about 70% of cases according to studies with less than 350 participants [56, 80]. Regarding the difference between genders, tattoos in women tend to be smaller than in men, usually smaller than 182 cm², both in Europe and in the US.

In the general tattooed population more than 50% usually have their tattoos placed on the extremities, followed by the trunk and by the head/neck, which generally represent less than 5%. Localisation seems to depend on gender and women more often tattoo

their trunk compared to men who rather do it on their extremities (arms and legs) [56, 67, 70, 71, 74, 78]

Apart from few exceptions, both data from the questionnaires and from the literature showed that at least half of the tattooed people have more than one tattoo. No clear trend related to gender can be derived from the data available. However, according to the biggest study [70] the majority of women and men have 2-3, or 4 and more tattoos respectively.

Most tattoos are single coloured and black (50-60%). Other popular colours in descending order are red, blue, green, yellow and white [70, 80].

## 5.3. Regrets and removals

Together with the increase of the number of tattooed people also the number of regrets, sometimes associated to a request for removal, has increased during the last years. Reasons behind the decision to undergo a removal procedure include aesthetic reason, medical problems or simply whish not to have it anymore [81].

Early removal procedures, no longer in use, consisted of mechanical destructive methods (often resulted in permanent scars, important residual tattoo and infections), such as dermabrasion or salabrasion. The use of trichloroacetic acid and of the so called glycolic acid mixture (lactic, tartaric, malic and glycolic acid) also became of routinely use and it is still used nowadays as cheap alternative to the modern laser technique. It is worth mentioning the surgical excision of tattoos that is still considered in emergency cases (strong allergic reaction to the tattoo to be treated immediately). Finally, thermal procedures such as electrocautery, infrared coagulation, argon lasers, and $CO_2$ lasers have also been exploited with mediocre results.

Nowadays, the most widespread technique to achieve a safe, selective and efficient tattoo removal is represented by Quality-switched lasers which represent, since early 90s, the gold standard for tattoo removal [82, 83]. Although Q-switched lasers have made tremendous steps in advancing safety and selectivity of removal, both temporary and permanent side effects might still occur and are discussed in Chapter 9 of this document. QS Lasers produce short pulses of intense light that cross the skin to fragment the pigment into small particles [13].

Although data are scarce, questionnaires and publications did provide some figures that can be summarised as follows (Figure 5.6): regrets in Europe range from 5-20%, while in the United States values are more consistent and spread around 14-17% and in Canada are estimated at 17% [2, 10, 37, 38, 55-57, 67, 70, 78]. The number of removals is generally smaller than the number of regrets.

However, in a recent review, Laux reported that up to 50% of the tattooed individuals regret their tattoos [84].

According to a German study, 33% of the individuals who did the removal process were not satisfied with the results, while 38% reported a complete removal of pigment [85].

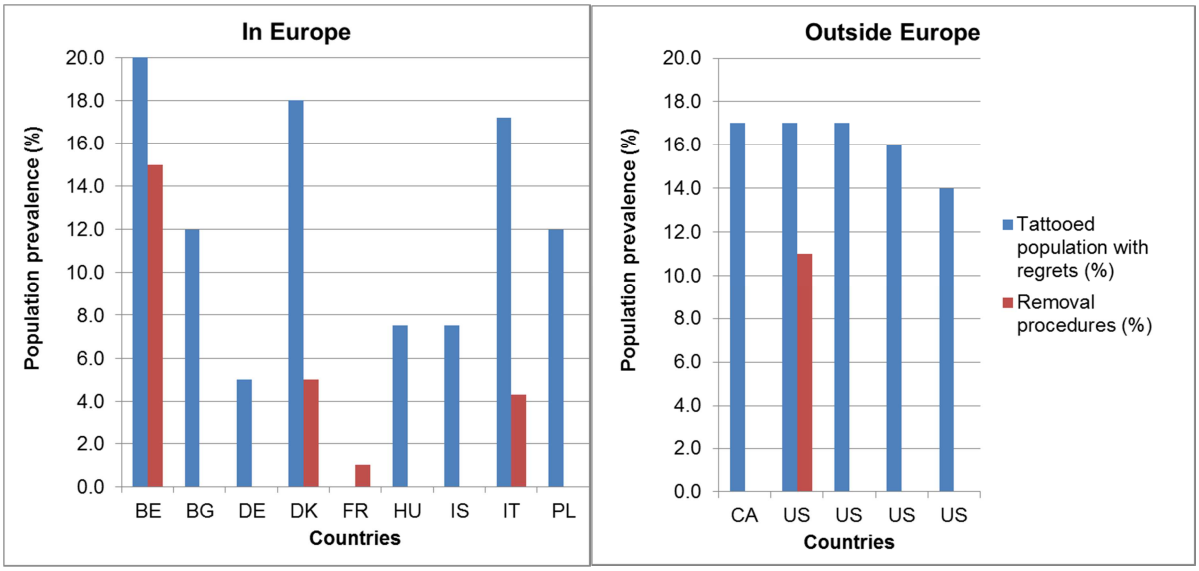



**Figure 5.6:** Prevalence of regrets and removals in and outside Europe.

## 5.4. Market

### 5.4.1. Studios and artists

As expected, the bigger the country, the more tattooist studios, whether professional or non-professional, were reported in the questionnaires and/or in the literature: 50-8000 registered studios and 100-5000 non-registered studios per European country. At the same time, 8-10000 and 16-30000 registered and non-registered artists were estimated, respectively.

When comparing the ratio of number of professional tattooists to the number of inhabitants, the north of Europe takes the lead with up to 9.4 tattooist/30000 inhabitants in Sweden, lowering down to around 1.4 in France or Italy for example. The data also show that tattooist usually work alone in their studio. In view of the widespread number of studios, the legislation application and overseeing can thus prove to be challenging.

The detailed data set is available in the previous JRC report (JRC, Annexes III and VI) and in the literature [20, 27, 37, 47].

### 5.4.2. Tattooist associations

Tattooist associations note that the distinction between professional and non-professional studios/artists is a challenge as an official registration system is not in place (Sweden) and the estimation of so-called 'home scratchers' is difficult (Italy, Sweden, Spain). These associations are an attempt to 'monitor' somehow the profession. Although Sweden, Norway and Denmark have the most tattooists/inhabitant, two more southern countries (Italy, Germany) and the United Kingdom account for half of the identified European tattooist associations (Figure 5.7). According to the membership in these associations, a minority of tattooists are affiliated.

Several tattooist associations were reported also for Canada and the United States, 10 and 13 respectively.

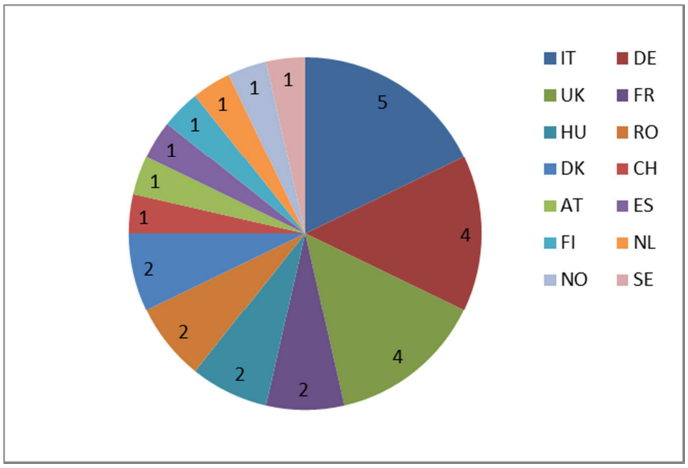



**Figure 5.7:** Tattooist and/or PMU professional associations per European country.

### 5.4.3. Ink origin and manufacture

According to both questionnaires and literature [86], the majority (70-80%) of the tattoo inks available on the European market are manufactured outside Europe, mainly in the United States. According to Michel's presentation and paper, it seems that professional tattoo artists would preferably use the US inks, while the non-professionals favour the Chinese products [86, 87].

On the contrary, 70-80% of the PMU inks on the EU market are made in Europe. Germany, Italy, Spain and the United Kingdom are the main EU manufacturers of tattoo/PMU inks.

While the above market trends for identifying the major producing countries are clear, when searching deeper for more market details, the situation becomes more confused. This study identified a non-exhaustive list of ink manufacturers/distributors/private labels based on the member states responses to the questionnaires and an internet search with 92 and 35 companies producing and/or distributing tattoo and PMU inks, respectively. The situation is complex and it was not possible to differentiate between manufacturers and distributors. An additional difficulty is represented by the fact that the same manufacturer may produce more than one brand of products and that in the market there are the so called "private labels", meaning that some manufacturers produce for other companies that put their brand name on the final products.

### 5.4.4. Brands and labelling

Internet data also enabled to prepare a non-exhaustive list of 72 and 22 tattoo and PMU ink brands, some of which can be purchased online on many different web sites. This study identified as many as 39 tattoo ink web suppliers. The most popular brands were selected on the base of the number of web sites selling those (Tables 5.6 and 5.7).

**Table 5.6:** Top tattoo ink brands sold on-line (ordered by presence in web-sites).

| Brand name | Suppliers Nr | Price €/ml | Capacity ml |
|---|---|---|---|
| Eternal Inks | 28 | 0.35 | 30, 60, 120 |
| Intenze Tattoo Inks | 22 | 0.35 | 30, 60, 90 |
| Panthera Tattoo Inks | 19 | 0.20 | 150 |
| Kuro Sumi Tattoo Inks | 16 | 0.15 | 180 |
| Starbrite Colors Inks | 14 | 0.35 | 15, 30, 60, 90 |
| Silverback Inks | 13 | 0.30 | 120 |
| Cheyenne Inks | 12 | 0.35 | 50 |
| Dynamic Tattoo Inks | 12 | 0.15 | 240 |
| Fusion Inks | 10 | 0.35 | 60 |
| Mom's Inks | 10 | 0.15 | 15, 30 |
| Alla Prima Inks | 8 | 0.35 | 30 |
| Sacred Color Tattoo Inks | 7 | 0.60 | 15, 30 |
| Bloodline & Skin Candy Tattoo Inks | 7 | 0.35 | 30, 60 |
| Atomic Inks | 6 | 0.65 | 30 |
| Talens Inks | 6 | 0.10 | 490 |
| Makkuro Sumi Inks | 5 | 0.15 | 120, 360 |
| Fusion Inks | 4 | 0.70 | 15, 30 |
| Electric Inks | 3 | 0.30 | 30, 60 |
| Polynesian Inks | 3 | 0.10 | 200 |

**Table 5.7:** Top PMU ink brands sold on-line (ordered by presence in web-sites).

| Brand name | Suppliers Nr | Price €/ml | Capacity ml |
|---|---|---|---|
| Cosmetic Partner | 2 | 3.8 | 15 |
| Pure Colours | 2 | 3.2 | 15 |
| Bella Pigment | 1 | 2.5 | 15 |
| Glam Colours | 1 | 4.3 | 2, 15 |
| Maube | 1 | 2.6 | 15 |

The responses of the manufacturers to the questionnaires were very low probably due to confidentiality and competition issues. Although the mailing list counted 38 recipients, only 7 answered and from 2 countries, Germany and Italy.

The few data received regarding volume, price and container type are summarised in Table 5.8.

**Table 5.8:** Tattoo and PMU inks in figures.

| | Production volume ($m^3$/year) | Price (Euro/ml) | Type of container |
|---|---|---|---|
| **Tattoo** | 2-10 | 0.1-0.5 | Single/Multiple use |
| **PMU** | 0.05-1.15 | 0.45-5.9 | Single/Multiple use |

The list of items on the label of ink containers is similar for all respondents even if some do add additional items in certain cases:

- List of ingredients (using INCI, International Nomenclature of Cosmetic Ingredients, CI, Colour Index, or IUPAC, International Union of Pure and Applied Chemistry, numbers in decreasing order of concentration);
- Manufacturer name and address;
- Date of minimum durability;
- Conditions of use and warnings;
- Batch number;
- Guarantee of sterility of the contents.

# 6. Ingredients of tattoo and PMU inks

Tattooing consists in the injection of inks in the derma stratum of the skin. Therefore, tattoos and PMUs are aimed to be permanent, causing a life-long exposure to chemicals which entails possible adverse health effect that may be linked to their toxicity. For such reason, the knowledge of ink ingredients and their fate in the body, including under light irradiation, is extremely important.

This chapter aims to give an overview of the ingredients currently used in tattoo and PMU ink formulations and to present what is known about colorants' fate. For more detailed information, please refer to the JRC report on Work Package 2 [2].

As mentioned in chapter 2, the information was collected through questionnaires, as well as web and literature searches.

Tattoo and PMU inks are complex formulations containing several ingredients, both inorganic and organic, plus by-products and impurities. Nowadays, they are generally ready-to-use-products that consist in mixtures of insoluble pigments (responsible for the colour) in a liquid made of binder(s) and solvent(s). The suspension is stabilised by additives, which among other actions help slowing down the sedimentation of pigments and re-dispersing them quickly under slight manual shaking. In order to avoid microbiological contamination, favoured by the usual high content of water and organic substances, preservatives are often added to the mixture [88]. Besides intentional ingredients (colorants and additives), other substances might be present as impurities for example originating from their synthetic processes. The main impurities found in tattoo and PMU inks are primary aromatic amines (PAA), from azo-colorants, polycyclic aromatic hydrocarbons (PAH), mainly from black inks, and metals, from inorganic and organometallic pigments.

## 6.1. Colorants

Colorants are by far the major ingredients of tattoo and PMU inks, being present in a concentration that can reach almost 60% by weight. They are responsible for the ink colour and can be classified into two main groups, namely pigments and dyes. While **dyes** are soluble in the vehicle in which they are incorporated and fast biodegradable, **pigments** are insoluble, photo-stable and chemical resistant thus making them the preferred choice for tattoo and PMU applications. Dyes are scarcely used and, when this is the case more often in PMU than in tattoo inks, they are made insoluble by precipitating them onto an insoluble inorganic compound, like barium sulphate and aluminium hydroxide, to form a **lake**, more stable to both light and other chemicals.

From the chemical point of view, pigments can be classified as organic or inorganic substances. **Inorganic pigments** show dull and not-brilliant shadows of colour and for these properties they are more frequently used in PMU than in tattoo inks. They are oxides of several elements, in particular iron, titanium and chromium.

In comparison, **organic pigments**, besides being more brilliant, show higher colour strength when mixed with barium sulphate and titanium oxide, cover a much wider range of colours and are mainly used in tattoo inks. Nevertheless, organic pigments show the drawback of having poorer dispersibility properties which are pivotal to obtain a good dispersion of the pigment (insoluble) into the vehicle.

According to the Colour Index classification made by chemical structures, the organic colorants identified as currently in use in tattoo and PMU products belong to the following classes: monoazo, diazo, xanthene, natural dyes, indigoid, anthraquinone, aminoketone, heterocycle, quinoline, triarylmethane, phthalocyanine, pyrrole ketone and oxazine.

The survey allowed identifying (Table 6.1) 113 colorants, currently used as ingredients in tattoo inks, and 100 in PMU inks (in total 126 different structures).

**Table 6.1**: Overview of colorants used in tattoo and PMU inks by colour.

| | Tattoo | | | | PMU | | | |
|---|---|---|---|---|---|---|---|---|
| | colorants | organic colorants | azo colorants | inorganic colorants | colorants | organic colorants | azo colorants | inorganic colorants |
| Colour | number | % | % | % | number | % | % | % |
| Red | 44 | 93 | 68 | 5 | 42 | 95 | 64 | 5 |
| Yellow | 27 | 93 | 78 | 7 | 25 | 96 | 80 | 4 |
| Orange | 10 | 100 | 70 | 0 | 8 | 100 | 75 | 0 |
| Blue | 7 | 71 | 13 | 29 | 5 | 60 | 0 | 40 |
| Green | 4 | 75 | 0 | 25 | 5 | 60 | 0 | 40 |
| Violet | 9 | 78 | 0 | 22 | 6 | 83 | 0 | 17 |
| Brown | 3 | 33 | 33 | 33 | 2 | 50 | 50 | 50 |
| Black | 6 | 0 | 0 | 83 | 4 | 0 | 0 | 100 |
| White | 3 | 0 | 0 | 100 | 3 | 0 | 0 | 100 |
| | 113 | | | | 100 | | | |

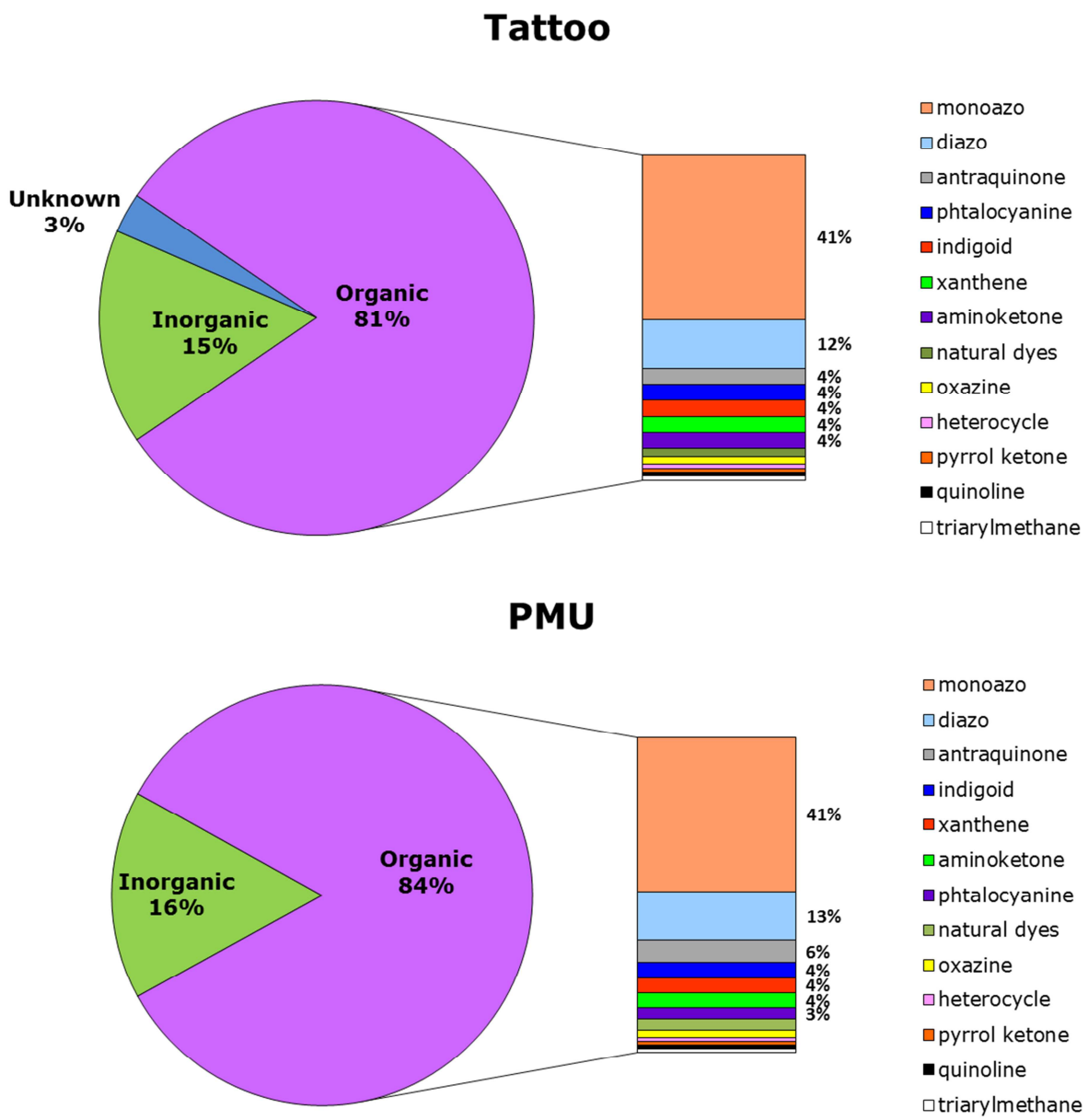



**Figure 6.1**: Classification of colorants. Organic/inorganic distribution and organic chemical classes.

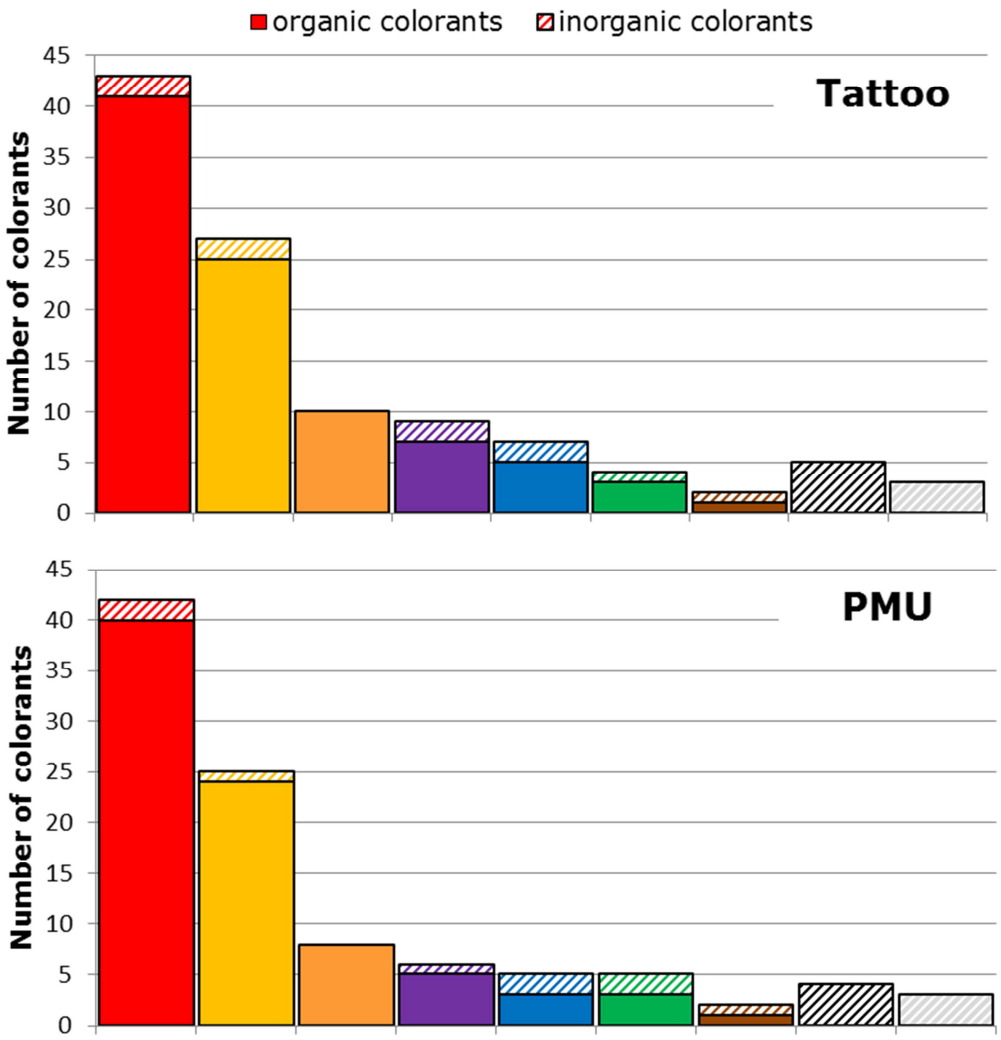



**Figure 6.2**: Number of organic/inorganic colorants used in tattoo and PMU inks by hue.

The survey pointed out that organic colorants nowadays represent the large majority of the pigments in use. The situation about 20-30 years ago was the opposite. It also highlights the fact that inorganic pigments linked to negative health effects, such as cadmium or mercury sulphide, are no more employed. They have been mainly substituted by synthetic colorants. Our results are in line with what reported by Bäumler et al. in 2003 [89].

In details, Table 6.1 summarises the percentages of organic, azo and inorganic colorants, divided by colours, used in tattoo and PMU products, respectively. As shown also in Figure 6.1, the large majority consists of organic colorants (92 and 84 corresponding to 81% and 84% for tattoo and PMU respectively). Among the organic colorants, the chemical class of azo pigments is the most represented (60 and 54, corresponding to 65% and 64% of the organic class and 53% and 54% of all colorants). It is worth noticing that for three colorants used in tattoo inks (pigment red 340, pigment brown 175 and pigment black 2) it was not possible to gather information on the chemical structure, therefore they were classified neither as inorganic nor as organic. Figure 6.1 provides also information about the frequency of organic classes. Organic pigments are dominated by azo colorants, followed by anthraquinone, phthalocyanine, indigoid, xanthene and aminoketone classes.

Figure 6.2 shows the prevalence of identified organic/inorganic colorants (expressed as number of colorants) for each hue of tattoo and PMU inks. The pigments used for black and white hues are all inorganic, whereas the orange ones are all organic.

Although none of the colorants in use is classified as carcinogenic, mutagenic or reprotoxic (CMR) substance under the EC Regulation 1272/2008 on Classification, Labelling and Packaging (CLP), 18% and 21% of the colorants used respectively in tattoo and PMU inks are actually included in some negative lists mentioned in the CoE ResAP(2008)1. An overview of the aforementioned colorants, with the reference to the list where they are included, is given in Table 6.2.

The following pigments are only listed in Annex II of the cosmetic regulation for their use in hair colorants (HC): solvent red 1, pigments red 4, 5, 48:1 and 63:1, pigment yellow 12 and pigment blue 15. However, it is important to note that according to industry there is no better alternative to pigment blue 15.

**Table 6.2**: List of colorants in use included in some negative lists mentioned in the CoE ResAP(2008)1.

| Colour Index Generic Name | Chemical class | Tattoo(T)/PMU(P) | Negative lists |
|---|---|---|---|
| BR 1 | xanthene | T/P | CoEResAP(2008)1 Table 2 |
| SR 1 | monoazo | P | Cosmetics, Annex II in HC |
| PR 3 | monoazo | T/P | Cosmetics, column g Annex IV (only rinse-off) |
| PR 4 | monoazo | T/P | Cosmetics, Annex II in HC; **permitted** in Annex IV |
| PR 5 | monoazo | T/P | Cosmetics, Annex II in HC; **permitted** in Annex IV |
| PR 7 | monoazo | P | Cosmetics, column g Annex IV (only for rinse-off) |
| PR 48:1 | monoazo | T | Cosmetics, Annex II in HC |
| PR 53:1 | monoazo | T/P | CoEResAP(2008)1 Table 2 & Cosmetics, Annex II |
| PR 63:1 | monoazo | T/P | Cosmetics, Annex II in HC; **permitted** in Annex IV |
| PR 112 | monoazo | T/P | Cosmetics, Annex II in HC & column g Annex IV (only rinse-off) |
| PR 122 | indigoid | T/P | Cosmetics, column g Annex IV (only rinse-off) |
| PY 1 | monoazo | T/P | Cosmetics, column g Annex IV (no on mucous membranes) |
| PY 3 | monoazo | T/P | Cosmetics, column g Annex IV (no on mucous membranes) |
| PY 12 | diazo | T/P | Cosmetics, Annex II in HC |
| PY 83 | diazo | T/P | Cosmetics, column g Annex IV (only rinse-off) |
| PB 15 | phthalocyanine | T/P | Cosmetics, Annex II in HC; **permitted** in Annex IV |
| DB 86 | phthalocyanine | T | Annex II in HC & Annex IV (only rinse-off) |
| BV 10 | xanthene | T/P | CoEResAP(2008)1 Table 2 & Cosmetics, Annex II |
| PV 19 | indigoid | T/P | Cosmetics, Annex II in HC & column g Annex IV (only rinse-off) |
| PV 23 | oxazine | T/P | Cosmetics, Annex II in HC & column g Annex IV (only rinse-off) |
| PO 5 | monoazo | T/P | CoEResAP(2008)1 Table 2 & Cosmetics, Annex II |
| PO 43 | anthraquinone | T/P | Cosmetics, column g Annex IV (no on mucous membranes) |
| PG 7 | phthalocyanine | T/P | Cosmetics, Annex II in HC & column g Annex IV (no in eye prods) |

In addition, it is worth mentioning that only just above 30% of the colorants used in tattoo and PMU inks are authorised in cosmetic products without any restriction.

An important problem highlighted by several authors [90-93] and stakeholders is that the pigments used in the formulation of tattoo and PMU inks are not produced for such purpose and do not undergo any risk assessment that takes into account their injection into the human body for long term permanence. They are usually produced by the

chemical industry for outdoor applications in products like textiles, cars and plastics, because they show good light fastness properties. Pigment producers do not state that their colorants can be used in tattoo and PMU products, even if this happen, and they are reluctant to take responsibility. In certain cases they refuse to sell their products to ink manufacturers when they know they are going to be used for manufacturing tattoo inks.

The fact that pigments are produced as technical products for different purposes poses the problem of their purity which has been reported to range between 70 and maximum 90% (depending on the source). They may contain harmful impurities and by-products such as: chromium VI in chromium oxides; nickel, chromium, copper and cobalt in iron oxides; aromatic amines in azo-colorants; and polycyclic aromatic hydrocarbons in carbon black.

Concerning the size of pigment particles, nanoparticles (NPs) can indeed be utilised to manufacture modern tattoo inks of high-quality and desired behaviour (e.g., brilliantness, fluorescence, persistence, photo stability) [94]. In a 2000 study on 41 tattoo inks, 16 different synthetic colorants were determined and $TiO_2$ was found as lightener, both in anatase and rutile form; the crystal size varied in the range 20 - 900 nanometres [95]. In 2011, NPs were actually found in tattoo inks, with black pigments containing the smallest particles (< 100 nm), white pigments having the largest particles and coloured pigments (green, blue, red and yellow) in between [96]. In 2015, NPs of tattoo inks were observed in human skin tissue, as well as on dermal fibroblasts *in vitro*, and analysed by atomic force microscopy [97, 98]. Recently, some authors have reported that tattoo inks contained metal-based NPs [99, 100]. Black colours contained the smallest particles (< 100 nm), mainly constituted of carbon black. Coloured tattoo inks (violet, blue and green) contained aluminium (Al) and titanium (Ti) in the form of $TiO_2$ as micron and submicron sized particles and aggregates. On the contrary, copper (Cu) was almost exclusively found (ca. 90%) in the form of NPs (< 100 nm) in blue, green and black pigments.

The presence of NPs in tattoo inks requires an accurate assessment of their interaction with the human skin, as well as an investigation to understand if they can penetrate the derma reaching the bloodstream.

## 6.2. Ingredients other than colorants

Additives such as surfactants, thickening agents and preservatives are used in tattoo inks and PMUs, in concentrations generally lower than 5% by weight, to modify certain characteristics, stabilise the dispersion and avoid the growth of microorganisms in the product after opening.

Auxiliaries include a variety of compounds, among which:

- **surfactants**, employed to adjust surface tension, helping better dispersion and stabilisation of pigments;
- **thixotropic agents** (e.g. silica), which inhibit the sedimentation of pigment dispersions during long storage time;
- **binding agents** (e.g. polyethers, polyvinylpyrrolidone, block copolymer and Shellac) which are non-volatile high molecular mass compounds, whose function is to bind pigment particles both to each other and to the tattooing needle with the aim to make easier the injection of tattoo and PMU ink in the skin;
- **fillers**, usually inorganic substances (e.g. silica and barium sulphate), which influence dispersibility properties helping better re-dispersion of pigments after long storage. Barium sulphate is used in the flocculation of organic pigments to optimise their dispersibility [94].

**Preservatives** ensure the preservation of the product after opening and were found in concentration up to 1.5% by weight.

Alcohols, for instance ethanol and isopropyl alcohol, can be used to modify the drying properties, viscosity and dispersibility of inks. Glycerine can be added as ingredients as it acts as humectant and helps increasing viscosity, while propylene glycol can be used as humectant and to increase dispersibility. Their concentration can reach up to 30% by weight.

Finally, water is the main **solvent** in use, able to solubilise and solvate binder(s).

The information collected allowed identifying a list of 100 auxiliaries and 48 preservatives. 99 and 70 auxiliaries and 47 and 30 preservatives were reported to be used in tattoo and PMU inks, respectively.

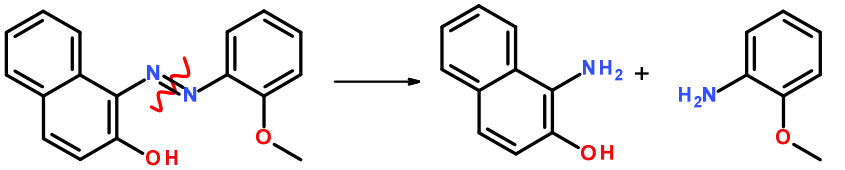
## 6.3. Fate of colorants

As already mentioned, the large majority of the organic colorants used in tattoo and PMU formulations belong to the chemical class of azo pigments. The fate of these compounds is discussed hereafter.

It is know from the literature that free azo dyes may undergo metabolic reductive cleavage into aromatic amines upon oral intake either in lumen of the gastric tract or in the liver after uptake from the intestine. According to Platzek T. et al. [101], such cleavage may occur even on the skin due to influence of the skin bacteria.

Cui Y. et al. [102] showed that pigments could be metabolised *in vitro* by expressing cytochromes together with rat and human microsomal proteins. In addition, both *in-vivo* and *in-vitro* studies proved that the reductive cleavage of azo pigments into aromatic amines can also be triggered by solar, UV or laser irradiation, the latter being the preferred technique for tattoo removal [12, 26, 91, 103-108].

In total 31 out of the 67 azo colorants in use in tattoo and PMU products, corresponding to 46%, contain and might release, by simple reductive cleavage of the azo bond, one of the amines included in the negative lists cited in the CoE ResAP(2008)1, including Annex II of the cosmetic regulation and Table 3.1 of the CLP regulation. Figure 6.3 reports the example of solvent red 1.




Solvent Red 1

o-Anisidine
Carc 1B
Muta 2

**Figure 6.3:** Possible decomposition pathway of Solvent Red 1.

The scenario is further complicated by the fact that some of them may form aromatic amines included in the negative lists cited in the CoE ResAP(2008)1 also by cleavage of a different type of bond (e.g amide bond) [12, 26, 91, 103-108]. Therefore, it would be extremely important to take the full decomposition pathway, also under irradiation, in consideration when carrying out the risk assessment of a colorant for tattoo and PMU applications. One example of secondary reaction that leads to the formation aromatic amine classified as CMR is reported in Figure 6.4.

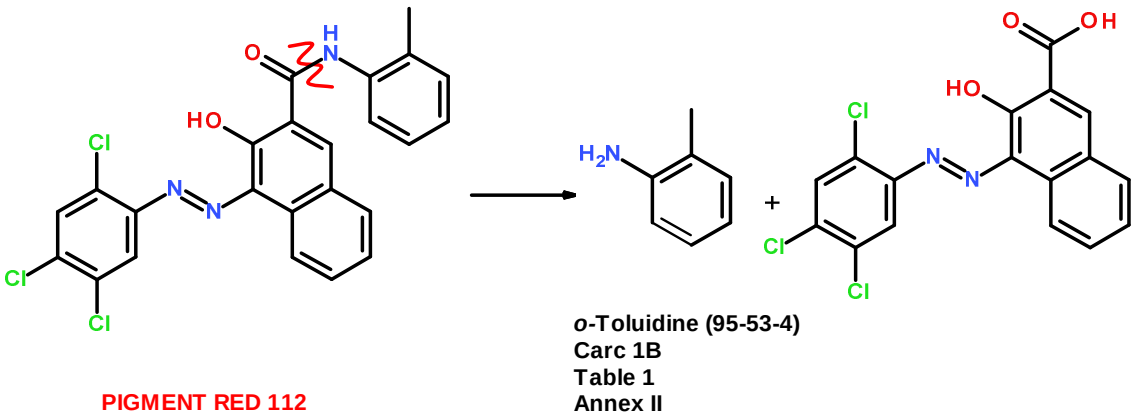



**Figure 6.4:** Possible decomposition pathway of Pigment Red 112.

When amide hydrolysis and simple reductive cleavage are taken into account all together, the number of azo-colorants that could potentially lead to the formation of one of the amines included in the negative lists cited in the CoE ResAP (2008)1 rises up to 44, corresponding to 66% of the 67 azo colorants in use (including tattoo and PMU). Table 6.3 contains the list of azo pigments in use that, theoretically, might release unsafe amines through one of the reaction mentioned above.

**Table 6.3:** List of azo-colorants in use that might potentially lead to unsafe amines by decomposition.

| | Cleavage of azo bond | Amide hydrolysis |
|---|---|---|
| PR 2 | halogenated derivative of aniline (Annex II, ref 22) | 62-53-3, aniline (Annex II ref 22, Table 3.1) |
| PR 7 | 95-69-2, 4-Cl-o-toluidine (Table 1, Annex II ref 32, Table 3.1) | 95-69-2, 4-Cl-o-toluidine (Table 1, Annex II ref 32, Table 3.1) |
| PR 9 | halogenated derivative of aniline (Annex II, ref 22) | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) |
| PR 12 | | 95-53-4, o-toluidine (Table 1, Annex II ref 32, Table 3.1) |
| PR 14 | | 95-53-4, o-toluidine (Table 1, Annex II ref 32, Table 3.1) |
| PR 15 | | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) |
| PR 17 | 99-55-8, 5-nitro-o-toluidine (Table 1, Annex II ref 1195, Table 3.1) | 95-53-4, o-toluidine (Table 1, Annex II ref 32, Table 3.1) |
| PR 22 | 99-55-8, 5-nitro-o-toluidine (Table 1, Annex II ref 1195, Table 3.1) | 62-53-3, aniline (Annex II ref 22, Table 3.1) |
| PR 48:1 | sulphonated and halogenated derivative of toluidine (Annex II, ref 32) | |
| PR 51 | sulphonated derivative of toluidine (Annex II, ref 32) | |
| PR 53:1 | sulphonated and halogenated derivative of toluidine (Annex II, ref 32) | |

| | Cleavage of azo bond | Amide hydrolysis |
|---|---|---|
| PR 57:1 | sulphonated derivative of toluidine (Annex II, ref 32) | |
| PR 57:2 | sulphonated derivative of toluidine (Annex II, ref 32) | |
| DR 53 | 92-87-5, benzidine (Table 1, Annex II ref 26, Table 3.1) | |
| PR 112 | halogenated derivative of aniline (Annex II, ref 22) | 95-53-4, o-toluidine (Table 1, Annex II ref 32, Table 3.1) |
| PR 146 | | 62-53-3, aniline (Annex II ref 22, table 3.1) |
| PR 210 | | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) |
| PR 222 | | 106-50-3, p-phenilendiamine (Table 1, Table 3.1) |
| PR 269 | | 62-53-3, aniline (Annex II ref 22, table 3.1) |
| SR 1 | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) | |
| PO 13 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | |
| PO 16 | 119-90-4, 3,3'-dimethossibenzidine (Table 1, Annex II ref 709, Table 3.1) | 62-53-3, aniline (Annex II ref 22, table 3.1) |
| PO 22 | halogenated derivative of aniline (Annex II, ref 22) | |
| PO 34 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | |
| PO 74 | | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) |
| AY 9 | sulphonated derivative of aniline (Annex II, ref 22) | |
| AY 23 | sulphonated derivative of aniline (Annex II, ref 22) | |
| AY 104 | sulphonated derivative of aniline (Annex II, ref 22) | |
| Diarylide Y | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | |
| FY 3 | sulphonated derivative of aniline (Annex II, ref 22) | |
| PY 1 | | 62-53-3, aniline (Annex II ref 22, table 3.1) |
| PY 12 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | 62-53-3, aniline (Annex II ref 22, table 3.1) |
| PY 14 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | 95-53-4, o-toluidine (Table 1, Annex II ref 32, Table 3.1) |
| PY 55 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | 95-53-4, p-toluidine (Annex II ref 32, Table 3.1) |
| PY 65 | | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) |
| PY 74 | | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) |
| PY 83 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | |

| | Cleavage of azo bond | Amide hydrolysis |
|---|---|---|
| PY 87 | 91-94-1, 3,3'-dichlorobenzidine (Table 1, Annex II ref 712, Table 3.1) | |
| PY 93 | | halogenated derivative of toluidine (Annex II, ref 32) |
| PY 97 | | 62-53-3, aniline (Annex II ref 22, table 3.1)-from sulphonamide hydrolysis |
| PY 100 | sulphonated derivative of aniline (Annex II, ref 22) | |
| PY 194 | 90-04-0, o-anisidine (Table 1, Annex II ref 708, Table 3.1) | |
| PB 25 | 119-90-4, 3,3'-dimethossibenzidine (Table 1, Annex II ref 709, Table 3.1) | 62-53-3, aniline (Annex II ref 22, table 3.1) |
| PBr 25 | halogenated derivative of aniline (Annex II, ref 22) | |

It has been proved that the initial quantity of pigment injected in human skin during tattooing processes decreases over time [106, 109]. Several mechanisms, such as bleeding, dispersion in the skin, phagocytosis, metabolism, transportation through the lymphatic or blood vessel systems and photodecomposition, have been suggested to explain these findings [102, 110]. So far, pigment particles have been found in macrophages, in the cytoplasm of cells in secondary lysosomes and in lymph nodes [111-120]. Moreover, it has to be considered that, once the degradation occurs, the increased solubility of the aromatic amines thus formed makes the transportation into the body fluids more likely.

Finally, it should not be neglected that not only colorants but also impurities, by-products and additives could be transported away from the skin. In this view, the fate of toxic substances, such as polycyclic aromatic hydrocarbons, primary aromatic amines and heavy metals is a concern. Lehner [115] reports that PAHs (originally present in black inks) remain partially in skin or can be found in the regional lymph nodes.

A further point to consider is the probable production of reactive oxygen species (ROS) from inks components and impurities in the presence of (sun) light. In particular if tattooed skin is exposed to UV radiation, some PAHs might generate singlet oxygen [121].

Høgsberg [122] proved that, in the absence of light, aggregation of tattoo pigment particles correlates with ROS production, independently of chemical composition including PAHs.

Cellular lipids and proteins could be oxidised by ROS and thus their functions might be compromised up to the point of causing in tattooed parts of the body adverse effects like sensation of pain, itching and discomfort [121-123].

Notwithstanding the formation of ROS can be diminished by the use of physical barriers to light, by sunscreen application on tattoos and by the intake of antioxidants [123].

# 7. Analytical methods

The CoE ResAP(2008)1 includes some negative lists of dangerous chemicals that should not be present or should not exceed a certain recommended concentration in tattoo and PMU inks:

- Table 1 (27 aromatic amines);
- Table 2 (35 colorants);
- Table 3 (suggested maximum concentration for 15 impurities).

The resolution also recommends adopting additional negative lists available in various EU legislations:

- Annexes II and IV (only colorants with restrictions in column g) of the Cosmetics Regulation [39];
- substances classified as carcinogenic, mutagenic and reprotoxic (CMR) categories 1A, 1B and 2, in Annex VI, Table 3.1 of the CLP Regulation [40].

In addition, the minimum requirements for further organic impurities for colorants used in foodstuffs, as specified by the Directive 95/45/EEC [41], should be respected.

The purpose of this chapter is to present the available analytical methods that can be used, as such or after modifications, for detecting the presence of these hazardous chemicals in tattoo/PMU products.

Particular attention was devoted to the test methods to determine aromatic amines, colorants, elements and polycyclic aromatic hydrocarbons (PAHs). Some of those substances are in Tables 1-3 of the CoE ResAP(2008)1, as well as in the other negative lists mentioned in the ResAP. More details about test methods and the complete inventory of the substances belonging to the before mentioned classes, which should not be present in tattoo/PMU inks, can be found in the JRC report on Work Package 1 [1]. It has to be noted, however, that the document does not have any legal value.

Phthalates and nitrosamines were also considered to some extent, as they were found in tattoo and PMU products and some of them are CMRs and are listed in Annex II of the cosmetic regulation [12, 122, 124].

Data on available methods were collected through a questionnaire that was specifically aimed to gather information on the following issues and via a web search of standard methods in the ISO (International Organization for Standardization) and CEN (European Committee for Standardization) catalogues:

1. international standard methods (harmonised at ISO and/or CEN level);
2. national standard methods (harmonised at national level, e.g. in Germany by DIN);
3. in-house validated methods (developed and validated in Member States' laboratories, not harmonised neither at national nor at international level);
4. analytical methods described in the literature.

As no standard test methods are available for the analysis of tattoo and PMU inks, analytical methods applicable to similar matrices, for instance cosmetics, food, textiles, toys and environment, were taken into consideration. With an adaptation of the sample preparation procedure these methods could be applied to tattoo and PMU products.

To complete the investigation, some analytical methods described in the literature were also collected.

A short description of all the identified test methods, including information about scope and field of application, principle, description of test method, type of instrumental

analysis, repeatability (r) and reproducibility (R), limit of detection (LOD) and limit of quantification (LOQ) was reported in the JRC report on Work Package 1 [1].

For each chemical class taken into consideration, Table 7.1 reports the current availability of analytical methods.

**Table 7.1**. Availability of analytical methods for the chemical classes of concern.

| Chemical class | International standard methods on different matrices | International standard methods adapted for tattoo/PMU matrix | National standard methods on different matrices | National standard methods adapted for tattoo/PMU matrix | In-house validated methods | Methods described in literature |
|---|---|---|---|---|---|---|
| PAAs | x | x | x | | x | x |
| Colorants | x | | | | x | x |
| PAHs | x | | x | | x | x |
| Heavy metals | x | x | x | | x | x |
| Phthalates | x | | | | | x |
| Nitrosamines | x | | | | x | x |

**Primary Aromatic Amines (PAA):** The presence of PAA in tattoo/PMU inks is linked to the use of azo pigments. PAA represent either impurities of these colorants ("free aromatic amines") or degradation products of them (in this case they are released through a mechanism called "reductive cleavage"). According to Table 1 of the CoE ResAP(2008)1, 27 aromatic amines should neither be present nor released from azo colorants in tattoo and PMU products; 25 of them are classified as CMR in categories 1A, 1B or 2 and 19 are listed in Annex II of the cosmetic Regulation.

No specific limit value is established for their content; nevertheless the resolution states that they should not exceed the concentration defined as "technically avoidable" when operating according to Good Manufacturing Practices. The same resolution states that "these aromatic amines should be determined by using appropriate test methods which should be harmonised across the Member States in order to ensure comparable health protection of the consumers and to avoid divergent enforcement, drawing on existing methods which can serve as models". Two analytical methods, which can serve as models for harmonising test methods, are proposed and summarised in the document. They are the adjustment of two existing international standard methods (EN 71-7:2002 and EN 14362-1) for the determination of aromatic amines in toys and textiles. Both of them entail the chromatographic (either GC-MS or LC-MS) analysis of the primary aromatic amines after a reductive approach that allows quantifying the sum of free and releasable aromatic amines. It is worth mentioning that EN 71-7:2002 reports also the conditions to be applied for the determination of just the free aromatic amines (impurities).

**Colorants:** Among the 35 colorants in the negative list (Table 2) of the CoE ResAP(2008)1, 7 are CMRs in categories 1A, 1B or 2, 13 are listed in Annex II of the cosmetic regulation and none of them is allowed to be used in cosmetics as they are not listed in Annex IV to the same regulation. The pigments in Table 2 belong to the following chemical classes of colorants: azo (16), triarylmethane (11), antraquinone (4), xanthene (3) and nitro (1).

In the resolution, no limit values are set and no analytical methods are proposed for the determination of their content.

**Impurities:** The impurities reported in Table 3 of the CoE ResAP(2008)1 include 13 elements (As, Ba, Cd, Co, Cr, Cu, Hg, Ni, Pb, Se, Sb, Sn, and Zn), mainly originating from inorganic pigments, the chemical class of polycyclic aromatic hydrocarbons (PAHs) and benzo[a]pyrene (one of the most toxic PAH), which can be found in tattoo inks based on carbon black.

Concerning elements, cadmium, mercury and nickel are of particular concern as they are classified CMRs in categories 1A, 1B or 2. Moreover, arsenic, cadmium, chromium,

mercury, nickel, lead and selenium are also in the negative list of the cosmetic regulation (Annex II). The Resolution states that the presence of chromium (VI) and nickel should be clearly indicated on the package together with a warning, as they can cause allergic reactions.

Analogously, benzo[a]pyrene and the PAHs mentioned in parenthesis (dibenzo[a,h]anthracene, benzo[a]anthracene, benzo[e]pyrene, benzo[j]fluoranthene, benzo(e)acephenanthrylene, benzo(k)fluoranthene and chrysene) are CMRs and are listed in Annex II of the cosmetic regulation too.

Contrary to aromatic amines and colorants, maximum recommended concentration values are indicated for the content of impurities. However, no methods are proposed in the resolution for their identification and quantification in tattoo and PMU inks.

Nickel is often found when inorganic pigments based on iron oxides are used as pigments. Its concentration shall be as low as technically achievable. This requirement may originate problems when implemented, as the test results obtained by the analysis of products cannot be compared to a numerical value to decide if the products are or not compliant. As a consequence, various actors could interpret differently the same analytical results. For such reason, it would be recommendable to establish a limit value for nickel.

Chromium (VI) impurities may be found in inorganic pigments based on chromium oxides. The recommended limit of 0.2 ppm (parts per million, mg/kg) applies to chromium (VI) and not to its total content. This means that the analytical methods shall allow the speciation of chromium and the separation of chromium (VI) and (III).

25 ppm is the limit recommended for soluble copper. The Resolution prescribes that soluble copper should be determined after extraction to an aqueous solution with pH 5.5. Various phthalocyanines (organic pigments of green or blue colour) contain copper in their structure, however this copper is linked and not soluble under the experimental conditions just mentioned for the extraction of soluble copper.

For the other elements the limits apply to their total content and are: 50 ppm for barium, tin and zinc; 25 ppm for cobalt; 2 ppm for arsenic, lead, selenium and antimony; 0.2 ppm for mercury and cadmium.

PAHs can be found as impurities in black tattoo and PMU inks, in particular carbon black, depending on the production processes. The limit of 0.5 ppm applies to the sum of the PAHs found in tattoo and PMU products; only benzo[a]pyrene has an individual limit equal to 5 ppb (parts per billion, µg/kg).

## 7.1. International standard methods

As anticipated, neither ISO nor EN standard methods are available specifically for the analysis of aromatic amines, colorants, elements, polycyclic aromatic hydrocarbons, phthalates and nitrosamines in tattoo and PMU inks. However, some international standard methods for aromatic amines and elements, developed for other matrices, have been adapted by some Member States. Table 7.2 shows the complete list of available international standard methods with the indication of those adapted to the analysis of tattoo and PMU products.

**Table 7.2**: List of available international standard methods by chemical classes.

| | Field of application | Analytical technique(s) | Adapted to the analysis of tattoo inks |
|---|---|---|---|
| **AROMATIC AMINES** | | | |
| EN 71-11:2005 | Toys | GC-MS | |
| EN ISO 17234-1:2010 | Leather | GC-MS | Italy |
| EN ISO 17234-2:2011 | Leather | HPLC-DAD; HPLC/DAD/MS; CE/DAD; TLC; HPTLC | Italy |
| EN 14362-1:2012 (corresponding to ISO 24362-1:2014) | Textiles | HPTLC; HPLC-DAD or HPLC-MS; GC-FID or GC-MS; CE-DAD | Slovenia and Sweden |
| EN 14362-3:2012 (corresponding to ISO 24362-3:2014) | Textiles | GC-MS; HPLC-DAD | Slovenia and Sweden |
| EN 71-7:2014 | Toys | GC-MS; HPLC-DAD | |
| **PAH** | | | |
| EN 71-7:2014 | Toys | GC-MS | |
| CEN/TS 16621:2014 | Food | HPLC-FD | |
| **COLORANTS** | | | |
| EN 71-11:2005 | Toys | HPLC-DAD; HPLC-MS | |
| EN ISO 16373-2:2014 | Textiles | HPLC-DAD; HPLC-MS | |
| EN ISO 16373-3:2014 | Textiles | HPLC-DAD; HPLC-MS | |
| **PHTALATES** | | | |
| EN 16521:2014 | Cosmetics | GC/MS | |
| EN ISO 14389:2014 | Textiles | GC/MS | |
| ISO 8124-6:2014 | Toys | | |
| **NITROSAMINES** | | | |
| ISO 10130:2009 | Cosmetics | HPLC | |
| EN 71-12:2013 | Toys | HPLC-MS/MS | |
| ISO 15819:2014 | Cosmetics | HPLC-MS-MS | |
| **INORGANIC IMPURITIES** | | | |
| EN 13806:2002 | Food | CVAAS (Hg) | Germany |
| EN 14082:2003 | Food | AAS | |
| EN 14083:2003 | Food | GFAAS (Pb, Cd, Cr, Mo) | Germany |
| EN 14084:2003 | Food | AAS | |
| EN ISO 17294-2:2003 | Water | ICP-MS | Austria and Sweden |
| EN 14332:2004 | Food | GFAAS | |
| EN 14546:2005 | Food | HGAAS | |
| EN 14627:2005 | Food | HGAAS | |
| EN 15111:2007 | Food | ICP-MS | |
| EN ISO 5398-1:2007 | Leather | Titration | |
| EN ISO 5398-3:2007 | Leather | AAS | |
| EN ISO 5398-4:2007 | Leather | ICP-OES | |
| EN ISO 11885:2007 | Water | ICP-OES (Total metal content) | Sweden |
| EN ISO 17075:2007 | Leather | | |
| EN 15517:2008 | Food | HGAAS | |
| EN 15505:2008 | Food | AAS | |
| EN ISO 5398-2:2009 | Leather | Colorimetry | |
| EN 15763:2009 | Food | ICP-MS (As, Cd, Hg, Pb) | Austria |
| EN 15764:2009 | Food | FAAS; GFAAS | |
| EN 15765:2009 | Food | ICP-MS | |
| EN ISO 17072-1:2011 | Leather | ICP; AAS; SFA (All metals extractable in an acidic perspiration solution) | Italy |
| EN ISO 17072-2:2011 | Leather | ICP; AAS; SFA (Total metal content) | Italy |
| EN ISO 12846:2012 | Water | AAS (Hg) | |
| ISO/TR 17276:2014 | Cosmetics | | |
| EN 71-3:2013+A1:2014 (see also ISO 8124-3:2010) | Toys | ICP-MS; ICP-OES; CVAAS; GC-MS (General elements, Cr (III and VI), Sn) | |
| EN 13805:2014 | Food | | |
| EPA 3051A (and EPA 3051) | Environment | FLAAS, GFAA, ICP-AES, ICP-MS (Total metal content) | Italy |
| EPA 3052 | Environment | FLAA, CVAA, GFAA, ICP-AES, ICP-MS (Total metal content) | Italy |
| EPA 3060A | Environment | Ion Chromatography with ICP-MS detection; HPLC-ICP-MS; CE-ICP-MS (Cr(VI)) | Italy |
| EPA 218.7 | Environment | Ion chromatography (Cr(VI)) | Italy |

### Aromatic amines

Test methods for aromatic amines can quantify the sum of free and releasable aromatic amines. These two types of aromatic amines show different hazard scenarios: the aromatic amines released from azo-colorants, assuming only a partial conversion, could produce a potential low level of chronic contamination; whereas the free aromatic amines are immediately available and could potentially cause high single dose exposure. Furthermore, there is strong evidence of photo degradation of pigments into aromatic amines under solar, UV and laser exposure. Therefore, it would be important to have a method able to discriminate between the two types of aromatic amines. However, a single analysis cannot provide information on the different scenarios and in order to evaluate the concentration of free aromatic amines a second analysis with a different test method, without the reductive cleavage, is needed.

The standard methods available show poor reproducibility and may provide both false negative and positive results. In fact, they were developed to quantify aromatic amines released from soluble azo-dyes and, when they are applied to insoluble pigments, only a small fraction of them, very much dependent on the experimental conditions of the test methods, are transformed into the original reagents (aromatic amines). Hauri (P2015) proved that only about 4% of the initial amount of pigment yellow 14 and orange 13 is transformed into aromatic amines using EN ISO 14362-1 and EN ISO 17234-1 modified, e.g. by adding dimethylformamide, to increase the solubility of pigments. The same author proved that pigments considered compliant when analysed with EN ISO 14362-1, actually resulted non-compliant when analysed with three different improved protocols of this test method.

The listed standard methods could also provide false positives. In fact, as reported by Hauri H. [91], when pigments like pigments yellow 65 and 74 are analysed using EN ISO 14362-1 and EN ISO 17234-1, results show the presence of o-anisidine deriving from the cleavage of the amide and not the azo bond. These test methods may also produce the reduction of nitro groups to amino groups.

### Elements

The majority of the listed methods are useful to determine the total content of elements.

Italy exploits a modified version of EN ISO 17072-1 to determine the soluble part of copper and EN ISO 17072-2, EPA 3051A and EPA 3052, which are based on microwave digestion of samples, for the determination of the total content of elements. EPA 3060A and EPA 218.7 are used for the determination of chromium VI. In Germany, modified versions of the standard methods EN 13806 and EN 14083 developed for foodstuffs, to analyse mercury and other elements, respectively, are used for tattoo and PMU inks. A German official method for cosmetic products (§ 64 LFGB K 84.00-29) is applied for the extraction and microwave digestion of tattoo or PMU samples. Austrian experts make use of EN 15763, Austrians and Slovenians use EN ISO 17294-2 and Swedish apply EN ISO 11885.

## 7.2. National standard methods

There are very few national standard methods for the analysis of aromatic amines, elements and polycyclic aromatic hydrocarbons (see Table 7.3). None of them was validated for tattoo and PMU products. They are applicable to textiles, water and polymer samples. In principle, they could serve as a model to develop specific methods for tattoo and PMU products.

**Table 7.3**: List of available national standard methods by chemical classes.

| Country | Field of application | Analytical technique(s) |
|---|---|---|
| **AROMATIC AMINES** | | |
| Sweden (64§ LFGB 82-02-2 ) | Textiles | HPTLC; HPLC/DAD or HPLC/MS; GC/FID or GC/MS; CE/DAD |
| **PAH** | | |
| Sweden (ZEK 01.2-08 then ZEK 01.4-08) | Consumer products | GC/MS |
| **INORGANIC IMPURITIES** | | |
| Austria K 84.00-29 (nach § 64 LFGB) | Cosmetics | Pb, Cd, Hg |
| Germany (DIN EN ISO 11885) | Water | ICP/OES (Total metal content) |
| Germany (DIN EN 1483 superseded by DIN EN ISO 12846:2012) | Water | AAS (Hg) |
| Germany (K 84.00-29 nach § 64 LFGB) | Cosmetics | |

## 7.3. In-house validated methods

Table 7.4 lists all the available in-house test methods, validated either for the analysis of tattoo and PMU inks or for other matrices.

**Table 7.4**: List of available in-house validated methods by chemical classes.

| Country | Field of application | Analytical technique(s) |
|---|---|---|
| **AROMATIC AMINES** | | |
| United Kingdom | Environment | HPLC |
| Austria | Food | HPLC/MS/MS |
| France | Dyes, cosmetics, finger paints and **inks** for pens and **tattoos** | HPLC/MS |
| Switzerland | **Tattoo inks** | HPLC/MS/MS |
| Switzerland | **Tattoo inks** | HPLC/MS/MS |
| Slovenia | **Tattoo inks** | HPLC |
| The Netherlands | **Tattoo/PMU ink**, and textile | GC/MS |
| Denmark | **Tattoo inks** | GC/MS |
| Denmark | **Tattoo inks** | GC/MS |
| **PAH** | | |
| Switzerland | **Tattoo inks** | HPLC/UV/FLD |
| The Netherlands | **Tattoo inks** | GC/MS |
| Italy | **Tattoo inks** | GC/MS |
| **COLORANTS** | | |
| Switzerland | **Tattoo inks** | MALDI/TOF |
| Switzerland | **Tattoo inks** | Colorimetry |
| Sweden | Cosmetics | HPLC/MS |
| Slovakia | | |
| **PHTALATES** | | |
| Austria | Cosmetics | GC/MS |
| Slovakia | Cosmetics | HPLC/DAD |
| **NITROSAMINES** | | |
| Switzerland | Cosmetics, finger paints and **tattoo inks** | HPLC/MS/MS |
| **INORGANIC IMPURITIES** | | |
| France | | ICP/MS |
| Slovenia | **Tattoo inks** | ICP/MS (Total metal content) |
| The Netherlands | **Tattoo inks** | ICP/MS |
| Denmark | **Tattoo inks** | ICP/MS |
| Slovakia | Cosmetics and food | GFAAS (Cd, Pb, Ni) |
| Slovakia | Cosmetics and food | AAS/AMA (Hg) |
| Slovakia | Cosmetics and food | Hg, Zn, Cu, Cr (VI), Co, Sb |
| Italy | Cosmetics | ICP/MS (Cd, Co, Cr, Ni, Pb) |

### Aromatic amines

Among all the available in-house validated test methods, two of them (France and Denmark) are suitable for the quantification of the free aromatic amines present as impurities. All the other methods are based on the reductive cleavage of the azo bond of colorants and can therefore quantify the sum of the free and releasable aromatic amines.

It is worth noticing that the British and Austrian methods were in-house validated in air and food.

### Colorants

Switzerland reported two in-house validated analytical methods for the analysis of colorants in tattoo and PMU inks. One using an expensive and not widely available high resolution mass spectrometer, the Matrix-Assisted Laser Desorption/Ionization Time Of Flight (MALDI/TOF) and a second method, based on simple colorimetric detection, which can identify, when used as main ingredients, several hazardous colorants, such as pigments violet 19 and 23, pigment red 122, pigment blue 15 and pigment green 7, and some possible replacements, like pigment red 202 and pigment green 36.

Methods were developed by Sweden and Slovakia for the identification of colorants in matrices other than tattoo and PMU inks.

### Elements

Out of 8 analytical methods, 3 were specifically validated for tattoo and PMU products. Namely they are Slovenian, Danish and Dutch methods. They require the sample digestion in microwave oven in the presence of strong acids or acids and hydrogen peroxide mixtures and allow the determination of the total content of elements. They all use Inductively Coupled Plasma Mass Spectrometry (ICP-MS) for the instrumental analysis.

Other methods have been in-house validated in other countries on matrices other than tattoo and PMU inks (mainly food contact materials and cosmetics).

### Polycyclic aromatic hydrocarbons

Three in-house validated methods are available for the analysis of PAH in tattoo and PMU products.
PAHs are extracted from the tattoo inks either with benzene/acetone mixture in ultrasonic bath, or with toluene in pressurised microwave oven or with toluene/acetone mixture. The quantification is carried out either with gas chromatography coupled with Mass Spectrometer detector or with high performance liquid chromatography coupled with UV or fluorescence detector (FLD).

### Nitrosamines

One in-house validated method, proposed by Switzerland, is available for the determination of N-nitrosamines by Liquid Chromatography with tandem Mass Spectrometry (LC/MS/MS).

### Phthalates

No analytical methods were in-house validated for tattoo and PMU products. They are applicable to cosmetics and could be, in principle, adapted to tattoo and PMU inks.

## 7.4. Methods described in the literature

A non-exhaustive list of test methods published in the literature and used for the analysis of aromatic amines, colorants, elements and PAHs in tattoo and PMU inks and other products is presented hereafter (Table 7.5).

**Table 7.5**: List of analytical methods available in the literature by chemical classes.

| Author | Title | Applied to tattoo/ PMU inks |
|---|---|---|
| | **AROMATIC AMINES** | |
| 2012, Margraf | Determination and Quantification of Primary Aromatic Amine in Printer Inks | |
| 2012, The Danish EPA | Chemical Substances in Tattoo Ink Survey of chemical substances in consumer products | X |
| 2005, Mortensen | Specific determination of 20 primary aromatic amines (PAA) in aqueous food simulants by liquid chromatography-electrospray ionization-tandem mass spectrometry | |
| | **PAH** | |
| 2012, The Danish EPA | Chemical Substances in Tattoo Ink Survey of chemical substances in consumer products | X |
| 2010, Regensburger | Tattoo inks contain polycyclic aromatic hydrocarbons that additionally generate deleterious singlet oxygen | X |
| | **COLORANTS** | |
| 2013, Djelal | The use of HPTLC and Direct Analysis in Real Time-Of-Flight Mass Spectrometry (DART-TOF-MS) for rapid analysis of degradation by oxidation and sonication of an azo dye | |
| 2012, The Danish EPA | Chemical Substances in Tattoo Ink Survey of chemical substances in consumer products | X |
| 2012, Vila | Analysis of the chemical composition of red pigments and inks for the characterization and differentiation of contemporary prints | X |
| 2011, Hauri | Inks for tattoos and PMU (permanent make-up)/organic pigments, preservatives and impurities such as primary aromatic amines and nitrosamines | X |
| 2009, Schäning | Pigment classification of synthetic organic pigments by multivariate data analysis of FTIR spectra | |
| 2008, Poon | In situ chemical analysis of modern organic tattooing inks and pigments by micro-Raman spectroscopy | X |
| 2006, Engel | Establishment of an extraction method for the recovery of tattoo pigments from human skin using HPLC diode array detector technology | |
| 2006, FBI Laboratory Chemistry Unit | FTIR Analysis of Paints, Tapes, and Polymers | |
| 2006, Instrument data sheet | Analysis of organic pigments using a direct exposure probe on JMS-T100GC 'AccuTOF GC' | X |
| 2005, Fang | Determination of EU-Banned Disperse Dyes by LC/MSD TOF | |
| 2004, Cui | Photodecomposition of Pigment Yellow 74, a pigment used in tattoo inks | X |
| 2004, Vasold | Tattoo pigments are cleaved by laser light- the chemical analysis in vitro provide evidence for hazardous compounds | X |
| 2001, Timko | In vitro quantitative chemical analysis of tattoo pigments | X |
| 2001, Vandenabeele | Non-destructive analysis of paintings using Fourier transform Raman spectroscopy with fibre optics | |
| 2000, Bäumler | Q-Switch laser and tattoo pigments: first results of the chemical and photophysical analysis of 41 compounds | X |
| Learner | The use of a diamond cell for the FTIR characterization of paints and varnishes available to twentieth century artists | |
| | **INORGANIC IMPURITIES** | |
| 2014, Eghbali | Determination of heavy metals in tattoo inks | X |
| 2013, Wellington Ministry of Health | Survey of Selected Samples of Tattoo Inks for the Presence of Heavy Metals | X |
| 2012, The Danish EPA | Chemical Substances in Tattoo Ink Survey of chemical substances in consumer products | X |
| 2009, Forte | Market survey on toxic metals contained in tattoo inks | X |
| 2006, Kang | Quantification of para-phenylenediamine and heavy metals in henna dye | X |
| 2006, Kang | Determination of hexavalent chromium in cosmetic products by ion chromatography and post-column derivatisation | |

| Author | Title | Applied to tattoo/ PMU inks |
|---|---|---|
| | **PHTALATES** | |
| 2013, Høgsberg | 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 | X |
| 2011, Lehner | Black tattoo inks are a source of problematic substances such as dibutyl phthalate | X |
| | **NITROSAMINES** | |
| 2014, Hauri | Tinten für Tattoos und Permanent Make-Up / Pigmente, Konservierungsstoffe, Aromatische Amine, Polyaromatische Kohlenwasserstoffe und Nitrosamine | X |

[12, 17, 31, 58, 95, 103, 104, 121, 122, 124-141]

# 8. RAPEX notifications and market surveillance

This chapter aims to give an overview of the alerts notified through RAPEX (Rapid Alert System for non-food dangerous products) in the last decade and of the results of market surveillance activities carried out in the European countries.

For more detailed information, please refer to the JRC report on Work Package 2 [2].

## 8.1. RAPEX notifications

As foreseen by the General Product Safety Directive 2001/95/EC (GPSD), since 2004 a rapid alert system for non-food dangerous products, called RAPEX, has been set up. This tool facilitates communication among 31 countries (28 EU MS, plus Norway, Iceland and Liechtenstein) and the Commission on products posing serious risks to consumers' health and safety and on the emergency measures taken by national authorities or manufacturers.

Reports on current RAPEX alerts are published weekly. During the last decade (2005-2015, week 15), 126 alerts related to tattoo and PMU inks have been reported, as shown in Figure 8.1.

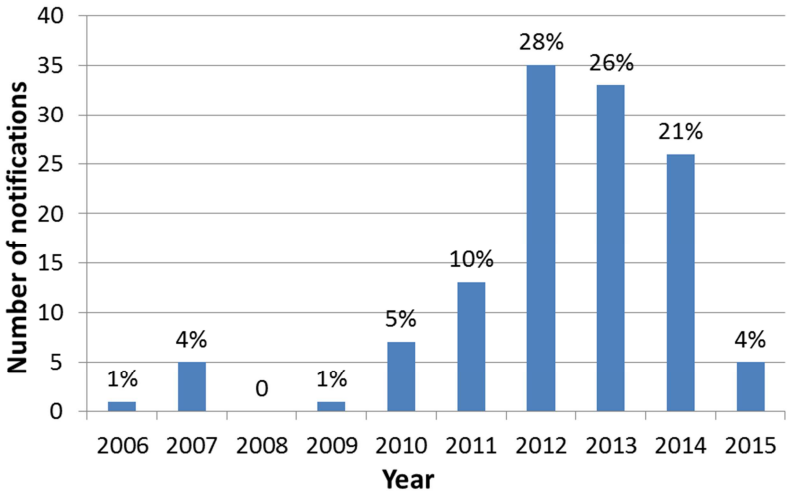



**Figure 8.1:** Notifications by year.

Out of the 126 notifications, 120 (109 referring to tattoo and 11 to PMU inks) were related to chemical risks, while the remaining 6 implicated microbiological risks of tattoo inks. Many of the notifications referred to inks containing two or more hazardous substances. Figure 8.2 gives the proportions among the type of risks and the category of products.

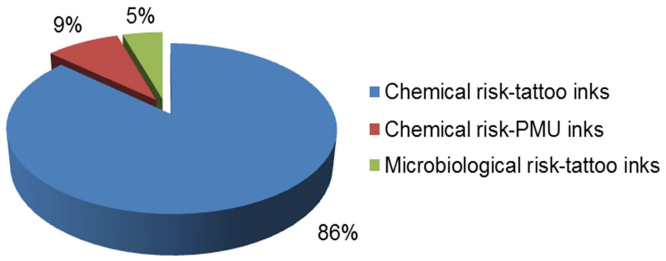



**Figure 8.2:** Notifications by category of products and type of risks.

As shown in Figure 8.3, two thirds of the notified inks were produced in the United States, 25% came from China, Japan and some European countries, whereas the provenience of 9% of products was unknown. Consistently, the majority (64%) of products not in line with CoE ResAP(2008)1 recommendations or with national legislations belonged to three American brands, Intenze (35%), Eternal ink (21%) and Starbrite 2 (8%).

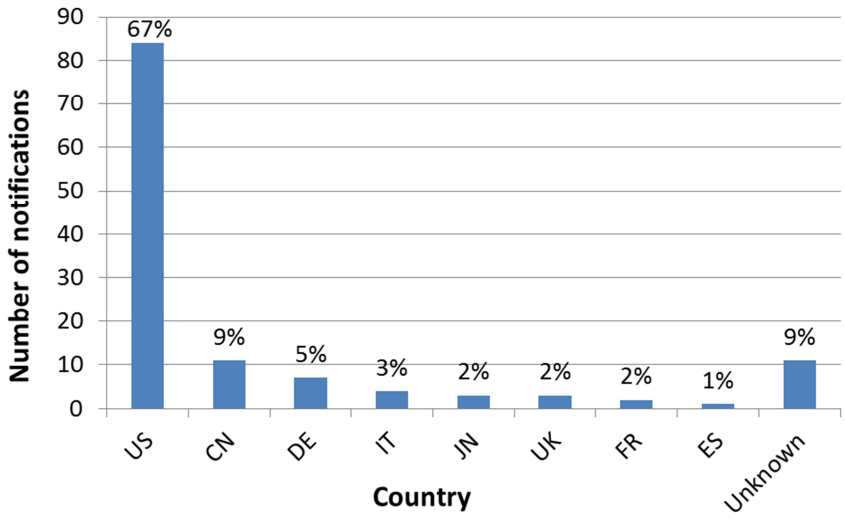



**Figure 8.3**: Notifications by country of origin of the products.

Most notifications were related to the presence of impurities, mainly primary aromatic amines (40%) followed by polycyclic aromatic hydrocarbons (30%, including 10% benzo[a]pyrene) and heavy metals (28%), see Figure 8.4.

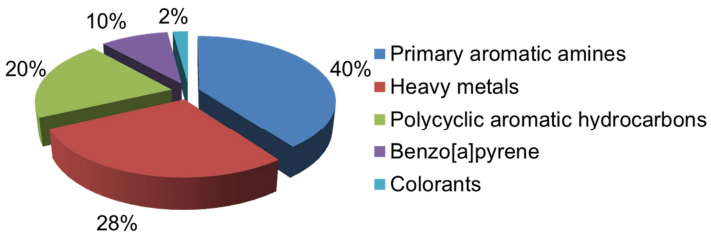



**Figure 8.4:** Chemical notifications by chemical class.

Amounts of primary aromatic amines in the range 3.4 – 5521 mg/kg were detected. The levels of total content of PAHs and of benzo[a]pyrene ranged between 0.5 - 96.5 mg/kg and 0.02 - 0.6 mg/kg, the suggested threshold values of the Resolution being 0.5 and 0.005 mg/kg, respectively.

Among all notifications, 28% showed heavy metals' contents above the threshold values in the CoE ResAP(2008)1. Alerts were related in particular to As, Ba, Cd, Cr(VI), Cu (soluble), Pb, Ni and Zn. High concentrations especially of Ba and Cu (soluble) were reached (7800 and 4310 mg/kg, respectively). Despite the content of nickel should be 'as low as technically achievable', the levels reported in RAPEX notifications ranged from 12 to 9690 mg/kg.

Notifications linked to microbiological risks are mostly related to the presence of aerobic mesophilic bacteria (up to $10^6$ cfu/ml) that compromises the sterility of ink packages before their opening. Recognised pathogenic species, such as Staphylococcus and Pseudomonas, were identified in some samples.

Different actions were taken after the identification of the risky products notified in the alerts, ranging from the voluntary recall from the market by the importer to the destruction of the products ordered by the authorities. As shown in figure 8.5, withdraw from the market was the measure taken in one third of the cases, followed by the ban on the marketing of the product.

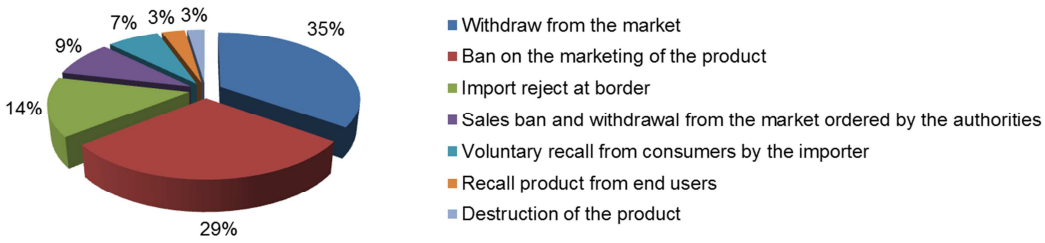



**Figure 8.5:** Notifications by measure/action taken.

## 8.2. Market surveillance in European countries

Data presented in this section was collected from market surveillance surveys carried out in some countries, national studies, peer reviewed articles, books and presentations given during the meetings of the CSN-STPM.

The highest number of analyses related to tattoo and PMU products were carried out in The Netherlands, Germany, Switzerland and Italy, see Table 8.1, [12, 14, 15, 21-23, 100, 142-144] and the most studied classes of impurities were PAHs, PAAs and heavy metals. Preservatives were also monitored in some campaigns. Additional market surveillance activities were performed in Slovenia [145], Sweden [24, 25, 27], Denmark [17, 146] and Belgium [10].

**Table 8.1:** Major market surveillance campaigns conducted in the last decade.

| Country | Year | Samples analysed (approx. number) | Substances analysed (chemical class) |
|---|---|---|---|
| **CH** | 2009-2014 | 600 | PAAs, PAHs, preservatives, nitrosamines, pigments |
| **DE** | 2007-2014 | 1000 | PAAs, PAHs, heavy metals, preservatives, nitrosamines |
| **IT** | 2007-2014 | 300 | PAAs, PAHs, heavy metals |
| **NL** | 2004-2015 | 3000 | PAAs, heavy metals, preservatives |

Figure 8.6 summarises the percentages of samples not respecting the chemical and microbiological requirements of the CoE ResAP(2008)1 and/or of national legislation in relation to the content of impurities, preservatives and microorganisms. The data do not refer to a single study or publication, but are derived from the analysis of several documents taken into account during this project.

Considering all information sources, overall 43% of the 358 inks analysed for total PAHs content presented concentrations well above the threshold of 0.5 mg/kg suggested by the CoE ResAP(2008)1 (0.5 – 55000 mg/kg) [12, 115, 121, 122, 147, 148]. The fact that 57% of them were compliant proves that it is technically feasible to produce carbon black with low levels of PAHs and that these products are also present on the market. Among PAHs, the following substances are classified as CMR in the CLP regulation: benzo[a]pyrene, dibenz[a,h]anthracene, benzo[a]anthracene, benzo[e]pyrene benzo[j]fluorantene benzo[k]fluorantene, benz[e]acephenanthrylene and chrysene. Concerning benzo[a]pyrene, 24% of the 300 samples analysed contained this substance

in levels higher than the maximum recommended quantity of 0.005 mg/kg (0.005 – 6.8 mg/kg).

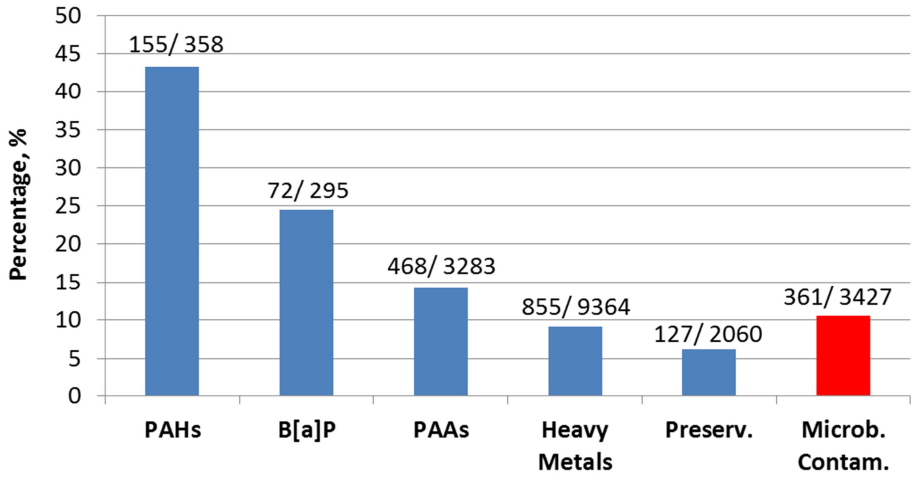



**Figure 8.6:** Percentage of analysed samples not respecting the chemical requirements of the CoE ResAP(2008)1 or of national legislation by chemical class (The red bar refers to microbiological contaminations).

Even if primary aromatic amines should not be present in tattoo/PMU inks, 14% out of the 3282 products analysed for the total content of PAAs contained these carcinogenic substances [12, 23, 142, 143, 148-150]. The PAAs that were mainly detected (o-anisidine, 4-chloroaniline, 3,3'-dichlorobenzidine, 4-methyl-m-phenylendiamine, o-toluidine and 5-nitro-o-toluidine) are reported in Figure 8.7, with the indication of the numbers of samples containing them against the numbers of the analysed ones. The measured concentrations ranged from 0.1 to 6900 mg/kg.

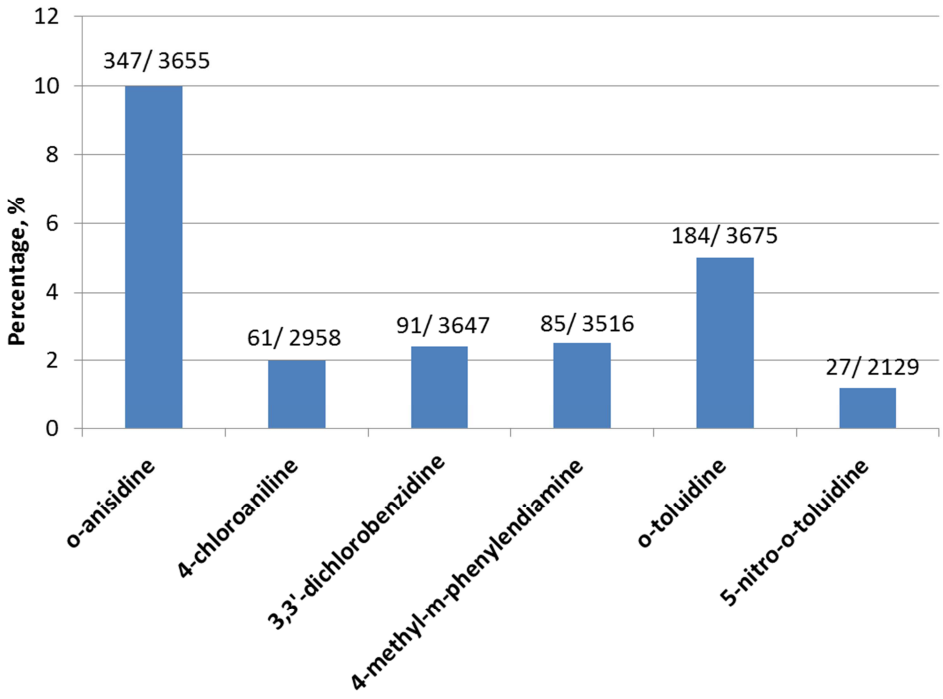



**Figure 8.7:** Percentage of analysed samples containing some carcinogenic aromatic amines.

Regarding the presence of metals [29, 58, 151-153], overall among all tattoo and PMU products analysed 9% of samples exceeded the recommended maximum concentrations mentioned in the CoE ResAP(2008)1. The percentages ranged from 1.4% to 32%, depending on the metals, as shown in Figure 8.8.

It was not possible to estimate the percentage of analysed samples containing Ni and Cr (VI). In the case of nickel because the CoE ResAP(2008)1 does not recommend a specific limit but suggests that the concentration should be as low as technically achievable. In the case of Cr(VI) because many studies reported only the total concentration of this element, even if the recommended limit applies to Cr(VI).

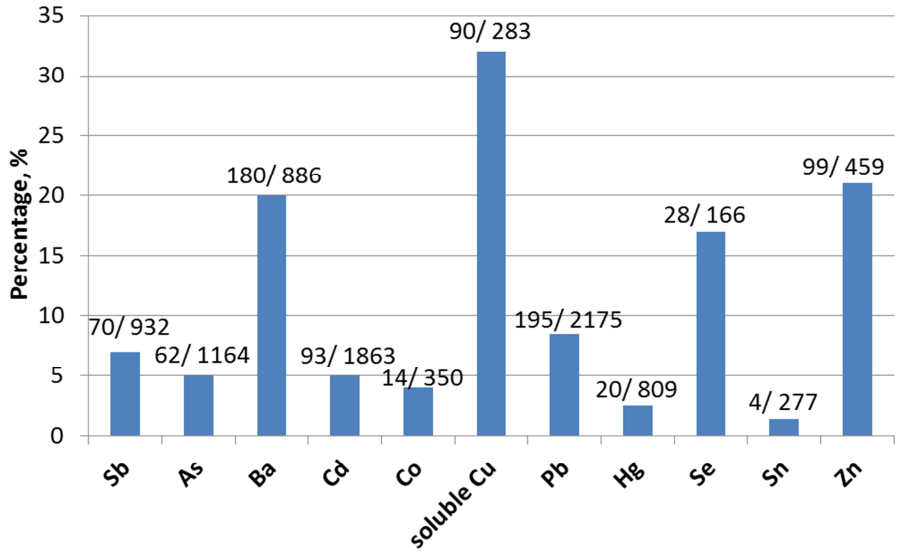



**Figure 8.8:** Percentage of analysed samples containing metals.

In 2007, 2008 and 2014 three studies from Germany, Switzerland and The Netherlands, which included nearly 2000 test results on preservatives, were published [12, 15, 23]. As shown in Figure 8.6, 6% of all considered products did not fulfil the recommendations or national requirements. In particular, Hauri [12] reported that benzoisothiazolinone, methylisothiazolinone and formaldehyde were found respectively in 24%, 8% and 7% out of the 229 inks analysed in his survey.

Other impurities like nitrosamines [12] and phthalates [122, 124] were detected in some cases. Some of them are classified as carcinogenic or toxic for reproduction or are listed in Annex II of the cosmetic regulation thus the CoE ResAP(2008)1 recommends they should not be present in tattoo/PMU inks.

Regarding microbiological contamination [15, 30, 78, 154-158], considering all the data collected in more than 3800 products, 11% of the ink bottles (sealed or in use) were not sterile (Figure 8.6). Pathogenic reported micro-organisms included Pseudomonas, Staphylococcus, Streptococcus and Enterococcus. The Netherlands was very active in this domain and conducted massive surveillance campaigns from 2004 to 2014 on more than 3000 samples [22, 23]. In particular, the presence of bacteria in 20% out of more than 800 analysed samples was revealed in the 2004 Dutch study.

Summarising, results indicated that tattoo/PMU products containing dangerous substances or biologically contaminated are available on the EU market. The main risks identified, in descending order, are the presence of PAHs, PAAs, microorganisms, heavy metals and preservatives. Thus it is of primary importance to continue market surveillance activities in all European countries.

It has to be noted that the total number of "non-complying" samples identified in market surveillance campaigns is by far higher than the total number of RAPEX notifications,

which concerns only those inks that are considered as causing serious risk to the health of consumers and fulfil the conditions to be notified through RAPEX.

Furthermore, some national studies carried out in various European countries, such as Belgium [10, 11], Denmark [17], Germany [14], Slovenia [145], Sweden [24] Switzerland [12] and The Netherlands [22] highlighted incomplete or missing information on the labelling of tattoo and PMU products. The absence of life date after opening and the incomplete list of ingredients were mostly reported; often there was no indication of durability, manufacturer, batch number or indication of use. A further issue raised from different studies was the presence on the market of counterfeit inks with not only fake product and manufacturers' names, but also false batch numbers with a list of ingredients not corresponding to the actual composition of the product.

A considerable market surveillance campaign has been conducted in the Netherlands from 2004 to 2014 [22], revealing that in 37% out of the 3000 samples analysed mandatory information were absent, thus non-complying with labelling requirements.

Incorrect labelling concerning the chemical composition of inks was also spotted in 1/3 of the samples collected by the German regional authorities [142], and highlighted both by the Slovenian [145] and Swiss [12] Competent Authorities in their national reports.

In Italy, campaigns carried out between 2009 and 2014 [150] showed that, even though nickel was present in nearly all samples, in no one this element was declared, as requested by the CoE ResAP(2008)1.

All details about data collected and summarized in this Chapter are available in the Annexes V and VIII of the JRC report 'Safety of tattoos and permanent make-up. State of play and trends in tattoo practices', by Piccinini et al. [2].

# 9. Adverse health effects linked to tattoo/PMU applications and removal

With the recent increase of popularity of tattooing and permanent make-Up among the general population, and particularly in the young generation, medical complications from tattoo applications and removal are more and more frequently described by physicians and medical literature. However the perception from the medical viewpoint might be partial, as tattoo recipients experiencing an adverse event are probably reluctant to seek medical care, especially if symptoms are minor. In the Klügl study [70] (see below) performed in German-speaking countries, only 1% of the tattooed people who took part in the survey consulted a physician, even though respectively 67.5% and 6.6% of them experienced skin or systemic problems directly after tattooing, and 6% and 3% of them experienced persistent problems linked or not to the skin. In the US, the Brady study [159] (see below) shows a higher proportion, i.e. 29% of the tattooed people with some adverse reaction had obtained medical care (16% from a dermatologist).

Serup [160] makes the distinction between (i) minor complaints of "discomfort and (ii) more serious "complications" requiring a medical advice and states that life-threatening incidents are extremely rare. Citing Kluger [161] "Dermatologists deal with two types of tattooed patients: most often those desiring tattoo removal and, more rarely, patients presenting with cutaneous reactions associated with tattoos". For PMU applications this aphorism is even more valid, as the most frequent complaint there relates to "patient's dissatisfaction resulting from misapplication of the pigment, pigment migration, and pigment fanning" [4]. Laux reported that up to 50% of the tattooed individuals regret their tattoos [84]. These psycho-social sequels are also to be considered after tattoo removals, which are in constant increase [162], due to regrets, aesthetic reason or medical complications of tattoos [85]. The post-removal side-effects presented in the following paragraphs focus only on the use of Q-switched lasers (QS), the gold standard for tattoo removal [82, 83], leaving voluntarily aside other sporadic and/or outdated removal techniques such as surgical, chemical and thermal procedures, or argon and $CO_2$ lasers. Complete pigment removal is successful in only 38% of cases, according to a self-reported non-medical study [85].

Adverse tattoo reactions may start either early, right after the tattoo procedure, or occur later on, months and years afterwards. Acute aseptic inflammation takes place already while the tattoo is placed or removed, immediately followed by a wound healing process. Skin bacterial infection (for permanent tattoo application) may occur after some days, while for allergic reactions, it can be delayed to weeks, or even years and decades for chronic dermatosis and immune reactions. A 2015 study performed by Brady [159] on 300 randomly selected tattooed people in Central Park (New York), reported 10.3% of adverse tattoo reactions. Out of these 31 individuals, 13 (4.3% of total participants) had mild acute effects (pain, itching, swelling) and 18 (6.0%) showed chronic reaction linked to a specific colour which lasted more than 4 months. However the author admits the limitations of such a survey approach, where self-reported reactions were not clinically ascertained, concluding that the overall extent and prevalence of post-tattoo adverse events is currently unknown because of scarce epidemiological data, and this is confirmed by other experts in this field, such as Kluger [161], or Desai [163].

Carrying out a web survey among tattoo recipients in 2010 [70] Klügl found that two thirds of the 3411 responders had acute dermal complaints, which were probably simple inconveniences, actually. This proportion is in the same range as the 76% of tattoo-recipients complaining of bleeding, in the Carney study [164], but much bigger if compared with the rate of acute minor disturbances reported by most authors (see point 9.1 below). After one month 9% of the German-speaking individuals declared to still present symptoms, be it local (for 6%) or general e.g. dizziness, headache, or nausea (for 3%) [70]. However the reliability of these responses to a questionnaire, without validation by a physician, is challenged by Wenzel et al, [165], and Klügl himself

recognises these figures might be inflated, as "people with health problems may be more willing to participate in such a survey".

Speaking about adverse health effects linked to laser tattoo removal, a similar internet survey performed by Klein [85] on 157 patients having undergone a laser tattoo removal, revealed the following rates of systemic effects: 6% (headache), 4% (dizziness), 1% (fever, vomiting). In two thirds of the individuals these complaints persisted up to 5 weeks, in 7% of them it lasted 6–9 weeks, and beyond 10 weeks in 4% of participants to the survey.

Apart the obvious dichotomy existing between infectious (only for permanent tattoo/PMU applications) and non-infectious diseases, a systematic categorisation of tattoo adverse events remains a challenging task, even under controlled clinical circumstances, according to Brady [159]. For the purpose of this report the adverse effects have been subdivided into the following categories:

- acute aseptic inflammation;
- infectious risks (bacterial and viral);
- allergic/hypersensitivity and auto-immune type reactions:
    - allergic reactions;
    - underlying dermatosis reactivated by tattooing;
    - other secondary effects;
- other secondary effects:
    - pigmentary disorders;
    - tumours;
    - medical diagnostic and treatment interference;
    - contraindication to tattoo procedure.

Among the inflammatory non-infectious events, an unavoidable step is represented by the acute needle trauma or laser burn, and subsequent inflammation always accompanying the tattoo application or removal (see point 9.1). In contrast with these mild discomfort claims, the main serious complications of tattoo procedures consist of infectious, hypersensitivity reactions (so called "allergic phenomenon") and chronic inflammation with possible immunity component, where the tattoo may reactivate underlying dermatoses. Further complications, like pigmentation disorders, are specifically linked to the laser removal process, but chronic post-inflammatory discolouration changes may also occur. Tumours form a separate group, because of the uncertainty of their pathogenesis. In addition tattoos can hamper or delay medical diagnosis and treatment.

Information reported in some key papers on adverse health effects are summarised in tables 9.1 (relationship between type of adverse effects and their prevalence) and 9.2 (type of adverse effects and onset).

**Table 9.1:** Prevalence of various types of adverse health effects.

| Number of persons surveyed | Number or % of persons with problems | Adverse effects | Type of study | Location | Reference |
|---|---|---|---|---|---|
| 300 tattooed | 10% (31/300) | experienced adverse tattoo reaction | street survey | US, New York | 2015, Brady |
| | of which 29% (9/31) | medical care for their syntoms | | | |
| | of which 16% (5/31) | care from dermatologists | | | |
| | 6% (18/300) of which 44% (8/18) to red and 33% (6/18) to black ink 23% (4/18) to other colours | chronic reaction releated to specific colour (>4 months)-itchy,scaly,raised,oedematous syntoms | | | |
| | 4.3% (13/300) | acute reactions (up to 4 months)-pain,itching,swelling,scabbing | | | |
| Unknown | 1-5% of tattooed people in general | bacterial infections after receiving a tattoo (from superficial skin infections to more severe systemic cases-pathogens bacteria, blood borne viruses hepatitis and HIV) | | | 2016, Laux |
| 35000 patients treated in the hospital (the number of tattooed is unknown) | 0.02% (7/35000 ) | severe adverse reactions (inflammatory lichenoid reaction, itch, acute edema,sarcoidal reaction, dermal granulomatous reaction, erythema nodosum, nodules, ulceration) | survey in dermatologic department of Dresda hospital | Germany | 2012, Wollina |
| 467 (144 tattooed) | 42% (60/144) | complaints | beach survey | Denmark | 2014, Hutton |
| | of which 52% (31/60) | sun induced reaction (red and black tattoos)-swelling (18/31),itching/pain (16/31), redness (8/31), more than one problem (11/31) | | | |
| | of which 48% (29/60) | reaction independent of sun-swelling (9/29), reaction to heat (12/29),allergic reaction (3/29) | | | |
| | of which 1% (2/60) | asked medical assistance | | | |
| 157 (ex tattooed reporting side effects after tattoo removal) | 97% (152/157) | reactions (blistering, edema, crusting, erythema and pain) | internet survey | German speaking countries | 2014, Klein |
| | 69% (108/157) | local effects within 5 weeks | | | |
| | 24% (38/157) | slightly visible scars | | | |
| | 8% (12/157) | important scars | | | |
| | 6% (9/157) | headache | | | |
| | 5% (8/157) | local effects persisted up to 30 weeks | | | |
| | 5% (8/157) | needed medicat treatment for side effects | | | |
| | 4% (6/157) | dizziness | | | |
| | 2% (3/157) | temporary disability | | | |
| | 1% (2/157) | vomiting | | | |
| | 1% (2/157) | fever | | | |
| | 1% (2/157) | more than 10 visits to their medical practitioner | | | |
| 280 (all tattooed patients reporting health effects) | 151/280 (54%) of which 21/151 (13.9%) black inks, 47/151(31.1%) coloured inks and 83/151 (55.0%) unknown colour | infections | review | | 2013, Wenzel |
| | 96/280 (34%) of which 12/96 (12.5%) black inks, 80/96 (83.3%) coloured inks and 4/96 (4.2%) unknown colour | granulomatous, lichenoid or hypersensitivity allergic reactions | | | |
| | 33/280 (12%) of which 10/33 (30.3%) black inks, 18/33(54.5%) coloured inks and 5/33 (15.2%) unknown colour | tumors | | | |
| | 2% (6/151) | hepatitis C | | | |
| 154 tattooed (342 tattoos) | 27% (41/154) | complains after 3 months (related to black and red pigments)-skin elevation and itching | study in a clinic of sexual transmitted diseases | Denmark | 2013, Høgsberg |
| | 16% (24/154) | complains related to sun exposure -skin elevation and itching (19/24 related to black tattoos) | | | |
| | 15% (23/154) | early complains (up to 3 months)-skin elevation, itching, ulceration, redness, fever, local infection | | | |
| 3411 tattooed | 67% (2285/3411) | immediate adverse tattoo reaction (bleeding, crusts, itching edema,pain, bacterial skin infections) | internet survey | German speaking countries | 2010, Klügl |
| | 8% (273/3411) | still have reactions after 4 weeks | | | |
| | 7% (239/3411) | systemic reactions directly after tattooing (dizziness, headache, nausea, fever) | | | |
| | 6% (205/3411) | persistent on going reaction (intermittent edemas, papules, itching,skin elevation) | | | |
| | 3% (102/3411) | psychic problems and light sensitivity of tattoos | | | |
| | 0.6% (20/3411) | positive to hepatitis test after tattooing | | | |
| | 33% (1126/3411) | no problems | | | |
| 234 tattooed | 2.1% (5/234) | tattoo complications-infectious,allergic and granuloma complications | study in dermatology clinic | Bulgaria | 2007, Kazandjeva |
| 500 (120 tattooed) | 18% (15/120) | medical problems during the first 2 weeks (disconfort, pain, tenderness, itching, bleeding, pus) | phone survey | US | 2006, Laumann |
| | of which 20% (3/15) | sun sensitivity within the first 2 weeks | | | |
| 454 (106 tattooed) | 0 | no reported medical complication from tattooing | students survey | US | 2002, Mayers |

[56, 70, 74, 80, 84, 85, 123, 159, 165-167]

**Table 9.2:** Onset of various types of adverse health effects.

| | Adverse effects | | Onset after tattooing | Comments | Reference |
|---|---|---|---|---|---|
| Inflammatory reactions in tattoos | Spongiotic reaction | | | red and black tattoos | 2015, Thum |
| | Psoriasis form reaction | | 1 week-few months | | |
| | Interface (lichenoid/vacuolar) reaction | | few weeks | black tattoo | |
| | Nodular and diffuse (granulomatous) reaction | Tuberculoid granuloma | | | |
| | | Sarcoidal granuloma | | | |
| | | Suppurative granuloma | 1/3 weeks | gray/black tattoos | |
| | | Necrobiotic/Palisading granuloma | 7 months- 1 year | blue and black tattoos | |
| | Nodular and diffuse (pseudolymphomatous) reaction | | extremely variable | red tattoos but also purple/blue-green/black | |
| | | Vesiculobullous reaction | | | |
| | | Vasculitis | days- 1 month | | |
| | Fibrosing reaction | | | | |
| | Pseudoepitheliomatous reaction | | 1 week-few months | | |
| Infectious complications of tattoos | Acute Pyogenic infections | | within days to few weeks | | |
| | Atypical Mycobacterial infections | Non-tuberculous mycobacterial | within one month | | |
| | Mycobacterium infections | Lupus vulgaris/leprosy | years | | |
| | Syphilis | | | | |
| | Fungal infections | | | | |
| | Leishmaniasis | | | | |
| | Viral infections | HCV/HIV | | | |
| | | Herpex Simplex virus | | | |
| | | Human Papilloma virus | months to years | | |
| | | Molluscum contagiosum | weeks to months | | |
| Inflammatory reactions in tattoos | Granulomatous reactions | Sarcoidosis | from weeks to years | 50 reported cases of interferon induced sarcoidosis | 2014, Simunovic |
| | Pseudolymphoma | | months to years | red tattoos | |
| | Lichenoid | | recent tattoos | preponderant red tattoos but also other colors | |
| | Connective Tissue Disease | | | | |
| | Reactivation/Exacerbation of underlying dermatoses | Psoriasis | | | |
| | | Atopic dermatitis | | | |
| | | Pyoderma gangrenosum | | | |
| | | Lichen sclerosus | | | |
| Neoplasms in tattoos | Pseudoepitheliomatous hyperplasia | | | | |
| | Squamous-cell carcinoma and keratoacanthoma | Keratoacanthoma | recent tattoos | red tattoos | |
| | Melanocytic neoplasms and malignant melanoma | | | | |
| Inflammatory reactions in tattoos | Sarcoidosis on tattoos (59 cases-mostly traditional tattoos) | | 6 weeks - 45 years | red and black tattoos mostly involved | 2013, Kluger |
| | Sarcoidosis on PMU (8 cases) | | 2 years- 25 years | red and brown PMU | |
| | Isolated uveitis (8 cases) | | 6 months- 12 years | light blue tattoos | |
| Skin cancer | Squamous-cell carcinoma and keratoacanthoma (23 cases) | | days - 20 years | red tattoos | 2012, Kluger |
| | Melanoma (16 cases) | | 3 months-40 years | black and dark colored tattoos | |
| | Basal-cell carcinoma (11 cases) | | 1 year- 55 years | black and dark colored tattoos | |

[168-171]

## 9.1. Acute aseptic inflammation

In this paragraph, reactions such pain, redness, blistering, swelling, itching, erythema, flush, mild bleeding during the healing process, are considered evidences of an on-going acute aseptic inflammation that could follow tattoo application and/or removal.

Except for henna-based temporary body art decoration, which are applied on the skin in a non-invasive way, placing a tattoo implies to breach skin layers with a needle, hence to trigger an injury to the superficial vessels. Such inevitable bleeding usually disappears within few days without treatment. Other minor discomfort symptoms include redness, swelling, and lymphadenopathy. As long as the wound is not contaminated by microorganisms the inflammation process remains aseptic and phases out within one month, during which clients present an induration of the tattoo with superficial crusting. Possible complaints range from pain to itching and blistering. In rare cases this injection of foreign substances inside the skin may provoke a general flush.

The acute thermal stress inflammation induced by laser removal on the epidermis may give rise to various transient effects, crusting and blistering being the most frequent, the latter especially with unexperienced laser operators applying inappropriate parameters such as too low light intensity or too long pulse duration. Dermal capillary damage caused by higher peaks of laser energy may result in transient erythema and pinpoint bleeding, usually self-resolving after few days by ice application [172, 173]. One case of persistent erythema has been reported when using a long pulsed device [174]. Textural changes heal usually within 1-2 months [172]. Additional acute effects may include fibrosis, scaling, and induration.

As seen earlier, prevalence of such transient tattoo disturbances is difficult to measure because self-report questionnaires might be flawed by selection bias. In addition, tattooed individuals might confuse between true medical disorders and mild symptoms inherent to the wound healing process. The results reported in different surveys are thus extremely variable. While the Klügl on-line enquiry showed a complication rate of 67.5% in tattooed people, other authors give much lower figures based on much smaller samples. Kluger in a review [175], reports together with Klügl's results, two other studies where the prevalence of acute symptoms was estimated between 12.5% [56] to 31% [176], with pruritus on top of the list (21.6%). Brady, [159], calculates 10.3% adverse events among 300 US tattooed individuals, with only 4.3% of total participants showing acute symptoms (pain, itching, swelling). Serup, [177] contends that one third of tattooed people experience swelling and itching, the latter being also the main complaints reported by 60 tattoo recipients out of 144 by Hutton Carlsen study [123], the majority (31/60) in relation with sun exposure, the others described as "acne-like changes" or secondary to "alcohol or tomatoes consumption

This variability in prevalence is mirrored by the degree of symptom severity which can be evaluated very differently from one tattooed person to another. In the Klügl internet study, 11% of the subjects qualified their symptoms as "moderate", and 1.8% as "intense" or "very intense". In the abovementioned Klein internet study [85], almost half of the 157 patients having experienced a removal by laser therapy declared it was much more painful than tattooing itself, while a third of them said the level of pain of both processes was comparable.

27% these acute symptoms may become chronic (beyond 3 months) as evidenced by Hogsberg's 2013 survey of 154 tattooed Danes [80]. 16% of the same sample reported lasting sun-induced swelling and itching. In his New York study, Brady counted 6% of chronic complaints (beyond 4 months) among his 300 tattooed patients.

Other reported collateral effects include neurologic pain in upper limbs, papulo-nodular skin elevation from pigment overload, soft tissue lymph oedema, skin pigmentation around the tattooed area and in the regional lymph nodes [160, 177].

Apart from the adverse effects described on loco-regional level, also generalised contact dermatitis can be triggered by impurities present in tattoo inks, such as metals usually

but not always at trace levels (almost all inks contain nickel), or preservatives (e.g. parabens, methylisothiazolinone). Such hypersensitivity reactions may be confused with microbial infections or injury repairing inflammation, especially if they don't diffuse beyond the tattooed area.

Even if Klügl's survey showed more frequent skin reactions to coloured tattoos (83%) comparing to black tattoos (80%) calculated on the total of replies that could be multiple, Brady [159] notes the frequencies of reactions provoked by black tattoos are reported in the literature in an inconsistent way, emphasizing the need for larger studies in order to show the respective proportions of adverse effects for each tattoo colour.

## 9.2. Infectious risks

In the context of tattoo/PMU application pathogens may proliferate for various reasons, starting at the ink manufacturing step, or once the bottle has been opened and used without respecting the standard rules of asepsis. A common bad practice consists of diluting black ink with tap water in order to get different shades of grey. Other contamination sources include the tattooist poor hygiene, or the inappropriate use of tattoo equipment, such as using the same needle for successive clients without proper sterilisation. In registered parlours implementing standard hygiene guidelines, professional tattoo artists have succeeded in reducing the rate of contamination through pathogens, especially in the PMU sector. After the tattoo procedure, the wound may also be subject to infection, in particular if hygiene recommendations are not followed by the tattooed person.

In developed countries most frequent infectious complications are caused by bacteria. Blood borne viral transmission may also be involved if minimal hygiene requirements are not met, such as in prisons or in non-professional parlours or during home-tattooing parties [178]. Mycotic or parasitic diseases have only been described in exotic or anecdotal cases.

### 9.2.1. Bacterial infections

Within a couple of days after the tattoo application pyogenic bacteria (e.g. streptococcus or staphylococcus aureus) may seldom give rise to superficial skin papulo-pustules, folliculitis, impetigo or ecthyma. Rare cases of deeper regional infections, such as furunculosis, erysipelas and cellulitis of the entire limb, have been described [161]. However, following proper hygiene protocols, systemic infection, with associated gangrene, osteomyelitis, epidural abscesses, septicaemia, toxic shock syndrome involving lethal prognostic is exceptional, provided that there is no underlying heart valvular diseases or other previous health conditions. Having large and multiple tattoos increases the risk of complications like bacterial endocarditis [179] and it is advised to patients with known story of cardiac valvular disease (1% of the general population, [180]) to avoid tattooing, or at least to perform it under strict antibiotic umbrella [181].

Kluger [175] contends the actual incidence rate of superficial skin infections is unknown since many tattooed persons are reluctant to seek medical advice for minor transient symptoms. Furthermore, medical statistics do not exist. However, some authors like Laux [84] and Klügl [70] have estimated it at respectively 1-5% and 0.5% of the tattoo-recipients. Kaatz [157] suggests that the risk of infection is increased when the patient suffers simultaneously of concomitant diseases such as sarcoidosis (see below), but this rate depends first and foremost on the hygienic settings of the studio and the tattooist's experience and the way he uses material and tools. Bacterial contamination is for instance uncommon in the case of PMU application, usually performed by licensed and trained aestheticians in well-established shops [182]. Another important factor is the tattoo inks' sterility. In the literature ink contamination figures of sealed tattoo/PMU ink bottles range from 10 to 50% according to various authors (see Table 9.3), pointing out

the urgent need to enforce regulatory measures ensuring inks sterility. The survival characteristics of vegetative bacteria and endospores, fungi, and bacteriophage (as virus surrogate) in tattooing solutions have been documented [183].

**Table 9.3:** Bacterial contamination rate of sealed tattoo/PMU inks.

| Author | Year | Ink contamination rate (%) |
|---|---|---|
| Høgsberg et al. | 2013 | 10 (6/58) |
| Health Canada | 2011 | 20 (3/15) |
| Kaatz et al. | 2008 | 37 (3/8) |
| Baümgartner et al. | 2011 | 44 (17/39) |
| Charnock et al. | 2004 | 50 (1/2) |

[30, 78, 156-158]

It has to be pointed out that opportunistic germs, such as pseudomonas or Non Tuberculosis Mycobacteriae (NTM), have also emerged. This phenomenon may be linked to either the presence of these pathogenic bacteria in unopened tattoo ink bottles [32] or unsterile tap water used to dilute black inks in order to obtain different grey shades [184]. Atypical Mycobacteriae infections may appear on the grey lines of the tattoo from 3 days up to 1 month after application, as unspecific red papules, pustules or lichenoid plaques accompanied by pruritus. Histologic examination shows suppurated or tuberculoid granulomatous patterns, which may be confused with pseudoepitheliomatous hyperplasia (PEH, see below). Mycobacterium abscessus, a species of rapidly growing mycobacteria, was also reported causing skin infections with erythematous papules [185].

Home tattooists operating under questionable hygiene conditions have also been associated with emerging "cluster outbreaks" of Community acquired-Methicillin-resistant Staphylococcus aureus (CA-MRSA) infections, facilitated by the high percentage of asymptomatic carriers in some US Communities [33, 186]. Tap water used for ink diluting purposes has been incriminated as well in the proliferation of these germs [165]. Last but not least, as with any antibiotics use (here in the form of topical aftercare ointment) there is the theoretical risk of germs developing resistance against some antibiotics.

### 9.2.2. Viral infections

Tattooists operating in unsanitary facilities may also contaminate tattoo recipients with the human papilloma virus (HPV) or molluscum contagiosum (MCV) because of a poor hygiene causing so viral warts after 2 weeks to 10 years after tattoo application (Wenzel, 2013, dermatology). Given such a long latency Kluger [161] has equated these viral reactions to a Köbner phenomenon (tattoo reactions on pre-existing skin lesions, see below section 9.3.2). Latent HPV can be also reactivated by UV exposure 2.5 years after tattooing took place [187]. So far only one case of a herpes rash within a tattoo has been reported by Kluger [175], but since it occurred 3 days after the application, Kaatz, [157] wonders whether the virus was directly inoculated during the tattoo procedure itself, or if the latter only reactivated a latent herpes infection.

Hepatitis viruses (HBV or HCV) which are responsible for severe systemic diseases, such as hepatic failure, can be transmitted during tattoo application. Conflicting results are available in the literature regarding the risk of hepatitis among tattooed people. On this basis in 2012 and 2010, Jafari published two systematic literature reviews and meta-analyses which aimed to determine whether tattooing can be considered a risk factor for the transmission of hepatitis C and B, respectively [188, 189]. The odds ratio (OR) was used to quantify how strongly hepatitis was associated with having tattoos in a given population. As reported in Figure 9.5, the calculated odds ratios are higher than one,

meaning that having tattoos (compared to not having them) raises the chances of getting hepatitis. Even considering the limitations of the studies and the fact that these findings do not establish a formal causality between the two events, the association between tattooing and the risk of transmitting hepatitis was present in all subgroups, strong in the case of hepatitis C with ORs values higher than 2. In addition, results suggested a stronger association between tattoos made in non-professional parlours and hepatitis C (pooled OR 2.80 based on 4 studies) compared to those made in professional studios (pooled OR 1.28 based on 4 studies). Jafari [189] reported that in countries with tattoo prevalence of 11-27% among inmates and 8% in the general population, 12-25% and 6% of hepatitis C in prison and in the community, respectively, are related to tattooing. Regarding hepatitis, in particular hepatitis C, similar conclusions were reported also by Aiyedun [28] that evidenced how needle stick injury and exposure prone procedures, including tattooing, are predisposing factors for the transmission of blood borne virus.

**Table 9.4:** Tattooing as risk factor for the transmission of hepatitis.

| | Hepatitis | Papers included in the meta-analysis | Total participants | Type of study | Pooled odds ratio (confidence interval at 95%) | Highest odds ratio in subgroup analysis (confidence interval at 95%) |
|---|---|---|---|---|---|---|
| **Jafari, 2010** | C | 83 | 132145 (from 26 countries) | 45 cross-sectional 30 case-control 8 cohort | 2.74 (2.38-3.15) based on all studies | 5.74 (1.98-16.66) (non-injection drug users) based on 6 studies |
| **Jafari, 2012** | B | 31 | 665169 (from 19 cuntries) | 19 cross-sectional 9 case-control 3 cohort | 1.48 (1.30-1.68) based on all studies | 1.64 (1.32-2.03) (high risk behaviour group) based on 5 studies |

[188, 189]

Recent unpublished data, reported in an epidemiological study realised by Italian Surveillance System (SEIEVA) in the period 2010-2014, showed strong association between placing a tattoo and acute B- or C-hepatitis without proving a formal causality between the two events: subjects who had placed a tattoo in the last 6 months had a significant and almost double risk of acute B- or C-hepatitis as compared to subjects without a tattoo (in the age group 15-54 year-old, adjusted OR=2.1 with confidence interval (CI) at 95% 1.4-3.1 for hepatitis B and OR=2.2 with CI at 95% 1.1-4.4, for hepatitis C were calculated). Klügl [70] calculated a post-tattoo hepato-seroconversion rate of 0.6% against the total number of tattooed people showing any kind of adverse reaction.

In contrast to hepatitis virus, which can easily infect a person, direct transmission of the HIV virus needs a huge and prolonged body fluid contact, hence AIDS contamination through tattoo application remains theoretical, and has been indeed documented only once in the whole medical literature, in a possible case that concerned two inmates in 1988 [175].

## 9.3. Allergic/hypersensitivity and auto-immune type reactions

This group of inflammatory unpredictable responses includes both acute allergic and delayed hypersensitivity reactions, very close clinically and histologically to auto-immune skin pathologies reactivated up to years after by tattoo procedures.

### 9.3.1. Allergic reactions

Though hypersensitivity is cited in medical literature as the most common reaction to tattoos and PMU inks, in particular the classical lichenoid reaction to red pigments (in the past often related to the mercury contained in cinnabar), classifying a tattoo reaction specifically as an 'allergy' remains a challenge for Brady [159]. Some "granulomatous/lichenoid" response may be mixed up, both clinically and histologically,

with and in some case be the first stage of underlying systemic disorders like sarcoidosis, lichen planus, or lupus erythematosus (see below point 9.3.2).

In the past, pigments based on or containing mercury sulphide (cinnabar, once used in tattoo red inks), chromium (in green), cobalt (in blue), cadmium (in yellow) or manganese (in purple) have been traditionally linked to allergic phenomena, but these pigments have been mainly phased out in most modern inks, being present only as trace level [168], and yet allergy continues to be mostly associated with red tattoos, throwing suspicion to primary aromatic amines (PAA)-containing azodyes. Besides use of compounds and elements such as cadmium selenide, ferric hydrate, aluminium, carbon, barium, copper and strontium still remains frequent. Titanium oxides are used in white pigments but trigger no allergic response [190]. Light-blue and green pigments cause seldom allergic reactions, mostly in relation to elements and compounds such as chromium, aluminium or chloride cobalt [190]. Despite granulomatous allergies reported for magnesium, chromium, mercury, cobalt, Serup [177] sustains that chromate VI and nickel are apparently not a clinically important inducers of delayed allergy (sometimes after months or years), as nickel, even if present in all inks [191], is swiftly washed out of the tattooed skin. We already mentioned that predisposed patients may experience a few days after the tattoo/PMU placement a widespread rash due to impurities such as nickel. Preservatives like parabens can provoke similar systemic eczema, sometimes 2 months later [192].

As far as black pigment is concerned, only a few allergic reactions have been so far described [168]. On the contrary, for temporary black henna body decorations, made of combination of red henna (little sensitising) plus PPD (p-phenylenediamine, a powerful antigen, used also in permanent black hair dye), and applied by street artisans to young people in fashionable venues (e.g. holiday resorts, festivals, attraction parks), the bulk of reported side-effects are of hypersensitivity type, i.e. local or widespread contact dermatitis, and hypertrophic or keloid scars [168, 193-195]. However, Calogiuri [196] stressed the possibility that metals (e.g. nickel, cobalt, mercury) and other ingredients such as thiurams and latex proteins might contaminate henna preparations, inducing hence as well contact dermatitis.

Overall the mediator of such allergic responses is hard to determine because the composition of these low-purity industrial products remains generally undocumented. Furthermore, superficial skin patch tests are mostly of no help, in particular with the granulomatous and lichenoid types of allergy (see below). The patch test study on 90 patients realised by Serup [191] suggests that chronic allergy is not induced by specific ink components as such, but by a slow intra-skin formation of pigment protein complex called "hapten" in the following months or years.

Both onset and duration of the hypersensitivity reaction are unpredictable, as they can start right after the tattoo procedure, or decades after (up to 45 years!), and may last lifelong [197]. The clinical appearance is not specific (papules, oedema and induration), and can be limited to tenderness and itching of extremities (typical), or develop until a tumour-like wart. Especially red tattoos show ulceration, necrosis and hyperkeratosis. Plaque elevation is very frequent in red, appears sometimes also in blue/green tattoos. [160].

In the case of tattoo removal inks degradation products scattered by the laser beam may elicit an hypersensitivity local response [82, 84, 167, 198, 199], or widespread immediately to the whole organism through the lymphatic system, provoking an anaphylactic shock [82, 83, 167]. Such a risk is increased if allergy already occurred at tattoo placement stage.

Histopathology classically distinguishes "lichenoid, granulomatous, or pseudolymphomatous" patterns, but such a classification does not correspond to a clear-cut clinical diagnosis and is rather challenging, as different patterns may coexist in the same biopsy. The following disorders may thus not be used to define specific tattoo reactions [165].

The development of allergy to latex proteins originating from the tattooist's gloves and introduced into the skin via the needle has been reported [177]. Serious complication may arise, with a risk of life-threatening anaphylaxis upon further exposure to latex. Sensitised persons can immediately elicit anaphylactic shock when they get into contact with latex particles either by a new tattooing session or by another direct contact with latex containing articles.

#### 9.3.1.1. Eczematous dermatitis

Acute or chronic eczema appears generally as a scaly and itchy papulovesicular rash after a tattoo application or removal, usually in individuals sensitized to medications such as topical disinfectants and antibiotics. This contact dermatitis is more frequent with red pigments, but may also involve black pigments or other dyes (green, blue, yellow). Originally limited to the tattooed area the erythema can then spread to the entire body, as reported by Caucanas [200] in the case of paraphenylenediamine contained in "black henna" temporary tattoos . For the latter, the incubation period may vary from 1 to 20 days, and is shorter in case of previous sensitisation.

#### 9.3.1.2. Photosensitivity

Light sensitivity may touch about 20% of tattooed individuals [201], mainly on sun-exposed body parts, such as face and hands. Hogsberg's 2013 survey [80] reported that 16 % of 154 tattooed Danes showed lasting sun-induced swelling and itching. Yellow cadmium-containing pigments after laser removal might also elicit local photo allergy [163].

Hutton Carlsen [123] performed a survey on sunbathers, 144 of which were tattooed. Among them, 21.5% experienced complaints linked to sun exposure. The major symptoms were swelling, itching/stinging/pain and redness, predominantly correlated to black and red tattoos, with blue following. The onset may vary from few second to the following day lasting from minutes up to several weeks. Results in terms of sun-induced complaints related to tattoo colour are reported in Table 9.5 (31 people expressed sun-related complaints, however multiple replies were allowed). Black tattoos were responsible for the larger number of complaints, but in percentage red tattoos were predominant.

**Table 9.5:** Sun-induced complaints related to tattoo colour (data from [123]).

| Tattoo colour | N° of persons | N° of complaints | % of complaints |
|---|---|---|---|
| **Black** | 133 | 20 | 15 |
| **Red** | 45 | 14 | 31 |
| **Pink** | 8 | 1 | 13 |
| **Orange** | 9 | 1 | 11 |
| **Purple** | 5 | 1 | 20 |
| **Blue** | 25 | 7 | 28 |
| **Green** | 31 | 2 | 6 |
| **White** | 10 | 1 | 10 |
| **Yellow** | 25 | 4 | 16 |

#### 9.3.1.3. Lichenoid and granulomatous reactions

**Lichenoid** (the most frequent type made of plaques and papules which can widespread to the whole body) and **granulomatous** (firm indurated nodules) patterns affect mostly the red portion of the tattooed area and provoke itching. Both lichenoid and granulomatous types can coexist in the same patient [202]. Mercuric sulphide (cinnabar) once used in red inks has been traditionally associated to the lichenoid type, but the recent shift towards organic pigments has not eliminated these kind of reactions, present

also after temporary henna tattoos application [168]. Greens and blues containing copper phthalocyanine pigments induce fewer allergies than those elicited by cobalt or chromium pigments. The role of manganese in inducing granulomatous allergic reactions in purple tattoos has not been proved [190].

Most of granulomatous reactions are foreign body encapsulation forms, appearing like papulo-nodular skin deposits of black pigment. They are not considered as allergic reactions by Serup, who classifies them as inflammatory non-infectious [192]. An allergic form with eczema and inflammation, probably due to aluminium, present in almost all tattoo inks as additive or pigment, may sometimes mimic the granulomatous forms [18] The purely allergic characteristic of such aluminium-induced granulomatous responses has been challenged, since they might also appear as sarcoidal granuloma involving, in predisposed patients, immunotoxic factors responsible for systemic sarcoidosis [17]. Sweeney, [203], reports a case of uveitis (eye inflammation) concomitant with a tattoo reaction probably to cobalt-containing pigments, while Setlur, [204], described a fatal case of granulomatous reaction in a patient died from pneumonia upon foreign body type response to his tattoo. Post-tattoo ocular involvement has also been reported by Ostheimer [205] (bilateral uveitis in all 7 patients with elevated and indurated black tattoos on various locations, e.g. arms, chest and abdomen), and by Kaatz [157] (concomitant retinal vasculitis and cystoid macular oedema).

Other types of granuloma are extremely rare, and in the case of tuberculoid granulomatous reactions to ferric oxide and chromium salts used in eyebrow PMU, they can have similarities with skin infections practically erased from developed countries, such as tuberculosis or leprosy. Cases of inoculation cutaneous tuberculosis and leprosy have been observed after tattoing in jail, in communities with high disease prevalence or in endemic regions [169].

#### 9.3.1.4. Lymphomatoid reactions

Called also pseudolymphomatous reactions, these erythematous indurated and sometimes itchy nodulo-papules and plaques mimic clinically and histologically skin lymphomas, but in 80-90% of cases fail to transform into malignant tumours [206]. Only one case of such evolution has been described so far in relation to tattoo reactions [169]. This delayed (from weeks to 42 years after the tattoo event) hypersensitivity infiltrates mostly start within the red parts of the tattoos (79% of the 19 cases studied by Marchesi [206]) but may also grow beyond the tattooed area, and involve other pigments: blue (cobalt), green (chromium) and black. Patch-tests to detect the culprit antigen are inconclusive. Pérez-Cotapos [207] sustains that months or years after tattooing people allergic to metal can display eczema, lichenoid reactions, or *pseudo lymphoma*.

#### 9.3.1.5. Pseudoepitheliomatous hyperplasia (PEH)

Weeks or months after a tattoo application these infrequent wart-like nodules or plaques warrant a skin biopsy to differentiate them from tumours (see section 9.4.2.1). They might also be associated to cutaneous infectious [163].

#### 9.3.1.6. Scleroderma and scars

In the long run the inflammatory processes described above may end up to a fibrotic and indurated aspect including scarring and keloids, labelled as scleroderma or pruritic morphea-like pathology, very similar to isomorphic reactions (see next section) developed in patients suffering from underlying connective tissue disorders [169]. The etiopathogenesis mentions prior needle trauma (like in tattooing or vaccination), but Thum [168] found no correlation between these traumas and morphea/scleroderma

diagnosis, suggesting to be due to persistent inflammatory process elicited by ink ingredients.

In the case of rare sequels to allergic reaction to black henna, hypertrophic or keloid scars have been reported [168, 193, 194].

As far as tattoo removal is concerned, permanent hypertrophic scars may develop if the Q-switched laser therapy causes deep damage under misappropriate conditions, or is applied at high energies required by resistant multi-coloured tattoo's containing iron oxide or titanium dioxide [162, 207].

### 9.3.2. Underlying Dermatoses reactivated by tattooing

#### 9.3.2.1. Köbner phenomenon

Köbner described in 1872 the "isomorphic" phenomenon: a psoriasis-like eruption emerging within the tattooed area of an already psoriatic patient. In addition to psoriasis similar flaring reaction may concern many more chronic dermatoses such as lichen planus/sclerosus, lupus erythematosus, atopic dermatitis, sarcoidosis, pyoderma gangrenosum, vitiligo, and skin vasculitis. Patients suffering from such underlying disorders, and also those presenting latent herpes infections, have the risk to see their disease being reactivated by the tattooing procedure. This "Köbner phenomenon" is clinically difficult to grasp, being more frequent in immunosuppressed patients. The incubation period of this flaring ranges from 1 week up to decades after the skin injury (usually within 10-20 days. Thum [168] observed a case of psoriatic arthritis within a week after skin lesions. An unambiguous link between tattooing and widespread flare-up remains to be proved, according to Kluger [161].

#### 9.3.2.2. Sarcoidosis

One of the main "*dermatologic masqueraders*", as defined by Selim [208] remains sarcoidosis, whose etiopathogenesis and diagnostic are mysterious [209], just as its controversial links with tattooing [157]. This systemic autoimmune pathology affects between 10 and 20 individuals on 100,000 in the general population [170]. Genetic predisposition is a requisite, but needs added environmental factors, like old skin injuries and scars, or embedded foreign bodies (e.g. in the opinion of some authors, tattoo inks) to trigger the disease, in particular with patients treated with interferon [169]. Granulomatous skin reaction, even of the non sarcoidal type, may reveal the systemic sarcoidosis in 25-30% of latent patients. This may happen from some weeks after the trauma, up to 45 years later, as mentioned by Kluger who considers that "*The tattoo is most probably the target of sarcoidosis, rather that its cause*" [170].

Clinically, the local symptoms are unspecific, ranging from no complaints to tender itchy papulo-nodules, plaques or infiltrations within the tattoo. Accompanying lesions may include scaling, ulcers or blisters. Reviewing 75 patients with sarcoidotic skin reaction to tattoos/PMU, Kluger [170] found that cases with lesions confined to the tattooed area were twice as numerous as those where the nodules were present outside the tattoo, on other scars, or elsewhere on the skin. Histopathologically difficult to differentiate from foreign-body granuloma, cutaneous sarcoidal manifestations restricted to one colour of the tattoo might represent hypersensitivity to the ink pigment (red and black being the most frequent), or the initial and often sole symptom of a general sarcoidosis (extra cutaneous involvement). The latter involves typically blue pigments, but green and brown may be encountered as well. Most of multi-coloured tattoos' patients react within a single colour of the tattooed area. However in 40% of cases, different colours were involved simultaneously. 70% of patients suffered from systemic sarcoidosis (no follow up for the remaining 30% which might potentially also develop symptoms in the long run), and from those 69% had their mediastinal lymph nodes infiltrated, and some had

their lungs affected. Lo Schiavo [210] reported that 74% of patients with skin sarcoidosis in a tattoo would be diagnosed later a systemic form.

#### 9.3.2.3. Vasculitis

According to Thum, so far only 4 cases of post tattoo cutaneous vasculitis have been documented in the medical literature [168] with an incubation period comprised between 10 days to 28 years after the tattooing. The responsibility of ink ingredients has not been substantiated [175].

#### 9.3.2.4. Lupus erythematosus

Thum Chee reported one case of cutaneous lupus erythematosus lesions developed in a black tattoo 3 weeks after its application, which later on spread beyond the tattooed area. Patients without signs of systemic lupus erythematosus may present "Skin lupus erythematosus–like tattoo reaction" to an old tattoo. Several cases of patients with known systemic lupus erythematosus developing, sometimes 15 years later, discoid lupus erythematosus–like reactions within tattoos, have been published in the medical literature [157, 161, 168, 211].

#### 9.3.2.5. Lichen

In post-tattoo lichenoid eruption, differential diagnosis between a true lichen planus and a generalized lichenoid tattoo reaction can be difficult. Some other anecdotal manifestations include lichen sclerosus and atrophicus, perforating collagenosis granuloma annulare (associated with red tattoos), erythema multiform and scleroderma-like reaction restricted to the red parts of a tattoo, *Darier's disease (genetic Keratosis follicularis)* [161, 169, 212].

#### 9.3.2.5. Other chronic dermatoses

Juhas [198] mentions an usual complication, morphea. Other rare manifestations such as Pyoderma Gangrenosum (PG), especially in the lower limbs, have been described in only two patients, one of them affected concomitantly by hematologic cancer [169].

## 9.4. Other secondary effects

Other types of tattoo collateral effects relate to pigmentary disorders, especially after laser removal, and to diseases such as cutaneous tumours, which may appear coincidentally within a tattooed area, but without any clear link to the tattoo procedure. However, even though tattoos might not elicit skin cancer, they can blur its surveillance, and interfere with the diagnostic and treatment of several other pathologies. Finally, a recap of main contra-indications to tattooing is presented in 9.4.4.

### 9.4.1. Pigmentary disorders

*QS* Laser removal is major responsible of pigmentary disruptions, grouped in *hypopigmentation, hyperpigmentation, and paradoxical darkening*. As part of the risk communication strategy, tattoo candidates should be warned that due to these collateral effects, the laser therapy, on top of being painful, might represent a lengthy and frustrating process, sometimes without achieving the same level of completeness as the patient expected. Table 9.6 lists the main Q-Switched lasers in use together with the indication of the wavelength at which they operate.

**Table 9.6:** Summary of Q-Switched lasers currently in use.

| Q-Switched Laser | Wavelenght (nm) | Tattoo Colours |
|---|---|---|
| Nd:YAG | 532 | Red; Orange |
| | 1064 | Black; Blue |
| Ruby | 694 | Black; Blue; Green |
| Alexandrite | 755 | Black; Blue; Green |

#### 9.4.1.1. Hypopigmentation

At certain QS laser wavelengths (especially in the ultraviolet range) the epidermal melanocytes are destroyed preferentially, leading, from one up to several months after treatment, to unwanted hypopigmentation, especially present in patients with tanned or darker skin [83, 173]. Sun exposure should therefore be avoided before laser treatment, while proper 10-days aftercare (treated area to be kept elevated and cooled) reduces the formation of bulla in most cases. Operating with Nd:YAG laser at its longest wavelength (1064 nm) would minimise that risk [162]. However, in order to remove tattoos coloured in red, yellow and orange, its shorter wavelength (532 nm) is required, making hypopigmentation unavoidable. This melanin pigment deficit is usually transient, but might last for years and or even life long, in particular in case of multiple laser sessions [82, 163, 172, 173]. Such permanent hypopigmentation could affect up to 10% of the individuals having removed their tattoos with laser [82, 162, 163].

#### 9.4.1.2. Hyperpigmentation

Especially with darker-skin individuals and people having been treated before with gold salts for diseases such as rheumatoid arthritis, laser irradiation increases dermal UV sensitivity, leading to transient hyperpigmentation in 5-10% of cases, the incidence climbing with repeated laser treatment [82, 162, 172, 173, 213].

The use of gold salts and exposure to UV light sources is known to induce chrysiasis (permanent alteration of skin pigmentation due to deposition of gold and triggered by UV radiation). For this reason, people treated with such salts or affected by chrysiasis should be advised to carefully consider the possibility to undergo QS laser tattoo removal in order to avoid worsening hyperpigmentation disorders.

#### 9.4.1.3. Paradoxical darkening

Occurring frequently after QS laser therapy, and in particular removal of multicolour tattoos, paradoxical darkening is probably induced by metals oxides contained in tattoo pigments. Therefore, it is often observed while treating white inks based on titanium oxide and flesh-toned colours for PMU containing iron oxides. This modification is commonly temporary, but can sometimes become permanent [82, 83, 168, 207, 213]. In a study of 184 patients [213] having removed their non-black tattoo with QS laser, 33 suffered colour shifts from white, flesh-coloured, red, brown, yellow and crimson areas of their tattoos to mild grey or black.

### 9.4.2. Tumours

It is unclear whether tattoo inks may induce tumours, be it local or general. On the one hand, many substances contained in tattoo inks (such as PAHs in black pigments or PAAs) and their (photo) degradation products, sometimes with increased solubility properties, are classified as mutagenic, genotoxic and carcinogenic. On the other hand, cancer is considered a multifactorial disease, which may take decades to express. Thus a direct correlation between tattoo and tumour is challenging to establish and a straightforward causality between tattooing and cancer formation is far from being

demonstrated.. Hence most authors consider the growth of cutaneous tumours within tattooed areas as purely incidental [171, 203].

Considering that millions of people are tattooed, and compared to the 2-3 millions of skin cancers arising each year [177, 192], the 50 cases of skin tumours developed in tattoo areas reported during the last 40 years seem negligible and in the authors' opinion has to be considered thus far as coincidental [171]: 16 cases of melanoma, 11 cases of basal cell carcinoma (BCC) [214], and 23 cases of squamous Cell Carcinoma, SCC (difficult to distinguish from keratoacanthoma, KA), with a latency ranging from 1 month to 55 years after the tattoo. While melanoma and BCCs are more frequent within dark coloured tattoos, SCCs, KAs and pseudoepitheliomatous hyperplasia (PEH) appear mostly on red tattooed areas [171]. Further, old concerns about epidermal neoplasms following lumbar puncture through lower back tattoos have been discarded by Kluger [215], who stresses that "*there has never been a case of malignant melanoma,* basal-cell carcinoma (*BCC), or* squamous-cell carcinoma (*SCC) occurring on a single tattoo*".

#### 9.4.2.1. Pseudoepitheliomatous Hyperplasia

These benign nodules, warts, plaques or ulcerated lesions may develop from one week to a few months after tattooing, mainly within red coloured areas, in connection with infectious, inflammatory affections (see section 9.3.1.5). Kluger in his review reports 10 cases in the last 40 years [171]. Clinically and histologically, the distinction with KA or verrucous tumours remains a challenge [169].

#### 9.4.2.2. Keratoacanthoma and Squamous Cell Carcinoma

Post tattoo appearance and evolution helps to distinguish between benign PEH, borderline KAs (develop from one week to a year after tattoo, only associated to red inks in 82% of cases, regress spontaneously within a few months), and malignant SCC, which may grow more than 20 years after tattoo, albeit without causative link with it (Kluger 2012 Lancet onc) [167].

#### 9.4.2.3. Basal cell carcinoma

Rarely growing after a skin injury, this tumour may invade secondarily a tattoo from the adjacent non-tattooed skin.

#### 9.4.2.4. Melanoma

Kaatz' risk analysis [157] could not show tattooing was a meaningful risk factor for the growth of malignant melanoma. However this neoplastic lesion should not be confused with benign nevi which can also arise within a tattooed area, rendering the differential diagnosis very arduous (see point 9.4.3 hereunder).

#### 9.4.2.5. Cutaneous lymphoma and other rare skin tumours

The only documented case of pseudo lymphoma in tattooed area transforming after years into an invading skin lymphoma has been reported by Kluger [171], who also mentions other extremely rare malignancies appearing years after tattooing, yet without any causality with it, such as dermatofibrosarcoma protuberans, or leiomyosarcoma. Baker [216] reported one case of dermatofibrosarcoma protuberans (uncommon, locally aggressive cutaneous tumour of intermediate grade malignancy) arising in a tattoo.

### 9.4.3. Medical diagnostic and treatment interference

Dark coloured pigments used in tattoos may deposit in both skin and regional lymph nodes, and mask the possible growth and malignant transformation of pre-existing nevi in the tattooed area (false negative), or mimic metastatic invasion of a lymph node by a melanoma (false positive). However using modern immunohistochemical techniques it is now possible to distinguish between the two types of pigmentation.

Other false-positive results may occur in mammography when tattoo inks contain metals, and especially iron oxides able to blur diagnostic imaging such as MRI[8] and PET[9] scan. In rare cases MRI exams may also lead to complaints of pruritus and burning in tattooed individuals [157, 207, 217]. Spinal anaesthesia in the lumbar region, frequently used in obstetrics, is more difficult to carry out if the skin area is tattooed, in particular with dark colours, but the potential risks of such a procedure are still under debate with different opinions expressed by various authors [215].

### 9.4.4. Contra-indications to tattoo procedures

Many physicians advice to avoid tattoo procedures in customers, both presenting specific clinical peculiarities and suffering of different disorders, at dermal or systemic level.

#### 9.4.4.1. Skin Disorders

- Pre-existing moles or other pigmented dermal lesions in the tattooed area may display histological post-injury atypical changes, and complicate the surveillance of any potential malignant transformation years after the tattooing. Suspicious nevus or infectious reaction within the tattooed area warrants postponement of tattoo procedures until a reliable diagnosis is established and appropriate treatment carried out [82, 83, 162, 213, 218].
- Sun baths should be avoided in the period preceding laser removal to diminish the risk of skin blistering.
- Prior sensitivity to latex, nickel or other chemicals used in tattoo inks can be reactivated by the tattoo procedure. Eczematous patients may encounter a more difficult aftercare wound healing process. People having experienced an allergic reaction at tattoo placement stage should be warned against the risk of anaphylactic shock during the laser removal stage, and thus could be treated preventively by corticosteroids and antihistamines [83, 167].
- Years after the tattoo procedure, chronic skin disorders, such as psoriasis or lichen, might reactivate and induce a rash within the tattoo (Köbner phenomenon) [161]. Tattooing on the edge of a vitiligo lesion may trigger its extension [219]. Prior latent cutaneous herpes might be reactivated by tattooing procedures.
- Patients previously treated with gold salts and those suffering from chrysiasis (UV-induced skin hyperpigmentation due to deposition of gold) should be prevented from tattoo removal by QS laser to avoid aggravating the pigmentation disorder [82].
- Traumatic tattoos with embedded combustible material involve the risk of re-ignition during the laser treatment stage, which can give rise to substantial scarring [83, 213].

[8] Magnetic resonance imaging *(*MRI*),* or Nuclear magnetic resonance imaging (NMRI*)*
[9] Positron emission tomography (PET)

- Patients with known pre-existing Pyoderma Gangrenosum should be strongly advised against tattooing, particularly on the lower extremities [169].

#### 9.4.4.2. Systemic Disorders

- Haemophilic patients or those with coagulation disturbances may display extensive bleeding secondary to the needle injury, and need medical approval prior to proceed with tattooing [219].
- Patients with heart valvulopathy (1% of the general population) need antibiotic coverage before any tattoo procedure, or otherwise take the risk of infective endocarditis and fatal septicaemia [181].
- Underlying autoimmune systemic diseases (sarcoidosis, lupus erythematous, etc.) or treatment with interferon, might trigger delayed flaring of the latent disease within the tattoo [169].
- Immunosuppressed and diabetic patients should be aware that their risk of getting a post-tattoo infection or undergo a delayed wound healing process (during application or removal) can be increased [82].
- As a general preventive measure, it is advisable not to perform any tattoo procedure in pregnant or breast feeding women, even though no specific risk could ever be shown ([198]).

# 10. Experience with the CoE ResAP(2008)1

The first CoE ResAP was published in 2003 and it was substituted by an updated version in 2008. Since then various European countries have gained experience in the implementation of the recommendations of the resolutions, either because they have adopted national legislation largely based on them or because they perform market surveillance activities using the list of chemicals contained in the CoE ResAP(2008)1 as a reference for the RAPEX notifications on dangerous tattoo/PMU inks.

This chapter aims to revise such experience on the basis of the replies gathered via a questionnaire and the discussions held during the meetings of the CSN-STPM with the intention to evaluate if new recommendations to improve the safety of tattoo/PMU inks would be needed and could be put forward.

For more detailed information please refer to the JRC report on the Work Package 3 of the project [3].

## 10.1. Chemical requirements

The CoE ResAP(2008)1 recommends not to use about two thousands substances in tattoo/PMU inks. Some of them are listed in its Table 1 (27 aromatic amines) and Table 2 (35 colorants), but the large majority is enumerated in lists which are part of European legislations referred to in the resolution (cosmetics and CLP regulations, as well as Directive 95/45/EEC). In addition, Table 3 of the CoE ResAP(2008)1 suggests the maximum recommended concentrations for impurities.

On the one hand, many repetitions exist in the chemical recommendations of the resolution and the same substance is often cited in more than one list. For instance, out of the 27 aromatic amines present in Table 1 of the resolution, 25 are also classified as CMR in the CLP regulation and 19 are mentioned in Annex II of the cosmetics one. A similar situation is observed for colorants.

On the other hand, Table 1 and 2 do not list all the aromatic amines and colorants that the resolution advices not to be used in tattoo/PMU products; many additional ones are present in Annexes II and IV (with restrictions in column g) of the cosmetic regulation and in Annex VI (Table 3.1) of the CLP one, they were identified and listed in Annex I of the JRC report on Work Package 1 [1].

The presence of various negative lists in different documents complicates the implementation of the recommendation by stakeholders, such as enforcement laboratories and manufacturers. From this point of view, the preparation of comprehensive negative lists at least for the most important ingredients (colorants) and impurities/degradation products (aromatic amines) of inks was judged positively by a number of experts. In addition, several stakeholders indicated that the chemical requirements should be EU harmonised.

The aromatic amines in Table 1 of the CoE ResAP(2008)1 should neither be present in tattoos and PMU products nor released from azo-colorants in concentrations that are technically avoidable according to Good Manufacturing Practices. The experts of the CSN-STPM agreed on the need to specify limits for these compounds, even though not on the value(s) to be adopted.

Based on the discussions held during the CSN-STPM meetings and the replies to the questionnaires, the aromatic amines and colorants reported in Tables 10.1 and 10.2 could/should be evaluated for addition to the negative lists of Table 1 or 2 of the CoE ResAP(2008)1, respectively. The last column of Table 10.2 presents possible degradation products classified as CMRs, which might be formed by reductive cleavage of an azo bond or by break of an amide link. In the same Table, the colorants listed with an asterisk do not belong to those reported as currently in use.

**Table 10.1:** Aromatic amines that could be evaluated for inclusion in Table 1 of CoE ResAP(2008)1.

| | | EC Reg 1223/2009 | EC Reg 1272/2008 | |
|---|---|---|---|---|
| **Substances** | **CAS number** | **Annex II (ref. number)** | **Annex VI Table 3.1 (index number)** | **Classification (CMR, Skin/Eye Irrir./Sens.)** |
| **aniline** | 62-53-3 | X (22) (its salts and its halogenated and sulphonated derivatives) | X (612-008-00-7) | Carc. 2, Muta. 2, Eye Dam. 1, Skin Sens. 1 |
| **2-ethoxyaniline** | 94-70-2 | | | |
| **N-isopropyl-N'-phenyl-1,4-phenylenediamine** | 101-72-4 | | | Skin Sens. 1 |

**Table 10.2:** Colorants that could be evaluated for inclusion in Table 2 of CoE ResAP(2008)1.

| | | EC Reg 1223/2009 | | EC Reg 1272/2008 | | |
|---|---|---|---|---|---|---|
| **CI Generic Name** | **CAS number Colorant class** | **Annex II (reference n.)** | **Annex IV (column g) (reference n.)** | **Annex VI Table 3.1 (index number)** | **Classification (CMR, Skin/Eye Irrir./Sens.)** | **Possible degradation products** |
| **P Blue 15** | 147-14-8 phthalocyanine | X (1367) (when used as a substance in hair dye products) | | | | |
| **P Green 7** | 1328-53-6 phthalocyanine | X (1369) (when used as a substance in hair dye products) | X (107) (not to be used in eye products) | | | |
| **P Red 5** | 6410-41-9 monoazo | X (1347) (and its salts when used as a substance in hair dye products) | | | | |
| **P Red 17** | 6655-84-1 monoazo | | | | | 5-nitro-o-toluidine (Table 1, Annex II, CMR) o-toluidine (Table 1, Annex II, CMR) |
| **P Red 181 VAT Red 1** | 2379-74-0 indigoid | X (1365) (when used as a substance in hair dye products) | | | | it may cause reactions in the skin |
| **P Violet 1** | 1326-03-0 xanthene | | | | | |
| **P Yellow 1** | 2512-29-0 monoazo | | X (4) (not to be used in products applied on mucous membranes) | | | aniline (Annex II, CMR) |
| **P Yellow 2*** | 6486-26-6 monoazo | | | | | p-chloroaniline (Table 1, CMR) |
| **P Yellow 3** | 6486-23-3 monoazo | | X (5) (not to be used in products applied on mucous membranes) | | | |
| **P Yellow 5*** | 4106-67-6 monoazo | | | | | aniline (Annex II, CMR) |
| **P Yellow 74** | 6358-31-2 monoazo | | | | | o-anisidine (Table 1, CMR) |
| **S Yellow 14*** | 842-07-9 monoazo | X (1107) | | X (611-056-00-6) | Carc. 2, Muta. 2, Skin Sens. 1 | aniline (Annex II, CMR) |

Considering the scientific evidences of the possible degradation of azo pigments in the skin and under light irradiation, for aromatic amines a different approach could also be taken into consideration. In fact, all those azo pigments that by reductive cleavage or break of amide bond could give rise to aromatic amines classified as CMRs or mentioned in Annex II of the cosmetic regulation could be inserted in the negative list of colorants.

Several national Competent Authorities and stakeholders would welcome an EU harmonised legislation on the chemicals present in the CoE ResAP(2008)1, as well as the establishment of a positive list of colorants allowed to be used in tattoo/PMU products and the harmonisation of analytical methods.

There was also a consensus among experts that limits for impurities in Table 3 of the CoE ResAP(2008)1 need to be revised or established, for instance for nickel, or added (strontium); however further discussions and evidences would be necessary to agree on values.

## 10.2. Labelling requirements

A general consensus was gathered on the need to add the following labelling requirements:

- period of maximum durability after opening (PAO);
- storage conditions;
- product type (ink for tattoo or PMU);
- health warnings;
- quantitative composition label.

No agreement was reached on the benefit to include in the label the production date, the distributor's address and the indication of the sterilisation method used for the inks.

## 10.3. Register of complaints/side effects and pre-marketing requirements

The majority of respondents were in favour of the establishment of a compulsory register of complaints and side effects.

On the contrary, opinions diverged on the proposal to set up a pre-marketing authorisation for tattoo/PMU inks.

## 10.4. Hygiene/sterility requirements

Some national Competent Authorities were in favour of making compulsory the specification of the ink and tool sterilisation methods (in the label), as well as the premise disinfection methods.

## 10.5. Other proposals

Among the additional proposals, the following were suggested by several Competent Authorities:

- to establish Good Manufacturing Practices for tattoo/PMU inks;
- to make safety assessment of inks compulsory;
- to prepare guidelines for risk assessment of tattoo/PMU products;
- to develop harmonised hygiene guidelines;

- to carry out market surveillance on products sold on the web;
- to establish compulsory training for tattooists (in accordance with national legislations);
- to enhance the collaboration among manufacturers and authorities;
- to ban backyard tattooing and illegal sales of "start-kits".

# 11. Risk perception and communication

Information about communication and perception of the risk associated to the permanent tattooing practice was collected through a questionnaire distributed to national authorities, as well as through a literature survey. The results are presented in the following sections.

## 11.1. Answers to questionnaires

### Risk communication

Nine national Competent Authorities provided data about the information campaigns that were conducted either at national or at local level in their countries. Their characteristics in terms of target audience and means used are summarised in Figure 11.1.

Targets included possible customers, tattoo artists and studios, physicians and school teachers; while means comprised printed materials, media coverage and events.

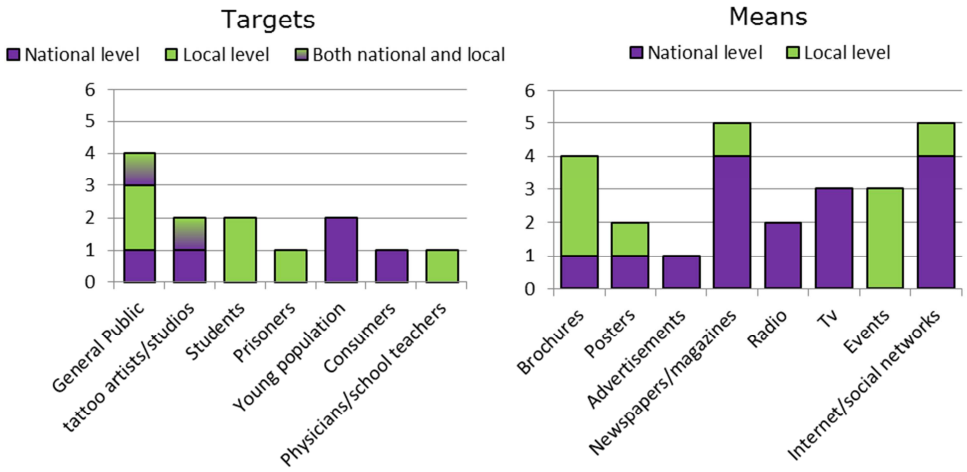



**Figure 11.1:** Characteristics of the information campaigns carried out by respondents.

General public seemed to be the preferred recipient of information campaigns, having been indicated by four different Member States with media (newspapers, radio, TV and internet) as the preferred means distribution, mainly at national level.

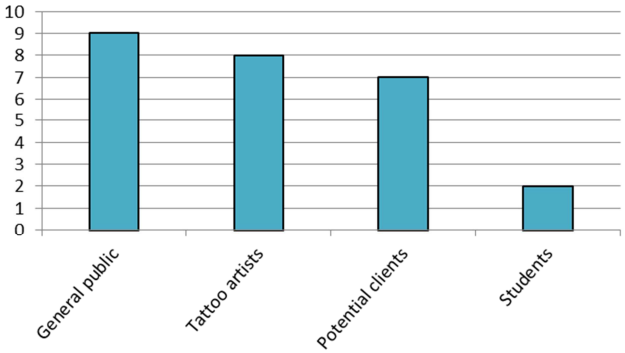



**Figure 11.2:** Need for additional information campaigns.

In the opinion of the majority of respondents and of experts of the CSN-STPM, to provide information on the risks of tattooing is indispensable to improve the safety of tattoo/PMU

practices and campaigns should be intensified towards tattoo artists, potential clients (including students) and general public (Figure 11.2).

If and when used, the prior informed consent document is a way to inform customers about the risks associated to the practice they are going through. One Member State, Italy, replied that a compulsory prior inform consent has to be signed by customers and seven that this is not mandatory, even if three of them recommend tattooists to use it. A recent survey performed by the Italian Institute of Health, in 2014-2015 on 7608 persons aged 12-75+ years old, showed that 50.8% of tattooed people signed the informed consent, 22.3% did not remember and 26.8% did not sign. Figure 11.3 reports the replies of six national authorities regarding the information available or requested in the prior informed consent document.

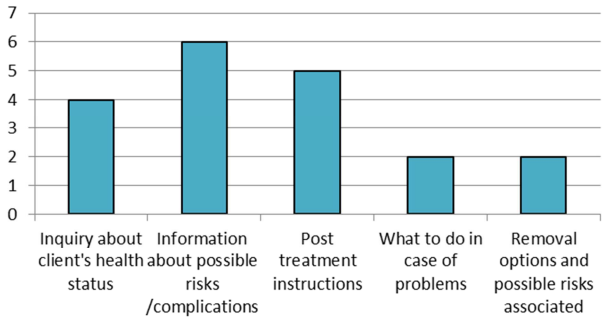



**Figure 11.3:** Content of the prior informed consent document.

### Risk perception

Only three national Competent Authorities were able to provide indications about risk perception of risks among the general and/or tattooed population, while six reported that they had no information at all. In their opinion, risk perception is mainly based on:

- awareness of prior aggravating medical conditions;
- awareness of the risks, such as infections and disease transmission.

Surprisingly, the choice of tattooists (professional or not), the safety of premises and tools in terms of sterility and hygiene, or the permanency and risks associated to removal options were not mentioned as reasons of concern for the general and/or tattooed population.

## 11.2. Literature

The perception of the risks linked to tattoo/PMU application and removal and their communication has been approached in many studies on adverse health effects, as a consequent issue [10, 70, 164, 188, 220, 221].

As for risk perception, these studies revealed that individuals desiring a tattoo are usually not aware of the ink ingredients, safety of tattoo inks and health risks connected to tattoo application/removal, including prior aggravating medical conditions. For instance, in an internet survey launched by Klügl and collaborators [70], emerged that 41% of the sample (3411 tattooed individuals) were not interested in the chemicals injected in their skin and about 33% of participants considered safe the injection of tattoo colorants in the human body.

Concerning risk communication, information campaigns and educational programs addressed to public, tattoo artists, ink and pigment manufacturers, and health care professionals and covering adverse health effects linked to both tattoo application and

removal are considered pivotal by many authors, e.g. to avoid the risk of bloodborne infections such as hepatitis [164, 188] and non-tuberculous mycobacterium skin infections [220]. Young people were identified as the most important target of information campaigns by the Belgian Superior Health Council [10].

Finally, all the aforementioned authors agree on the fact that tattoo artists should be obliged to keep records of their clients and to report any adverse effects related to tattoos to health authorities.

In the literature eight studies focussed specifically on risk perception related to body art practices, including both tattoo/PMU practices and piercing. Six were conducted in Italy [63, 64, 222-225], one in Denmark [226] and one in Canada [75]. They were all based on anonymous questionnaires addressed to students (ranging from secondary school to university), except the Danish study that was targeted to a representative sample of Danish population. 6.3-31.7% of the participants taken into consideration had at least one tattoo. When reported, the mean age at first tattoo was below 18 years old. The prevalence of interviewed people interested in getting a tattoo was in the range 25-57%. Among the tattooed and/or pierced individuals, 27-90% referred to an authorised operator to get their body art practiced and 28-76% observed the use of sterile/disposable instruments. Table 11.1 summarises the main findings linked to risk perception and communication.

Among the people aware of the possible risks associated to body art practices, those able to identify infections as a source of risks (36-90% of respondents) were by far more than the ones aware of non-infectious risks (26-65%). This knowledge seemed to be superficial as only 3.5-60% of respondents could correctly identify hepatitis B, C and HIV viruses among the transmittable agents and 2-5% were able to identify allergies, bleeding and cysts as non-infectious risks. These results support the opinion that information campaigns are needed.

Tattoo artists and piercers were reported as being the main source of information on possible risks. The informed consent was signed by 7-31% of Italian respondents and was considered the source of information about possible risk by 19% of the undergraduate university student interviewed by Quaranta and collaborators [64].

**Table 11.1**: Available literature data on risk perception/communication.

| | | | Risk perception | | | | | Risk Communication | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sample | Target | Awareness of a "General Risk" | Awareness of a infection risks | | | Awareness of a non-infectious risks | Information before undergoing the practice | Signed informed consent | From tattoois/piercer | From another person | From informed consent |
| | | | | General | Ability to identify HBV, HCV, HIV as infectious risks | Ability to identify tetanus as infectious risks | General | Ability to identify any of non-infectious risks | | | | | |
| **2013, DK YouGov** | | Danish population | | | 34% (HCV, HBV); 29% (HIV) | | | 48% (allergies); 37% (swelling); 35% (inflammation); 33% (photosens.); 19% (cancer); 15% (lump/node formation) | 55% | | 11% (swelling); 11% (allergies); 6% (inflamm.); 4% (lump/node formation); 2% (cancer) | | |
| **2013, Majori** | 2712 | Italian Students | | 81.6% | 50% | | | | | | | | |
| **2012, Gallè** | 3132 | Italian Students | | 84.4% | 4.1% | | 59.2% | 5.4% | | | 57.9% | | |
| **2011, Quaranta** | 1598 | Italian Students | | 90% | 34-60% | 34% | 65% | | 74% | 31% | 52% | 29% | 19% |
| **2011, Gallè** | 3610 | Italian Students (university) | 57.1% | 87% | 15% | | 59% | 3% | | 15.30% | Main | | |
| | 9322 | Italian Students (high school) | 24.7% | 79% | 3.50% | | 46% | 2% | | 6.90% | Main | | |
| **2010, Sidoti** | 1200 | Italian Students | | 36.5% | | | 26% | | | | | | |
| **2010, Cegolon** | 4277 | Italian Students | | 54.4% | | | | | | | | | |
| **2006, Deschesnes** | 2145 | Canadian Students | | | | | | | | | | | |

[61, 63, 64, 68, 223-226]

# 12. Data gaps and research needs

The data gaps and research needs described in this chapter were identified during the project through a questionnaire sent to national authorities (10 replied), data available in the literature and the discussions held during the meetings of the Consumer Safety Network Subgroup on Tattoos and Permanent Make-up.

In order to improve the safety of tattoo/PMU inks and practices the following actions were considered essential:

- to develop guidelines for the risk assessment of tattoo/PMU products;
- to develop and harmonise analytical methods for ingredients and impurities (heavy metals, AAs and PAHs) in tattoo/PMU products;
- to gather data on normal usage of inks, including on the amount applied when tattooing, and on exposure to tattoo inks (surface of application, body area, colour, population group);
- to collect further data on inks' chemical composition, stability and shelf-life, as well as ingredients' purity and concentration;
- to gather data needed to carry out the risk assessment of both inks' ingredients and inks, such as:
    - physical-chemical properties of ingredients, including their stability (to solar/UV and laser irradiation, enzymes, bacteria), cleavage products and impurities;
    - absorption level, distribution, metabolism and excretion (ADME) of ingredients, including their fate in the body in particular pigments migration and photo-degradation [10, 191];
    - derivation of No Adverse Effect Level (NOAEL);
    - toxicological data on ingredients (also nanoparticles), such as corrosion, irritation (skin, mucous membranes), phototoxicity, immunotoxicity (sensitisation, photo-sensitisation, etc.), in vitro genotoxicity, including test of cleavage products and photo-genotoxicity;
- although costly, to perform long term epidemiological and prospective cohort studies in order to investigate the correlation between tattoos and adverse health effects, in particular skin carcinogenesis [10, 171, 211].

As several adverse reactions linked to tattoo removal were registered in the last years, more studies on the techniques employed for tattoo removals are required. Interesting starting points could be the development of tattoo pigments easier to be removed if needed, the study on the wavelengths of absorption of colorants involved in the tattooing process and the development of more efficient lasers equipment for easier laser removals [82, 227].

Finally, according to Kluger, the addition of tattoo data in national skin cancer registries would help define the true prevalence of malignancies in tattoos [171].

# 13. Conclusions

## Legislative framework

DG JRC made a regulatory review of legal schemes on tattoo/PMU in all EU/EFTA countries plus other jurisdictions, available as of November 2014. The outcome of that review underlines a complex and varied situation in the different European countries.

## EU/EFTA countries

Across EU/EFTA countries, 10 of them (**Belgium, France, Germany, Liechtenstein, Norway, Slovenia, Spain, Sweden, Switzerland** and **The Netherlands**) have embedded in their national regulatory framework recommendations from the 2003/2008 Council of Europe Resolutions on tattoo/PMU products and services. In addition **Austria, Denmark** and **Latvia** have notified draft national legislation in line with CoE ResAP(2008)1, which are on hold as were not in line with REACH provisions. **Czech Republic, Finland, Italy, Malta, Romania** and **Slovakia** have regulated several health and safety aspects of tattoo practice, in particular the hygiene standards of parlours. Moreover, two of them i.e. Italy and Slovakia, ensure tattoo inks do not contain the hazardous chemicals listed in ResAP(2008)1. **Bulgaria, Croatia, Cyprus, Estonia, Greece, Ireland, Luxembourg, Poland** and **Portugal**, while not having yet put in place any specific legislation on tattoo/PMU, implement the EU legislation on consumer products safety, cosmetics and chemicals. No information was available for Hungary, Iceland, Lithuania and the United Kingdom.

Those EU/EFTA countries following the ResAP recommendations have embodied into domestic regulations and guidelines different types of requirements applying to tattoo products and services. Chemical requirements impose to ban some harmful chemicals contained in tattoo/PMU inks. Most countries have adopted provisions along the lines of CoE ResAP(2008)1 hygienic (tattoo premises, tools and staff) and labelling (inks) requirements. Ink packaging criteria, followed by the 10 abovementioned countries, plus Italy, Malta and Romania, ensure sterility of tattoo inks before use. The safety period after opening of the bottle is indicated in Germany, Norway Spain and Sweden. Several countries (e.g. Czech Republic, France, Norway, Slovenia or Spain) impose to the manufacturer/importer of the tattoo/PMU product the obligation to prepare a safety assessment dossier prior to put it on the market, and to submit this file to the Competent Authorities. Spain is the only MS to have established a positive list of inks allowed for tattoo/PMU purpose on the Spanish market. Various forms of reporting/registering or monitoring system for adverse health effects from tattoo inks exist in different countries such as Austria, France, Norway, Romania, Sweden and The Netherlands. Tattooists in France, Liechtenstein, Malta, Norway, Slovenia, Sweden, Switzerland and The Netherlands, must duly inform the clients about the potential health risks and medical complications entailed by the tattoo application, including aftercare instructions and removal possibilities. In some countries like Norway and The Netherlands, such information is conveyed by the authorities through public campaigns targeting potential customers. To open and run a tattoo parlour, a specific license or diploma is mandatory in Belgium, Czech Republic, Italy, Liechtenstein, Luxembourg, Malta, Romania, Slovenia, Slovakia, Switzerland and The Netherlands, while specific training is required in France. Access to the profession and ad hoc training is also contemplated in draft legislation of Austria, Denmark and Latvia. With some exceptions, tattooing is generally forbidden to minors without a parental approval.

As far as tattoo removal is concerned, The Netherlands and Romania consider it as a medical act, to be performed only under medical supervision.

## Other jurisdictions

Beyond Europe, other developed countries have tackled the tattoo issue. **New Zealand** has adopted tattoo/PMU guidelines inspired by the last Council of Europe Resolution, and therefore limits the same chemicals as those listed in ResAP(2008)1. In **Australia, Canada** and the **USA**, tattoo procedures are regulated at respectively government

entities, provinces and states level, generating hence a wide variety of guidelines and hygiene standards. To our knowledge, tattoo inks are not regulated as such, and tattoo studios are not covered by a specific legislative scheme in **Japan**.

### Analytical methods

In order to implement the chemical recommendations of the CoE ResAP(2008)1 analytical methods aimed to detect and quantify different hazardous chemicals should be available. Yet standard methods specifically developed for the analysis of tattoo and PMU inks are lacking, both at national and international level. However, a number of test methods applicable in other areas (e.g. cosmetics, food and textiles) do exist and in some cases were adapted for tattoo/PMU products. In–house validated methods have also been developed by Member States' laboratories expressly for the analysis of aromatic amines, colorants, elements, PAHs and nitrosamines in tattoo and PMU products, but not yet for phthalates. These methods could represent the starting point for inter-laboratory validation and harmonisation. In addition a number of test methods for the analysis of tattoo and PMU products have been described in the literature.

### Tattoo/PMU prevalence and market

The tattoo phenomenon is no more linked as before to certain marginal. 12% of the European general population is now tattooed (21-24% in the USA). This trend is upwards from the previous surveys. In Europe, when breaking the data down according to age, 2-9% of teenagers placed a tattoo, and a peak of 20-30% is reached before 30 years-old. A net decrease happens after 50 years-old. There is not a standard size for tattoos, but they can range from less than 30 $cm^2$ (small) to more than 300 $cm^2$ (large). More than half of the tattooed individuals have more than one tattoo. Gender differences tend to disappear regarding the prevalence between women and men, but do include a reduced size for women (<300 $cm^2$), a preferred localisation (trunk for women and extremities for men) and a smaller number/person for women (2-3 compared to ≥4). Up to 50% of the tattooed people have regrets, but only a fraction of those do the removal.[10] Amongst the latter, two thirds are satisfied with the results.

Depending on the country size the surveys vary between 50-8000 registered studios and 100-5000 for non-registered studios. Although tattooists associations exist in most countries, only a limited number of tattooists are affiliated. Most tattoo inks on the EU market are manufactured in the United States, while PMU inks are generally produced in Europe, in particular in Germany, Italy, Spain and the United Kingdom. Non-professional tattooists, outnumbering the official ones in many countries, might not follow appropriate hygienic procedures and use cheap inks available on internet.

### Inks Ingredients

Colorants represent by far the major ingredient of tattoo inks (up to 60% by weight), followed by additives, usually in concentration lower than 5% by weight. Inks may also contain impurities. Currently, as the tattoo ink market represents only a marginal fraction of the global production of colorants, the pigments used in tattoo and PMU inks are not specifically produced for such purposes. This poses the problem of lacking high purity. Moreover, they do not undergo any risk assessment procedure that takes into account their intra-dermis injection and long term permanence in the human body.

There are a number of chemicals present in inks, either as ingredients or as impurities, which are banned in consumer products that get into direct contact with the skin under different legislative frameworks, like in cosmetics (Cosmetic Product Regulation) or in

[10] This estimate is different from what was reported in a previous JRC report (2. Piccinini, P., et al., *Safety of tattoos and permanent make-up. State of play and trends in tattoo practices.*, 2015: JRC Report, EUR 27528 EN, 10.2788/924128. p. 1-193, http://bookshop.europa.eu/en/safety-of-tattoos-and-permanent-make-up-pbLBNA27528/.), as new data have been published in 2016 and taken into consideration (84. Laux, P., et al., *A medical-toxicological view of tattooing.* The Lancet, 2016. **387**(10016): p. 395-402.).

textiles (e.g. REACH restriction for aromatic amines), but so far tattoo inks are not covered by these legislations.

Many of the colorants in use are actually included in the negative lists mentioned in the CoE ResAp (2008)1 and the majority are not allowed as ingredients in cosmetic formulations. More than 80% of the pigments in use are organic, and the majority of them are azo pigments. These colorants have been proved to undergo degradation via cleavage of azo bonds in the skin (sometimes induced by light irradiation) with formation of primary aromatic amines that can be carcinogenic. Colorants and other impurities contained in pigments (e.g. PAH in carbon black) were found in lymph nodes and could be widespread via the lymphatic or blood systems to the whole organism. They might eventually cause systemic toxicity, but further studies are needed to support such hypothesis. Limited information is available concerning the quality of additives.

### RAPEX and market surveillance

The main issues identified from the analysis of RAPEX notifications are in line with the results of market surveillance campaigns conducted in different countries and confirm that tattoo/PMU products containing hazardous chemicals, mainly produced in the United States, are on the European market. Polycyclic Aromatic Hydrocarbons (43%), Primary Aromatic Amines (14%), heavy metals (9%) and preservatives (6%), as well as microbiological contamination (11%) were detected in the indicated percentages of the analysed samples. On this basis, it is of paramount importance that the national authorities keep on monitoring the market situation through national surveillance campaigns.

### Adverse health effects linked to tattoo application and removal

As result of the trending popularity of tattoo and PMU practices, especially among youngsters, the literature reports more and more complications prompted by tattoo application and subsequent laser removal. Unfortunately, they may not reflect the full picture, as tattoo recipients are usually keener, especially for minor complaints, to return to their tattooist rather than to seek medical advice. As a matter of fact, and because there are no systematic data gathering on this issue, the actual extent and prevalence of tattoo adverse events is currently unknown and mainly of dermatological nature. In non-clinical studies based on self-reporting, precise incidence figures are variable and up to 67%, according to the definition of "adverse reaction", which may include factual medical symptoms or mere disturbance claims (e.g. pain, itching, swelling and redness), which are inherent to the wound healing process and usually disappear swiftly without treatment. Severe complications are not common and fatal cases exceptional.

Adverse effects can been subdivided into the following categories: acute aseptic inflammation, infectious risks (bacterial and viral), allergic/hypersensitivity and auto-immune type reactions and other secondary effects.

Acute local effects such as pain, swelling, redness, lymphadenopathy, bleeding and blistering are very common during and/or immediately after the tattoo procedure (placing or removal), in the form of an acute aseptic inflammation provoked by the needle trauma or laser burn (for the latter, especially if incorrect parameters are applied). They generally disappear after some days, unless the wound gets infected by microorganisms. Systemic symptoms (headache, dizziness, fever, vomiting) and chronic itching have also been described.

Infectious diseases, mainly from bacterial inoculation, sometimes from viruses, may complicate a tattoo/PMU application if minimal hygiene conditions (tattoo premises, tools and inks) are not fully met. The true incidence of such cutaneous bacterial infections appearing within several days after the placing of the tattoo remains unknown, but some estimations point at a range between 1 and 5% of all tattoo-recipients. Very rarely infections can further widespread, leading to regional abscesses and necrosis. Infective endocarditis with fatal septicaemia is exceptional in the general population, but should

be prevented in patients with prior valve heart disease, by an antibiotic umbrella before any tattoo application.

Blood borne viral transmission, involving for instance hepatitis virus B and C, is theoretically possible during a tattoo application procedure, especially in unsanitary settings like prisons. Even though findings are sometimes controversial, the two main systematic reviews on the issue assert that tattooing is associated with hepatitis, particularly hepatitis C. It has to be considered, however, that any pathogenic contamination could be virtually eradicated if strict hygienic measures are duly applied by tattoo practitioners.

The bulk of tattoo/PMU complications consist in hypersensitivity, called also "allergic" reactions, including photosensitivity, with unpredictable onset and duration, and nonspecific clinical appearance. They may occur either: 1) immediately (acute contact eczema by reaction to inks' ingredients , to latex proteins contained in tattooist's gloves, or to aftercare topical ointments), affecting mostly the red parts of the tattoos, and exceptionally provoke a general flush and cardiovascular collapse; or 2) after a long latency (months, years and even decades) in the case of chronic dermatosis and rare underlying auto-immune pathologies, such as systemic sarcoidosis, "revealed" rather than triggered in predisposed patients. Such reactions, sometimes exacerbated by sun exposure, are poorly predictable, and patch tests usually used for detecting allergies are mostly inconclusive for detecting the culprit substance (with frequent false negative results). Latent cutaneous herpes lesions might be reactivated by tattooing procedures. The risk of anaphylactic shock during a laser removal procedure is increased in patients with prior allergic reaction at tattoo application stage.

In the long term sequels to allergic reactions include post-inflammatory dyschromic changes and hypertrophic/keloid scars. For laser tattoo removal, further to local or systemic allergic responses to inks degradation products, permanent hypertrophic scars and pigmentary disorders have also been described (i.e. hypo/hyperpigmentation and paradoxical darkening, affecting 5-15% of the individuals treated with QS laser).

The risk of tattoo-induced tumours cannot be totally excluded, due to the carcinogenic properties of many inks' impurities, and of degradation products of ink ingredients, i.a. through laser treatment. However, in order to establish a direct cause/effect link, a risk assessment of those ingredients is necessary, together with prospective epidemiological studies. In any case, tattoos should be avoided in skin areas containing moles or pigmentary changes, as they could delay or complicate the diagnostic of potential malignant growth.

Tattoos may also interfere with PET scan and Magnetic Resonance Imaging, provoking in rare cases burning complaints, and should be avoided in patients with existing cardiac, blood or autoimmune pathologies. Those suffering from diabetes raise their risks of complicated tattoo aftermath. Sun exposure is not advised before tattoo laser removal.

### Experience with the CoE ResAP

According to experts from several Competent Authorities, in order to improve the safety of tattoo/PMU inks and practices the recommendations of the CoE ResAP(2008)1 should be revised. Practical suggestions ranged from the inclusion of additional substances in the negative lists, to the request of adding the period of maximum durability after opening and the indication of the ink sterilisation method on the label, to the establishment of a compulsory register for complications.

Furthermore, several members of the CSN-STPM, both stakeholders and representatives from Competent Authorities, considered that the recommendations in the CoE ResAP(2008)1, in particular on the chemicals listed, should be made binding by an EU harmonised measure.

The establishment of Good Manufacturing Practices for manufacturing tattoo/PMU inks, compulsory training for tattooists, measures to control products sold on-line, as well as the ban of "backyard" tattooing were also considered as necessary.

### Risk perception and communication

Additional information campaigns targeted to tattoo artists, potential clients and general public, with a particular emphasis on the young population, were considered as necessary both by the experts and papers in the literature.

These conclusions are supported by a number of studies made on students, which pointed out a generally poor knowledge of risks related to body art practices, in particular the non-infectious complications.

### Data gaps and research needs

The following data gaps and research needs were identified: development and harmonisation of analytical methods to assess the possible presence of impurities and/or banned ingredients, guidelines for risk assessment of tattoo/PMU products, including toxicological studies on ingredients, and exposure data from use of tattoo/PMU inks. The fate of those colorants in human skin and body (after tattoo application/removal) and their toxicokinetics (ADME for absorption, distribution, metabolism, and excretion) should be further investigated, including for their degradation products. Prospective epidemiological studies would be needed to ascertain the risk of carcinogenicity from tattoo inks constituents, including their degradation products.

Currently, the CoE is developing guidelines, expected for 2016, on the risk assessment of tattoo/PMU products.

### Other recommendations

In addition to addressing the abovementioned research needs, harmonised hygiene guidelines for tattoo/PMU professionals should be developed and further enforced. Currently, there is an on-going CEN project dealing with this issue.

A harmonised curriculum and training at EU level for tattooists and a register for professional tattooists would be both welcome. Clandestine tattooing, source of most post-tattoo infections, must be eradicated and consumers information play a key role to reach this objective.

Risk communication campaigns should be encouraged.

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# List of abbreviations and definitions

## Abbreviations

ISO two letters country code were used for the abbreviation of country names.

| | |
|---|---|
| AA | Aromatic Amine |
| AAS | Atomic Absorption Spectrometry |
| BCC | Basal Cell Carcinoma |
| CE-DAD | Capillary Electrophoresis with Diode Array Detector |
| CEN | Comité européen de normalisation (European Committee for Standardization) |
| CI | Colour Index |
| CoE | Council of Europe |
| CSN | Consumer Safety Network |
| CVAAS | Cold-Vapour Atomic Absorption Spectrometry |
| DG JRC | Directorate General Joint Research Centre |
| DG JUST | Directorate General Justice and Consumers |
| DG SANCO | ex-Directorate General Health and Consumers |
| EC | European Commission |
| EDQM | European Directorate for the Quality of Medicines and Health Care |
| EFTA | European Free Trade Association |
| EU | European Union |
| FLAA (or FAAS) | Flame Atomic Absorption Analysis |
| GC-FID | Gas Chromatography coupled with Flame Ionisation Detector |
| GC-MS | Gas Chromatography coupled with Mass Spectrometer detector |
| GFAAS | Graphite Furnace Atomic Absorption Spectrometry |
| GMP | Good Manufacturing Practices |
| GPSD | General Product Safety Directive |
| HBV | Hepatitis B Virus |
| HCV | Hepatitis C Virus |
| HGAAS | Hydride Generation Atomic Absorption Spectrometry |
| HIV | Human Immunodeficiency Virus |
| HPLC-DAD | High Performance Liquid Chromatography coupled with Diode Array Detector |
| HPLC-FD | High-Performance Liquid Chromatography with Fluorescence Detector |
| HPLC-MS | High Performance Liquid Chromatography coupled with Mass Spectrometer Detector |
| HPTLC | High Performance Thin Layer Chromatography |
| HPV | Human Papilloma Virus |
| ICP-AES | Inductively Coupled Plasma Atomic Emission Spectroscopy |

| | |
|---|---|
| ICP-MS | Inductively Coupled Plasma Mass Spectrometry |
| ICP-OES | Inductively Coupled Plasma Optical Emission Spectrometry |
| INCI | International Nomenclature of Cosmetic Ingredients |
| ISO | International Organization for Standardization |
| IUPAC | International Union of Pure and Applied Chemistry |
| KA | Keratoacanthoma |
| MALDI-TOF | Matrix-assisted laser desorption/ionization Time of Flight |
| MCV | Molluscum Contagiosum Virus |
| MRI | Magnetic Resonance Imaging |
| MRSA | Methicillin-Resistant Staphylococcus Aureus |
| MS | Member States |
| NDELA | N-nitrosodiethanolamine |
| NTM | Non Tuberculosis Mycobacteriae |
| OR | Odds Ratio |
| PAA | Primary Aromatic Amines |
| PAH | Polycyclic Aromatic Hydrocarbons |
| PAO | Period of maximum durability After Opening |
| PEH | Pseudoepitheliomatous Hyperplasia |
| PET | Positron Emission Tomography |
| PG | Pyoderma Gangrenosum |
| PMU | Permanent Make-Up |
| PPD | Para-phenylendiamine |
| OECD | Organisation for Economic Co-operation and Development |
| PRISMA | Preferred Reporting Items for Systematic reviews and Meta-Analysis |
| RAPEX | Rapid alert system for non-food dangerous products |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals |
| ResAP | Resolution (Council of Europe) |
| STPM | Subgroup Tattoos and Permanent Make-up |
| TLC | Thin Layer Chromatography |
| QS laser | Quality Switched laser |
| SCC | Squamous Cell Carcinoma |
| SFA | Spectrometry of Atomic Fluorescence |
| TIME | Tattoo Ink Manufacturers in Europe |

## Definitions

**Basal Cell Carcinoma** (BCC) is the most common form of skin cancer. More than two million cases of this skin cancer are diagnosed in the United States each year. This skin cancer usually develops on skin that gets sun exposure, such as on the head, neck, and back of the hands. People who use tanning beds have a much higher risk of getting BCC. They also tend to get BCC earlier in life. This type of skin cancer grows slowly, and rarely

spreads to other parts of the body, if untreated. (from American Academy of Dermatology)

**Eczema** (called also atopic dermatitis) is an inflammation causing symptoms such as itchy, red, and dry skin. The treatment may require oral or topical corticosteroids and light therapy. (from Web MD)

**Granulomatous reactions** are sub-classified into about four types. They can be tuberculoid, sarcoidal, pallisading or infectious (suppurative). Various diseases present as different types of granulomas. Foreign body material can cause any type of granuloma but usually it is sarcoidal. The sarcoidal granuloma is sometimes called the naked granuloma because there is just a collection of histiocytes without any surrounding lymphocytes or neutrophils. The tuberculoid granuloma contains histiocytes but also some central caseous necrosis. In the pallisading granuloma the cells are surrounding denatured collagen which goes under the name of necrobiosis or sometimes there is mucin or foreign body material at the centre of a pallisading granuloma. A suppurative granuloma has centrally numerous neutrophils and they are part of an infected abscess. The granuloma is the body's immune attempt at isolating this infective or inflammatory process. The most common granulomatous diseases encountered by dermatologists are ruptured follicular cyst, sarcoidosis, granuloma annulare, actinic granuloma, necrobiosis lipoidica, tuberculosis of the skin and leprosy. (from"Dermatopathology Made Simple", the teaching website of the Australian Institute of Dermatology)

**Keratoacanthoma** is a relatively common low-grade tumor that originates in the pilosebaceous glands and closely resembles squamous cell carcinoma (SCC). In fact, strong arguments support classifying keratoacanthoma as a variant of invasive SCC. In most pathology/biopsy reports, dermatopathologists refer to the lesion as "squamous cell carcinoma, keratoacanthoma-type." Keratoacanthoma is characterized by rapid growth over a few weeks to months, followed by spontaneous resolution over 4-6 months in most cases. Keratoacanthoma may progress rarely to invasive or metastatic carcinoma. Whether these cases were SCC or keratoacanthoma, the reports highlight the difficulty of distinctly classifying individual cases. (from Medscape)

**Lichenoid** reaction pattern implies histological changes at the dermal/epidermal junction due to an immune attack of lymphocytes at the dermal/epidermal junction. Classic conditions in this category include lichen planus, lupus erythematosis and erythema multiforme. There are variants on this such as fixed drug reaction, graft versus host reaction and some of the other collagen diseases that also are associated with damage to the dermal/epidermal junction and the greater that degree of damage the more it influences the clinical picture. (from "Dermatopathology Made Simple", the teaching website of the Australian Institute of Dermatology)

**Molluscum Contagiosum virus** (MCV) is a common disease of childhood transmitted by skin-to-skin contact or by contact with fomites. Molluscum may represent a sexually transmitted disease. It can also present as widespread lesions in the setting of immunodeficiency (AIDS) [169].

**Pseudoepitheliomatous Hyperplasia**: a benign marked increase and downgrowth of epidermal cells, observed in chronic inflammatory dermatoses and over some dermal neoplasms and nevi; microscopically, it resembles well-differentiated squamous cell carcinoma. (from: Farlex Partner Medical Dictionary © Farlex 2012)

**Sarcoidosis** is an idiopathic, multisystemic, granulomatous disease characterised histologically by non-caseating epithelioid granulomas. Lung disease, the most common systemic manifestation of sarcoidosis, is present in 90% of patients. (Ali [209] citing Howard A, White CR. Non-infectious granulomas. In: Bolognia JL, Jorizzo JL, Rapini RP, editors. Dermatology. London: Mosby;2003. p. 1455- 69).

**Squamous Cell Carcinoma**: a malignant neoplasm derived from stratified squamous epithelium, but that may also occur in sites such as bronchial mucosa where glandular or

columnar epithelium is normally present; variable amounts of keratin are formed, in relationship to the degree of differentiation, and, if the keratin is not on the surface, it may accumulate in the neoplasm as a keratin pearl; in instances in which the cells are well differentiated, intercellular bridges may be observed between adjacent cells. (from: Farlex Partner Medical Dictionary © Farlex 2012)

**Tattoo Complaints**: Any unusual condition, sensation or visible reaction in the tattooed skin that differs from normal skin of the same person. Usually mild, and treated ”at home” [80, 192].

Many tattooed individuals described fading of the tattoo colour over time. This was not included in the study as a complaint.

**Tattoo Complications**: More serious adverse reactions in tattoos associated with objective, clinical pathologies of the tattoo in combination with major subjective symptoms and significant discomfort, i.e. events that would typically make the patient consult a doctor [192].

**Uveitis:** eye inflammation affecting the middle layer of tissue in the eye wall (uvea). Warning signs often come on suddenly and get worse quickly. They include eye redness, pain and blurred vision. The condition can affect one or both eyes, primarily in people ages from 20 to 50. Possible causes of uveitis are infection, injury, or an autoimmune or inflammatory disease. Many times a cause can't be identified. Uveitis can be serious, leading to permanent vision loss. Early diagnosis and treatment are important to prevent the complications of uveitis. (Definition by Mayo Clinic Staff)

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