European Commission

JRC TECHNICAL REPORTS

Safety of tattoos and permanent make-up
Adverse health effects and experience with the Council of Europe Resolution (2008)1

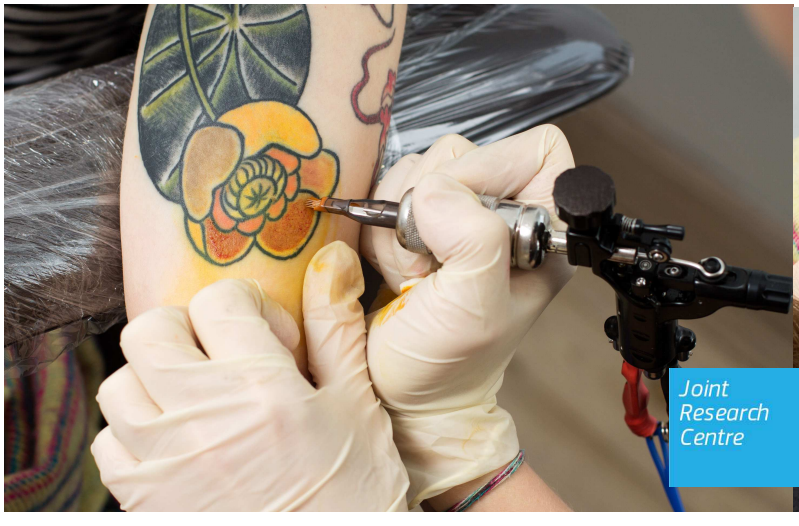
Report on Work Package 3

Administrative Arrangement N. 2014-33617

Analysis conducted on behalf of DG JUST

Paola Piccinini, Sazan Pakalin, Laura Contor, Ivana Bianchi

2016



Joint Research Centre

EUR 27672 EN

JRC Science Hub
https://ec.europa.eu/jrc

JRC99882

EUR 27672 EN

PDF ISBN 978-92-79-54234-3 ISSN 1831-9424 doi:10.2788/177900

How to cite: Paola Piccinini, Sazan Pakalin, Laura Contor, Ivana Bianchi; Safety of tattoos and permanent make-up. Adverse health effects and experience with the Council of Europe Resolution (2008)1; EUR 27672 EN; doi: 10.2788/177900

Luxembourg: Publications Office of the European Union, 2016

Table of contents

Abstract

In the last decades, the proportion of the tattooed population has been increasing all over the world, particularly in the young generations. Concerns about the possible health problems associated to tattoos and permanent make up (PMU) have also grown together with the number of tattoo/PMU applications and removals.

The Council of Europe Resolution (CoE ResAP)(2008)1 [1], on requirements and criteria for the safety of tattoos and permanent make-up, is a non-binding internationally recognised benchmark that was taken as a reference for the development of national legislation adopted in a number of European countries.

The European Commission launched the 18-month project "Tattoos - Permanent Make-up" with the aim of collecting data about the use, the ingredients, the European Union (EU) market and the possible health problems associated to tattoo and permanent make-up inks.[1]

This project is divided into 4 Work Packages: 1) preparatory work; 2) state of play; 3) assessment and update of the CoE ResAP(2008)1; 4) conclusions. The reports on Work Packages 1 and 2 [2, 3] are available at http://bookshop.europa.eu/.

The present report is the outcome of Work Package 3 which aims to gather data about adverse health effects and complications linked to tattoo/PMU application and/or removal, risk perception and communication, data gaps and research needs, as well as to evaluate the lessons learned from the experience in implementing the recommendations of the CoE ResAP(2008)1.

The information was collected through the following sources. (1) Two questionnaires were developed: one addressed to dermatologists on adverse health effects and the other one to national authorities on complications, experience with the CoE ResAP(2008)1, risk perception and communication, data gaps and research needs. They were sent to all EU Member States and European Free Trade Association (EFTA) countries and to 36 dermatologist associations in Europe with the request to circulate among their members. 14 Member States and 19 dermatologists filled-in the questionnaires. (2) A systematic review of the literature from 2003 on was carried out according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis) methodology. (3) The outcome of the meetings of the Consumer Safety Network Subgroup Tattoos and Permanent Make-up was taken into account.

The main findings show that:

It is not possible to conclude on an exact incidence of adverse health effects following tattoo/PMU applications. The majority of tattoo/PMU recipients report minor short-term discomfort and complaints during the wound healing process following the tattoo application. This could be confused with other more serious complications and makes the accurate calculation difficult.

Short term complications, such as skin infections, may appear some days after the tattoo placing, or within weeks, for allergic reactions. In the long run chronic inflammatory dermatoses may develop, sometimes after decades.

The precise frequency of microbiological (mainly bacterial, more rarely viral) contamination through inks, tools or procedures used in the tattoo application remains unknown, though it has been generally estimated at up to 5% of the tattoo-recipients in the case of bacterial infections.

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

The vast majority of tattoo/PMU adverse reactions are due to delayed and unpredictable hypersensitivity, involving allergy and/or autoimmunity. Direct causal relationship between tattooing and (skin) cancer has been so far neither proved nor excluded. However, tattoos may blur and hence delay a melanoma diagnosis. They can also interfere with diagnosis imaging, and should be avoided in patients with prior cardiac, blood or autoimmune pathologies, inter alia.

Similarly, also the process of tattoo removal is associated with side effects. The modern removal techniques, based on the use of Q-switched lasers, have improved the safety, efficiency and selectivity of the removal procedure, still side effects might occur, especially when incorrect parameters are applied to the laser device. The frequency of skin pigmentation disorders following laser therapy have been encountered in 5-15% of patients.

Henna based preparations are not permanently injected in the skin and therefore they cannot be considered as tattoos. However, as the use of henna for temporary body decoration has become also widespread it has been included in this report for completeness. Henna has been used for centuries for body painting and it is generally well tolerated. When p-phenylendiamine (PPD) is added to make the painting darker, side effects due to sensitisation to PPD have been reported in the literature.

The majority of the national authorities who replied to the questionnaire indicate that, in order to improve the safety of tattoo/PMU inks and practices, it would be necessary to update the list of recommendations in the CoE ResAP(2008)1. In particular, suggestions were put forward to include additional substances to the negative lists and to modify and/or introduce new limits. Other suggestions were to add new labelling requirements, such as the period of maximum durability after opening, to envisage the compilation of a register of complaints and to include information on the ink and tool sterilisation methods. Furthermore, several Member States pointed out the need to establish Good Manufacturing Practices for tattoo/PMU inks, to control products sold on-line, to establish compulsory training for tattooists, to enhance the collaboration among manufacturers and authorities and to ban backyard tattooing.

Risk communication has been addressed by means of information campaigns targeted to various audiences and using a variety of means in nine Member States, out of the twelve who filled-in this section of the questionnaire. Beside this, national authorities generally agreed on the need to organise further actions to reach tattooists and potential clients, particularly adolescents, to give them the correct instruments to be able to take an informed decision. Actually risk perception is based on the information given by the tattooist (e.g. via an informed consent form), or received through parents or friends, or read in mass media and internet. In addition, some studies estimated the level of knowledge of possible health risks among students, either school or university ones. In general, infectious risks were better known that non-infectious ones, even though the level of knowledge was in many cases only superficial and, for example, not specifically linked to the transmittable agents of possible infections or to the various possible non-infectious risks. These evidences support the need of further additional information campaigns.

Data gaps and research needs were identified, such as development of guidelines for risk assessment of tattoo/PMU products, harmonised analytical methods, data on normal usage of and exposure to tattoo inks, including their characteristics (physical-chemical properties, chemical composition, ingredients' purity and concentration). In order to carry out a risk assessment of tattoo/PMU inks, data are missing on absorption, distribution, metabolism and excretion (ADME) of ingredients, including migration in the body of pigments and their (photo)-degradation products, DNEL (Derived No Effect Level), as well as chemical and toxicological properties of ingredients. Moreover, several authors considered that, although costly, prospective cohort studies should be conducted to investigate the association between tattoos and (skin) carcinogenesis.

1. Introduction

The worldwide trend of increasing popularity for tattoos and Permanent Make-Up (PMU) applications among the total population has led to a parallel rise in health related complications [4-6]. Although a number of surveys, national reports and papers have become more and more available, a clear insight into the extent and frequency of adverse reactions remains difficult.

In 2003, the Directorate General Joint Research Centre (DG JRC) of the European Commission (EC), on behalf of DG Health and Consumers (SANCO), prepared a document describing the state of play in terms of prevalence of tattooing and piercing practices in the European Union (EU), chemicals involved, review of health effects and risks and regulatory review, which included recommendations on the safety of tattoos, body piercing and related practices in the EU such as risk assessment on ingredients, the development of a negative/positive list of substances and the use appropriate labelling [7]. In the same year, the safety of tattoo/PMU inks and practices was addressed by the Council of Europe in a resolution (CoE ResAP(2003)2) [8], which included several requirements about the chemical composition of tattoo/PMU inks, the labelling and safety assessment of these products, as well as the hygiene and information necessities. In 2008, an updated version of the resolution was published [9]. Since 2003, a number of Member States and EFTA countries adopted legislations which use the recommendations in the CoE resolutions as reference.

Since 2003, the state of play has changed significantly due to several factors, the most relevant being: the increasing prevalence of tattooed population; the new legislative framework in place; the enlargement of the EU; and the wider online availability of tattoo/PMU inks compared to 2003. Consequently, an updated evaluation of the situation related to the safety of tattoo/PMU inks and practices become needed.

1.1. Tattoos and Permanent Make-up Project

In April 2014, the Consumer Safety Network (CSN) Subgroup Tattoos and Permanent Make-up (CSN-STPM) was established by DG SANCO as a subgroup of the CSN. The first meeting of this subgroup was held on 23th June 2014 with representatives from 14 EU/EFTA national authorities, tattooists, ink manufacturers, consumer groups, medical professionals, the Council of Europe, etc. At the end of September 2014, DG JRC was entrusted by DG SANCO with the project on "Tattoos - Permanent Make-up".

The main goal of this 18-month project is to gather all the available information to describe the up-to-date situation and to understand what the current problems are, which their size is and how they can be addressed to improve the safety of tattoo/PMU inks and practices. This Work Package 3 focused on the collection of information regarding the adverse health effects linked to tattoo/PMU applications and removal, the experience gained by the European countries with the CoE ResAP(2008)1, the risk perception and communication and the data gaps and research needs.

This project is divided into 4 Work Packages:

1. Preparatory work: regulatory framework and analytical testing methods [2]
2. State of play: current trends in tattoo practices, prevalence, data on inks market and composition of tattoo/PMU inks, post marketing surveillance [3]
3. Assessment and update of the CoE ResAP(2008)1: including adverse health effects, lessons learned from the experience in implementing the recommendations of the CoE ResAP(2008)1, risk perception and communication, data gaps
4. Conclusions.

The results of Work Package 1 showed large differences in the regulatory framework across the Member States, together with a lack of harmonised analytical methods. Work

Package 2 concluded that around 12% of the European population has at least one tattoo and more than 20% in the United States. Regarding tattoo and PMU inks composition, colorants are the main ingredients, while additives, by-products and impurities are also present. According to market surveillance actions and studies carried out by the Member States, the CoE ResAP(2008)1 recommendations concerning e.g. primary aromatic amines, polycyclic aromatic hydrocarbons and metals are not always respected by the inks available on the European market.

This report covers the results of Work Package 3, which include:

- CSN-STPM meeting discussions
- Adverse health effects linked to tattoo/PMU applications
- Adverse health effects linked to tattoo removals
- Adverse health effects linked to henna-based temporary tattoos
- Experience with the CoE ResAP(2008)1
- Risk perception and communication
- Data gaps and research needs.

2. Methodology

The data were gathered from various sources:

1. the responses to two questionnaires sent to national authorities and dermatologist associations (Annexes II, III and IV);
2. a literature review, performed according to the guidelines "Preferred Reporting Items for Systematic reviews and Meta-Analysis" (PRISMA) [10], which included also national reports (References chapter);
3. and the discussions at the 9th November 2015 Consumer Safety Network Subgroup Tattoos and Permanent Make-up meeting (Annex I).

2.1. Questionnaires

Two different questionnaires were developed to collect information: one targeted specifically to dermatologists and the other one to competent authorities (see Annex II).

Questions

a) For dermatologists, the questions were focused only on health effects:

- complications following a tattoo/PMU application or removal (including skin and systemic symptoms and their frequency and severity, proportion of people with previous skin diseases, including allergy, allergic skin reactions, other inflammatory reactions, cutaneous/regional/systemic infections and tumours);
- correlations between health complications and certain tattoo characteristics/parameters (number of tattoos/patient, tattoo sizes, gender/age, colours, localisation).

b) For competent authorities, the queries covered a wider range of topics:

- health effects (frequency of different health issues amongst people having undertaken tattoos/PMU applications or removals and factors correlated to higher frequency of medical complications);
- experience gained with the CoE ResAP(2008)1 (in terms of chemical, labelling, hygiene/sterility and other requirements);
- risk communication and perception (information campaigns, information on risk perceived by the general public, signature of a prior informed consent);
- data gaps identification (research or technical development to improve the safety of tattoo/PMU inks and practices).

Distribution

Both questionnaires were sent to the 28 EU Member States' plus the 4 EFTA countries' authorities (through the Consumer Safety Network by DG JUST). MS were invited to distribute the dermatologist questionnaire among dermatologist associations in their country, who had to further circulate it among their members. This dermatologist questionnaire was also sent by DG JRC to 31 dermatologist associations from 24 countries, inviting them to share it with their members (Table 2.1).

Table 2.1: List of dermatologist associations involved in the survey.

Country	Dermatologists associations
AT	Österreichischen Gesellschaft für Dermatologie und Venerologie
BE	Union Professionnelle de Dermatologie et Vénérologie Belge
	European Academy of Dermatology and Venerology (BE, CH offices)
BG	Bulgarian Dermatological Society
CH	Schweizerische Gesellschaft für Dermatologie und Venerologie
CY	Cyprus Society of Dermatology and Venereology
CZ	Czech Dermatovenereology Society
DE	Deutsche Dermatologische Gesellschaft
	European Society of Contact Dermatitis
DK	Nordic Dermatology Association (DK, FI, SE)
EE	Estonian Society for Dermatovenereologists
FI	Finnish Dermatological Society
FR	Société Française de Dermatologie
HR	Croatian Dermatovenereological Society of the Croatian Medical Society
HU	Hungarian Dermatological Society
IE	Irish Association of Dermatologists
IT	Associazione Italiana Dermatologi Ambulatoriali
	Associazione Dermatologi Ospedalieri Italiani
	Associazione Italiana Dermatologia e Cosmetologia
	Società Italiana di Laser in Dermatologia
LI	Lithuanian Association of Dermatovenereologists
LT	Association of Dermato-Venereologists of Latvia
MT	Maltese Society of Dermatology and Venereology
NL	Nederlandse Vereniging voor Dermatologie en Venereologie
PL	Polish Society for Aesthetic Dermatologists
	Polish Dermatological Society
PT	Portuguese Society of Dermatology and Venereology
RO	Societatea Romana de Dermatologie
SE	Swedish Society for Dermatology and Venereology
UK	British Association of Dermatologists
	British Society for Medical Dermatology

Responses

a) Nineteen dermatologists from 6 countries replied on health effects (Annex IV): 4 BE, 5 DE, 5 DK, 1 FI, 3 NL, 1 SE.

b) 14 Member States completed the questionnaire developed for them (Annex III): BE, BG, CZ, DE, DK, ES, FI, FR, IT, NL, RO, SE, SI, SK. Replies from national authorities covered (Figure 2.1):

- health effects: 6 answers (BE, ES, FI, FR, NL, SE)
- CoE ResAP(2008)1: 12 replies (BE, CZ, DE, DK, ES, FI, FR, IT, NL, SE, SI, SK)
- risk perception and communication: 12 answers (BE, CZ, DE, DK, ES, FI, FR, IT, NL, SE, SI, SK)
- data gaps and research needs: 10 replies (CZ, DE, DK, ES, FR, IT, NL, SE, SI, SK).

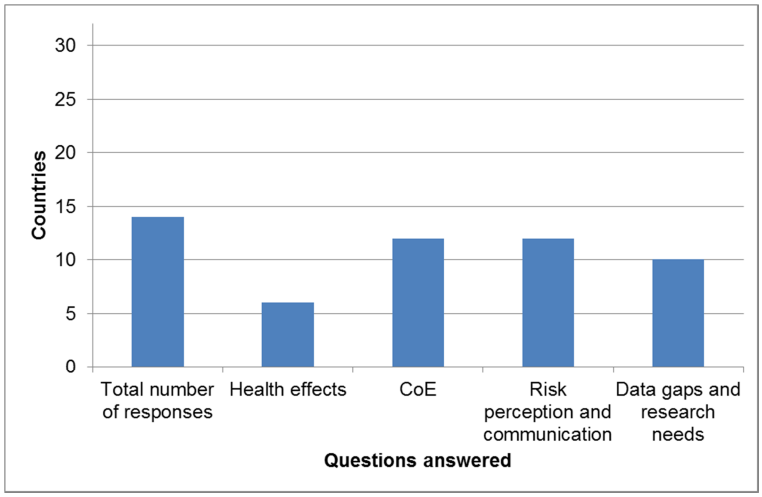


Figure 2.1: Rate of MS responses to the questionnaire.

Limitations impacting on conclusions

Despite the large number of dermatologists reached by the questionnaire, the rate of responses was very low. Among the 19 dermatologists who replied, 15 reported less than 15 patients per year with tattoo complications and 4 up to 150. Similarly, only 6 competent authorities filled-in the questionnaire section related to health effects, and among them just Belgium and The Netherlands reported on the individual complications.

Relatively to health effects, these facts strongly limited the representativeness of the exercise and prevented the possibility to draw sound conclusions. For this reason, the chapter regarding adverse health effects is essentially based on the literature review.

2.2. Literature

The PRISMA approach [10] for the literature review was used. The overall objective was to collect the available relevant information on adverse health effects and risk perception linked to tattoos/PMU application/removal published after 2003, not included in the previous JRC report of the same year [11]. The literature search was conducted in PubMed and Scifinder data bases.

The preliminary results were processed using the following exclusion/inclusion criteria:

- years included 2004-2015;
- key words present in abstract and title;
- removal of duplicates;
- filtering for relevance to health effects of tattoos, PMU or henna;
- focus on more than one case studies.

Search strategy

The inclusion search criteria used a combination of the following keywords with tattoo(s) or tattooing: adverse health effects/reactions, (skin) allergy, (skin) infections, risks, diseases, safety, laser, epidemiology and toxicology.

For permanent make-up, 42 references were found and combined with the same key words. On the resulting references, the exclusion criteria before 2004 and no patents lead to a final number of 5 articles.

For risk perception, tattoos were searched in combination with perception, attitudes, knowledge, experiences and awareness. A final number of 61 abstracts of publications were read to select 6 relevant articles for inclusion in the report.

PRISMA flow diagram and final results

The approach followed for adverse health effects is illustrated in Figure 2.2, where the 4 steps of the flow diagram are represented (identification, screening, eligibility and inclusion).

Following the identification of the articles using the above mentioned key words, the first screening excluded patents, publications before 2004, some languages (Japanese, Chinese, Polish and Russian) and documents classified as historical, dissertation, biography, commentary and conference.

In the eligibility step the abstracts were reviewed, according the following relevance criteria: 1) reviews, recent books and national reports; 2) clinical trials and 3) other papers. The pertinence to the objective of the study was checked, and preference was given to studies reporting more than one case.

The selected papers were read and used in the preparation of this report (see References).

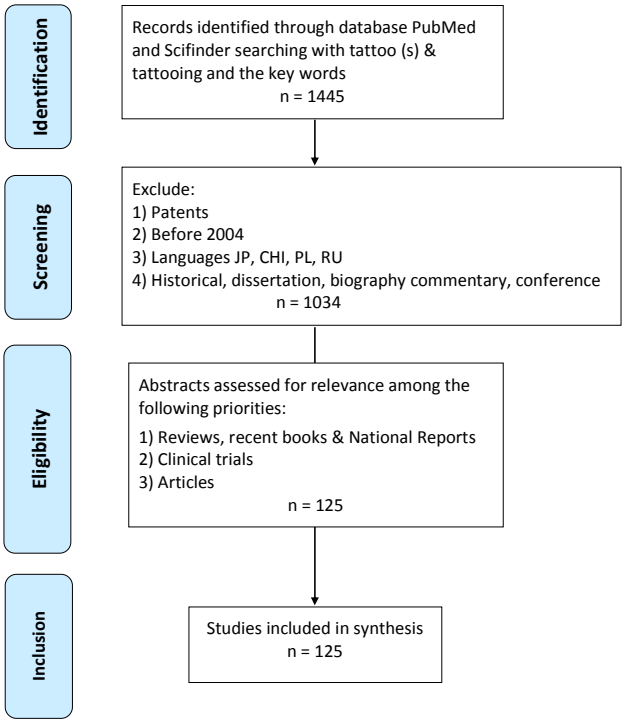


Figure 2.2: PRISMA flowchart on adverse health effects of tattoos.

3. Work Package 3: Assessment and update of the CoE ResAP(2008)1

A meeting of the CSN-STPM was held at the JRC in Ispra (Varese, Italy) on 9th November 2015 to discuss the issues to be tackled in Work Package 3. 24 participants were present, representing 11 Member States, plus Switzerland, and a number of stakeholders, such as dermatologists, professors from academia, representatives from tattoo artists', ink manufacturers' and consumers' associations.

The aim of the meeting was to share information and try to discuss conclusions and recommendations on the following topics: adverse health effects linked to tattoo/PMU applications and removal, experience with the CoE ResAP(2008)1 [9], risk perception and communication, data gaps and research needs.

The discussion was preceded by a number of presentations on the above mentioned topics, as well as by an overview of the literature and replies to the questionnaires.

The minutes, agenda and list of participants to this meeting are reported in Annex I.

3.1. Adverse health effects linked to tattoo/PMU applications

As the popularity of the body art phenomenon has been steadily increasing over the last decades, a wide range of medical side-effects of both tattoos and permanent make-up applications and removal are nowadays encountered by physicians, essentially dermatologists.

These associated adverse reactions can be acute or chronic according to the delay after the tattoo/PMU application.

At short term, accompanying the inevitable wound healing process that takes place already during the tattoo session, immediate complications may arise within days in the case of skin bacterial infection, or within weeks, for allergic reactions.

In the long run we may assist, sometimes after years or decades, at persistent inflammatory reactions and delayed hypersensitivity with chronic dermatosis. (Skin) tumour development has been incriminated, but it has been neither proved nor excluded.

There are different types of tattoos. According to the practitioner, they are classified as amateur or professional. Cosmetic tattoos, also known as PMU, are used to resemble make-up. Iatrogenic or medical tattoos are mainly carried out by physicians for diagnosis or therapeutic purposes. Finally traumatic tattoos may be provoked by accidents and explosions, where exogenous elements enter the human skin and colour it in an indelible way.

The following findings take stock of the previous JRC reports published in 2003 [7, 11] and are mainly based on a literature research carried out from 2004 onwards.

Frequency of secondary effects

The real incidence of tattoo reactions is currently unknown, according to many authors, such as Kluger [12] or Desai [13].

To establish the true nature of these lesions, a biopsy is mandatory, because there is no clear-cut correspondence between clinical aspects and histopathological findings. From October 2008 to June 2015, Serup [14] diagnosed and treated 493 tattoo complications. In 292 tattoo reactions, histopathological findings show a predominance of inflammatory patterns (70%), followed by granulomatous reactions (21%, among which 7% of the sarcoidal-type).

Serup [15] distinguishes between on one hand "discomfort" or "complaints", which are mild by nature, experienced by 42% of tattooed individuals [16], and more severe reactions qualified as "complications" for which the patient would normally consult a physician.

In a US study on 300 tattooed individuals [6], 10.3% (31 out of 300) reported adverse tattoo reactions; of which 13 (4.3% of total participants) were acute (pain, itching, swelling) and 18 (6%) lasted beyond 4 months. Høgsberg [17], analysing complaints from 154 Danish tattoo-recipients in 2013, found 15% of minor acute effects (redness, swelling, itching) within 3 months after tattooing, and 27% of symptoms (predominantly plaque elevation and itching related to sun exposure in the majority of cases, 58%) persisting beyond 3 months, mainly in black and red tattoos.

According to the Klügl [18] survey performed over the Internet among German-speaking tattooed persons in 2010, 67% of the 3411 responders complained spontaneously over acute dermal symptoms (which could be merely inconveniences, in fact). This figure, is comparable to the 76% of bleeding complaints amongst tattoo-recipients, cited by Carney [19], but much higher than the incidence of acute minor symptoms signalled by many authors (see below). In Klügl's study, after one month persistent effects were mentioned by 9% of tattooed customers, 6% locally and 3% on a systemic level (dizziness, headache or nausea). Yet life-threatening situations remain exceptional. Overall, Klügl himself admitted the limitations of his study, as "*people with health problems may be more willing to participate in such a survey*" and Wenzel [20] challenged the reliability of these responses given without validation by a physician. Precise data on the extent and frequency of adverse reactions are not available so far. Probably because, in case of minor symptoms, tattoo recipients prefer rather return to their tattooist than consult a physician. Actually, only 1.6% of the Klügl study tattooed people showing health problems did so. As Kluger [12] put it "*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*". This is particularly true in the case of PMU applications, where the most common complications and patients' dissatisfaction result from "*misapplication of the pigment, pigment migration, and pigment fanning*" [21].

These psycho-social consequences, even though frequent, will not be further treated in the present document, neither will be the psychiatric impact of chronic pain and itching. On the contrary, the aftermath and sequels of tattoo removal are considered in chapter 3.2.

Categories of medical complications

In addition to the minor inflammatory symptoms accompanying necessarily the tattooing act itself, adverse reactions to tattooing and PMU can be divided into two main categories according to the transmissible character of the adverse effects (infectious vs. non-infectious complications). The non-infectious reactions may be of allergic nature or not. Many authors, like Kaatz [22], use the words "coincidental diseases", regrouping both the underlying dermatoses reactivated or triggered by tattooing ("concomitant diseases" such as sarcoidosis, amongst other auto-immune pathologies), and tumours arising within a tattoo.

Furthermore, tattoos may interfere in some cases with diagnosis, disrupt various imaging exams and hamper medical procedures and treatments. In addition, patients with specific clinical status or pre-existing pathologies should be warned against placing a tattoo.

The relative frequencies of these various pathologies have been so far hardly estimated due to lack of epidemiologic studies. According to Serup's data on 405 sick tattooed patients treated in a specialised dermatologic clinic between October 2008 and June 2015 [14], 12% of adverse reactions are of infectious nature (at local, regional or systemic level, induced mostly by bacteria), while the bulk of the non-infectious

reactions (the remaining 88%) consists mainly (65%) of inflammatory nature (allergic or not). It has to be noted that no skin cancer originating from a tattoo was observed among these 493 adverse reactions, even though 1 case of invading Basal Cell Carcinoma (BCC) from surrounding skin has been reported. Yet these figures have to be taken with caution, as details about the selection modalities of these patients are not available ("recruitment bias"), making their representativeness questionable. With that respect, it is remarkable that 14% of the complications listed are attributed to amateur tattooing (meaning tattoos performed by non-professional tattooist), 80% to professional tattooing and 2% to PMU.

3.1.1. Acute aseptic inflammation

As the tattoo procedure consists of the skin layers' breach, the needle prick trauma to vessels is inevitably associated with a superficial bleeding, which normally fades away within a week without any specific medical care. Individuals getting a tattoo experience immediate discomfort, swelling and erythema during the procedure and the days after, together with transient bleeding and lymphadenopathy. This acute inflammatory reaction of variable intensity remains in principle aseptic, unless cases of bacterial contamination. During the healing phase lasting 1 to 4 weeks, a superficial crusting and induration takes place in the tattooed area and patients may complain about pain, itching, blistering and burning sensation, like after sun exposure.

Reactions such as itching, tenderness, pain or fluid discharge occur normally in all tattooed individuals, as they are inherent to the needle injury and the intradermal injection of foreign substances with subsequent histamine release, which may trigger a general flush. These so-called “complications” are part of the natural history of tattoos.

Consequently, results of self-report questionnaires from tattooed individuals are difficult to interpret and statistics about their prevalence are highly variable, not only because of the methodological bias, but also due to the confusion, by the respondents, between real complications and symptoms that are almost always present during the wound healing phase. While the Klügl on-line survey [18] with 3411 responders mentioned figures of 67%, other authors come with much lower complication rates calculated on smaller groups.

Laumann [23] reported that 15 out of 120 tattooed people (12.5%) developed medical problems within two weeks after tattooing.

Antoszewski [24] wrote that 31% of the 416 interviewed tattooed recipients experienced complications, including mainly pruritus (21.6%) and bleeding (7.7%).

Hutton Carlsen [16] counted 60 tattooed persons out of 144 (42%) who expressed complaints (mainly swelling and itching), of which 31 (52%) sun-related, especially with black, red and blue tattoos. Symptoms may disappear immediately or last several weeks. Problems not related to sun exposure included "swelling after consumption of alcohol or tomatoes", "acne-like changes", tenderness, itching, etc.

Høgsberg's 2013 study on 154 Danish tattoo recipients showed that 27% of them had chronic discomfort, especially in black and red tattoos, with itching and skin elevation as main symptoms.

On a sample of 493 tattoo reactions, Serup's 2015 study [14] , reported the following prevalence for various symptoms according to patients' history (more than one symptom could be associated to one tattoo reaction): 80% swelling, 65% itching, 30% pain, 24% scaling, 20% redness, 19% wounds, 17% photosensitivity, 7% scar tissue and 2% thermal/alcohol/hash mechanic deterioration.

The gradation of severity is also a matter of subjectivity and might vary from one individual to the other. In the abovementioned German internet survey of 2010 [25] the adverse effects have been described as "negligible" by 31.4% of the respondents

reporting complications, "slight" by 49.8%, "moderate" by 16.2%, "intense" by 2.1% and "very intense" by 0.6%. Differential evaluation of bleeding during tattooing might explain discrepancies in "slight bleeding" reported from 7.7% up to 76% of the tattooed individuals.

The Klügl survey [25] showed slight more frequent skin reactions to coloured tattoos (83.%) than to black tattoos (80%), calculated on the total of replies that could be multiple. It has to be noted, however, that the majority of tattoos are black.

Serup [26], reported also soft tissue lymph oedema, together with a pigmentation of the surrounding skin (pigment drift) and sometimes of regional lymph nodes. He further mentioned papular or nodular thickening and elevation in certain tattooed areas, as a result of 'pigment overload' with injection of too much ink. In addition he described tattoo-related pain in the segment of the radial nerve i.e. hand, fore-arm and arm [15].

Apart from these local symptoms, a systemic contact dermatitis with generalised rash can occur in in previously sensitised persons to, in particular, nickel and also to other metals or preservatives (e.g. parabens, methylisothiazolinone), if these substances are present as trace element and impurities. If limited to the tattooed area, this allergic reaction can be confounded with the wound healing process and also misdiagnosed as a bacterial infection.

Generalised allergic reactions, e.g. to methylisothiazolinone, can also be induced by the use of local products (cleaning products, liquid soaps, body lotions for aftercare, etc.); the same is true for some topical antibiotics and antiseptics.

3.1.2. Infectious risks

The source of infection may be the tattooist, the instruments, the ink or the tattooed individual himself. Infections may occur if tattoo instruments are not properly sterilized and from tattoo inks microbiologically contaminated at manufacturing phase or after the opening of the bottle, due to deficient hygienic conditions and e.g. by diluting inks with non-sterile water. Infection can further take place during the healing phase of a tattoo.

The risk of blood borne transmission is low in registered parlours respecting the hygiene requirements. Fungal or parasitic contaminations have only been reported in historical or exotic cases.

By applying standard hygiene measures for both instruments and inks, professional tattooists and established PMU providers can minimize the risk of infections.

Various studies were carried out on sealed tattoo/PMU inks to evaluate the microbiological contamination. Høgsberg [27] analysed 58 samples and found an ink contamination rate of 10%, Health Canada [28] 20% (3/15), Kaatz [22] 37% (3/8) and Bäumgartner [29] 44% (17/39).

3.1.2.1. Bacterial infections

Skin infections in the form of papulo-pustules provoked usually by pyogenic strains, such as staphylococcus aureus or streptococcus, may appear quickly within the first few days after the tattoo procedure. Both acute superficial pyogenic infections, such as folliculitis, impetigo or ecthyma, and deep regional pyogenic infections, like furunculosis, erysipelas and cellulitis of the entire limb, are seldom [12], while systemic involvement and life-threatening outcome (by gangrene, osteomyelitis, epidural abscesses, septicaemia, toxic shock syndrome, etc.) remains exceptional under correct hygienic circumstances. Infective endocarditis has been mostly documented in patients getting extensive and repeated tattoos [30]. As a preventive measure every customer suffering of heart valvular diseases should be refrained from undergoing a tattoo procedure without a prior antibiotic prophylaxis, because of the potential risk of bacterial endocarditis [31].

Cutaneous superficial infections have been scarcely described by the medical literature, but the number of publications has increased in recent years, probably due to better clinical identification or improvements in mycobacterial testing. In his review Wenzel [20] considered 122 publications which included 280 patients. The published cases were classified into the following three categories: 1) granulomatous, lichenoid or hypersensitivity allergic reactions; 2) infections; 3) tumours, which represented 34.3%, 53.9% and 11.8% of cases, respectively.

Yet the real frequency of cutaneous infections remains difficult to estimate [32], as in minor cases the patients go rather to see their tattooist than a physician and this is not recorded in medical statistics. Laux [33], estimates the rate of bacterial infections at 1-5% of the tattoo-recipients. Klügl's survey [18] indicated that 0.5% of tattoo respondents had pus-filled skin areas, especially at extremities. Bacterial contamination is clearly influenced by the hygienic conditions of the tattoo shop equipment and tools, and by the ink sterility. Tattoos performed in dubious hygienic settings by inexperienced amateurs with poor instrumentation and inks of unknown origin or composition, present obviously more risks than procedures carried out by trained professionals in licensed tattoo parlours, or aesthetician shops in the case of PMU, for which bacterial infections are rare [34].

According to some authors, these enhanced disinfection measures might have facilitated in the last years the development of commensal (coli bacteria) and opportunistic germs, such as pseudomonas or Non Tuberculosis Mycobacteriae (NTM). These pathogenic bacteria could be either present in unopened tattoo ink bottles [35] or in unsterile tap water used to dilute black inks in order to obtain different grey shades [36, 37].

Incubation of NTM infections after tattooing varies from 3 days to 1 month, with the development of unspecific itchy erythematous papulo-nodules, pustules or lichenoid plaques on the grey lines of the tattoo. The responsible pathogens of these suppurated (or tuberculoid) granulomatous patterns (sometimes pseudoepitheliomatous hyperplasia-like, see below) are usually *Mycobacterium chelonae* or *Mycobacterium abscessus*.

Special concern has also been expressed for emerging outbreaks of Community Acquired-Methicillin-Resistant Staphylococcus Aureus (CA-MRSA), essentially by nose secretions of asymptomatic carriers, who could be as numerous as 50% of the individuals in some US communities, whilst in Germany they account for some 20% of the population [38] . Since grey colour of tattoos is often involved, the influence of diluting tap water has been evoked as well [20]

The CDC reported the outbreaks of CA-MRSA in the states of Kentucky, Ohio, and Vermont [39]. These outbreaks were traced back to unlicensed tattooists operating in unsanitary facilities.

Quality control measures ensuring sterile inks are hence clearly needed, together with more stringent hygiene practices in tattoo parlours. However as Conaglen [36] noted, "*Any such interventions must balance the benefits of stricter controls with the risks of alienating the tattoo industry or increasing tattoo prices as these, in turn, could increase the prevalence of illegal tattooing with potentially grave public health consequences*".

Last but not least, linked to the increased use of topical antibiotics for mild infections following a tattoo, there is the theoretical risk of germs developing resistance against some antibiotics.

3.1.2.2. Viral infections

Isolated cases of viral warts caused by the human papilloma virus (HPV) or molluscum contagiosum (MCV) transmitted during the tattoo process or due to the presence of HPV in the tattoo ink have been observed [20] after an incubation period of 2 weeks to 10 years, but these events rarely take place within professional settings.

The fact that these verrucae are sometimes restricted to one tattoo ink colour, namely black, and that they might appear from 1 month to 10 years after the tattoo procedure have lead Kluger [40] to consider these viral reactions as a Köbner phenomenon (see below the section on coincidental diseases) on pre-existing skin lesions. UV exposure and sunburn 2.5 years after tattooing can represent another latent HPV triggering factor [41].

Blood-borne viruses of Hepatitis B (HBV) or C (HCV) may provoke serious systemic pathologies, such as hepatic failure, and several authors investigated the association among hepatitis and tattooing with conflicting findings.

Tohme [42] considered that there is no increased incidence of hepatitis C from tattooing in low-risk adults when sterile equipment is used. Mataix [43] mentioned that the HCV risk factor from tattooing is epidemiologically statistically irrelevant. Other authors mainly attributed the risk of getting hepatitis B or C to an inadequate hygienic environment [13, 32, 44] and Kluger [32] referred to home (or prison-) made tattoos, as well as to tattoos performed in unregulated settings as source of risks.

Analysing data from the Italian Surveillance System (SEIEVA) for acute viral hepatitis in the period 1997-2002, Mariano [45] suggested that tattooing plays a causal role in the transmission of acute hepatitis C (adjusted OR = 5.6, 95% CI 2.8 – 11.0). Tattooing was also associated to hepatitis B (adjusted OR = 1.7, 95% CI 1.0 – 3.1;). This study, however, did not indicate where the tattooing procedure had taken place (professional shops vs. home tattooing).

Carney [19] carried out a survey on 3871 patients, 1930 of which with chronic HCV infection. Tattooing resulted being associated with HCV infection (OR = 3.81, 95% CI 3.23 – 4.49). The same was true on a smaller sample of patients (1886, of which 465 HCV-positive patients) without traditional risk factors, such as drug injection and blood transfusion prior to 1992 (OR = 5.71, 95% CI 3.75 – 7.11).

Urbanus [46] performed a study on 434 individuals with multiple tattoos and/or piercings in The Netherlands, excluding possible confounding factors such as present or past drug users and men who have sex with men. There was neither a correlation with the number of tattoos, nor with the body surface area covered by tattoos. He concluded that "*in low HBV/HCV-endemic countries where strict hygiene guidelines for tattoo and piercing practices have been implemented, like in the Netherlands, tattoo and piercing practices are not associated with HBV/HCV infection*". The Dutch experience over the last years, reflected his paper, shows that a correct sterilisation of tattoo material and enforcement of robust hygiene guidelines by tattoo professionals in controlled premises prevents effectively virus transmission during the tattoo application. Exchange of good practices on this topic between the different countries is crucial for the eradication of blood-borne contamination.

In 2012 and 2010, Jafari [47, 48] published two systematic literature reviews and meta-analyses that evidenced a statistically significant association between tattooing and risk of transmission of hepatitis B and C, respectively (hepatitis B, odd ratio (OR) = 1.48, 95% confidence interval (CI) 1.30 – 1.68; hepatitis C, OR = 2.74, 95% CI 2.38 – 3.15). Higher odd ratios were calculated in the case of high risk behaviour groups. 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). He also estimated that, in countries with tattoo prevalence of 8% in the general population, 6% of the hepatitis C infections are related to tattooing, and that risk increases with the number of tattoos and surface area of the tattoo.

Serup [26] considered that the threat of HBV/HCV transmission through tattooing is overlooked since hepatic failure may take decennia to develop.

Recent epidemiologic unpublished SEIEVA findings (2010-2014) showed strong association between placing a tattoo and acute B- or C-hepatitis, without proving a

formal causality between the two events, in the age group of 15 to 54 years old. 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 (B, adjusted OR=2.1, CI at 95% 1.4-3.1; C, OR=2.2 with CI at 95% 1.1-4.4). Klügl [25] calculated a post-tattoo hepato-seroconversion rate of 0.6% against the total number of tattooed people showing any kind of adverse reaction.

As far as other viruses are concerned, Kluger [32] could only find one documented case of a herpes rash within a tattoo 3 days after the application. However, it was not proved that the cause was direct contamination and it has to be noted that latent herpes simplex and herpes zoster infections are known to be also reactivated through the tattooing procedure [22].

In his review, Kluger [32] also reported one possible case of AIDS contamination concerning 2 men who in 1988 received tattoos in prison with unsterilized needles used previously for other inmates. The risk remains thus theoretical, also because transmission of the HIV virus needs a massive and prolonged body fluid contact, which is unlikely to happen during a standard tattooing session, in contrast to HBV/HCV viruses, which require only a small inoculum to infect a person.

3.1.3. Non-Infectious risks

These types of complications comprise the allergic/hypersensitivity reactions and the coincidental diseases, who are both unpredictable and may occur years after the tattoo application. These coincidental pathologies may be further subdivided into concomitant underlying dermatoses, reactivated or triggered by tattooing, and cutaneous tumours developing within a tattoo.

3.1.3.1. Allergic reactions

The medical literature mentions hypersensitivity as the most common reaction to tattoos and PMU inks. These allergic manifestations are predominantly linked to coloured tattoos, and more specifically to red inks, in particular for lichenoid reactions (see below). Allergic reactions to black tattoo pigment are also rarely reported [49].

Older reports mentioned allergy to metals such as mercury sulphide (red pigment, cinnabar), chromium (green), cobalt (blue), cadmium (yellow) or magnesium (purple), but this view may have become partly obsolete, as nowadays inks are largely based on organic pigments and have eliminated some of these metals, except as impurities [49]. Nevertheless, metals such as chromium, cobalt and nickel are still present not only as impurities; some heavy metals, e.g. copper and titanium, are present as nanoparticles; and iron oxides are present in many PMU colours (such as in red, brown, pink and black inks (causing problems with Magnetic Resonance Imaging exams). As seen earlier, nickel contamination can, in already sensitive individuals, trigger a widespread rash the first days after the tattoo/PMU placement. Preservatives such as parabens can induce the same generalised eczema, sometimes after 8 weeks [14].

Notwithstanding this shift from metal salts towards organic dyes and pigments, allergic reactions are still more frequent with red tattoos, possibly due to primary aromatic amines (PAA)-containing azodyes. Modern inks' composition is highly variable, even among similar-coloured pigments, in addition to organic substances they may often contain, compounds or elements such as cadmium selenide, ferric hydrate, aluminium, titanium, carbon, barium, copper and strontium. Titanium oxide are one of the least reactive white pigments with no described allergic reaction [50]. A recent Danish study [51] found nickel, as a trace element or in higher amounts, on all the 61 tattoo inks analysed. Allergies to green and light-blue pigments are less common, often related to chromium, aluminium or chloride cobalt additives [50]. However, even though granulomatous reactions to chromium, mercury, cobalt, and magnesium have been

described, Serup [26] points out that apparently tattooing is not a clinically important allergy inducer to nickel and chromium VI, despite the presence of nickel in almost all tattoo inks, considering unlikely that allergy to nickel can explain chronic tattoo reactions, usually developing after months or years.

The difficulty to identify the culprit allergy-eliciting ink constituent is related, on the one hand, to the widely unknown composition of these low-purity industrial products and, on the other hand, to the often negative outcome of epi-cutaneous patch tests, especially with the granulomatous and lichenoid types of reactions. In the period 2009 – 2013, Serup [52] performed patch tests on 90 patients with non-infectious chronic tattoo reactions, whose results were negative. He suggested that chronic sensitisation is not elicited by an allergen directly present in the tattoo ink, but rather through metabolites produced in months or years probably due to haptenisation, i.e. the intra-dermis formation of a hapten, possibly helped by external factors such as light exposure. This slow haptenisation hypothesis and the possible pigment degradation, forming for example primary aromatic amines through photochemical cleavage of azo pigments upon sunlight exposure, could also explain why the results of patch tests were also negative in patients who had experienced concomitant reactions in another hitherto tolerated tattoo of the same colour as the reacting one. In its 2012 survey, [51] the Danish Environmental Protection Agency, sustained that "*Complex allergic reactions in the body mediated by tattooing in the form of widespread reactions in the vascular system, vasculitis, and in the form of iritis in the eye, also after tattooing, can be induced through an allergic reaction by a pigment protein complex and allergic reactions to tattoo colours are not obligatory limited to a simple chemical substance as mediator*". The onset of the inflammation is unpredictable, and can happen from immediately after tattooing up to 45 years later [53]. The duration is equally unpredictable, as the hypersensitivity reaction may last for ever.

Clinical aspect is non-specific, ranging from isolated pruritus to pseudo-tumoral wart [53]. Symptoms, which may disappear spontaneously or after decades, include itchy papulo-nodules, tenderness, swelling and induration. Papulo-nodular forms are especially noted with black tattoos and black linings. Ulceration, necrosis and hyperkeratosis are primarily encountered in red tattoos or red nuances [26]. Plaque elevation is typically seen in red, occasionally in blue/green [26].

The development of allergy to latex proteins originating from the tattooist's gloves and introduced into the skin via the needle has been reported [26]. 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. Latex particles from the tattooist's gloves can also provoke delayed type allergy causing hand eczema affecting the tattooist.

The histopathological findings refer traditionally to "lichenoid, granulomatous, or pseudolymphomatous" patterns, but these labels are imprecise, may overlap in the same biopsy without strict correlation to a clear clinical image, and should not be applied to distinguish various tattoo reactions. Consequently authors often opt for a histological pattern (e.g. 'granulomatous type IV inflammation') without specifying a clinical diagnosis [20]. The following manifestations are hence not specific, and attempt to classify them reveals challenging.

- **Acute or chronic eczematous dermatitis** presents usually as an itchy and scaly erythema in sensitized patients following any topical application during the healing phase, e.g. antibiotics, disinfectants, or by contact with gloves' latex, etc. The papulovesicular rash is typically localized at the tattoo site, but can secondarily spread as an urticarius to the whole body. These hypersensitivity reactions involve predominantly red pigments though black pigments also might be involved sometimes. Generalised erythema multiforme after localised allergic dermatitis from dark henna tattoo has been described [54].

Paraphenylenediamine has been designated as the contact dermatitis-triggering substance in "black henna" temporary tattoos [13].

- **Photosensitivity** following sun exposure affects, preferentially on light-exposed parts like face and hands, about 20% of tattoo recipients [55]. Høgsberg reported symptoms from acute swelling and itching to chronic nodulo-papules, lasting for months in 16% of the 154 tattooed Danes interviewed.

  Hutton Carlsen [16] performed a survey on 144 tattooed sunbathers, of which 21.5% experienced complaints linked to sun exposure. The major symptoms were swelling, itching/stinging/pain and redness. Photosensitivity was reported by 20/133 recipients bearing black tattoos, 14/45 for red, 1/8 for pink, 1/9 for orange, 1/5 for purple, 7/25 for blue, 2/31 for green, 1/10 for white and 4/25 for yellow tattoos (multiple replies were allowed). Black tattoos were responsible for the larger number of complaints, but in percentage (versus the number of tattoos of that colour) red tattoos were predominant. The onset may vary from few second to the following day lasting from minutes up to several weeks. The authors suggested that the formation of reactive oxygen species (ROS) in tattoos exposed to sunlight could cause symptoms with pain, discomfort and itching as well as signs, primarily manifested as redness and swelling.

  Some pigments (e.g. phthalocyanines) contained in the tattoo inks can act as photosensitizers [18]. Some purple pigments are photoreactive and lose their colour after prolonged exposure to light, but it remains to be confirmed whether manganese may cause granulomatous allergic reactions in some purple tattoos [50]. Rare cases of light-induced reactions resembling discoid lupus erythematosus have been associated with pigments contained in red inks [33].

- **Lichenoid** (papules or plaques) and **granulomatous** (firm indurated nodules) pruritic lesions are generally confined to the red portion of the tattooed area. The lichenoid type is the most frequently reported pattern [56], and can sometimes generalise [57]. It is historically linked with mercuric sulphide (cinnabar) used in red inks, but modern organic pigments, and Lawsonia inermis extracts of temporary henna tattoos have also been implicated [49].

  Kaatz wrote that the majority of the granulomatous inflammations are of foreign body type, but an allergic origin, like in the lichenoid forms, is also possible [22]. Allergy reactions of the granulomatous type, with eczema and inflammation, are probably related to aluminium, present in almost all tattoo inks. However it is still unclear if these reactions are purely allergic or involve an immunotoxic component, as aluminium-induced granulomas may be linked to sarcoidotic lung pathologies (see below) in predisposed individuals [51].

  Greens and blues made of copper pthalocyanine pigments are more stable than those containing cobalt or chromium pigments, and as such least likely to elicit allergy [50]. Setlur [58] reported the death of a patient from desquamative interstitial pneumonia upon foreign body reaction to his tattoo. Sweeney [59] cited a case of uveitis occurring simultaneously with a skin reaction possibly secondary to cobalt-containing tattoo pigments.

  Less commonly, these granulomatous reactions present sarcoidal type (especially associated with iron oxides and blue pigments). Both forms, lichenoid and granulomatous, may coexist in the same patient [60]. Serup [14] does not consider as allergic the papulo-nodular skin deposits of black pigment, but as a common foreign-body encapsulation phenomenon, which at histology manifests as sarcoidal type granuloma, evoking rather a systemic reaction pattern. Setlur [58] cited the case of a patient with a known sensitivity to metallic jewellery, who developed a sarcoidal granuloma in black pigment only, despite the presence of

turquoise colour that was also part of the tattoo but uninvolved by the granulomatous reaction.

Some granulomatous/lichenoid reactions may be confused clinically and histologically with sarcoidal or lichen planus manifestations (both hypertrophic and atrophic forms), and in some cases constitute an early manifestation of these systemic underlying pathologies (see below). The same holds true for lupus-like lichenoid patterns, potentially associated to the systemic lupus erythematosus.

According to both Simunovic and Wood, granuloma annulare- and necrobiosis lipoidica-like reactions are rare [57, 61]. Tuberculoid granulomatous reactions to ferric oxide and chromium salts used in eyebrow permanent make up may mimic inoculation diseases such as cutaneous tuberculosis or leprosy [49], which have virtually disappeared among Western non immunosuppressed citizens.

- **Lymphomatoid** reddish indurated nodulo-papules and plaques, sometimes pruritic, and much similar to cutaneous lymphomas at clinical and histologic examination, though without malignant evolution in the vast majority of cases (80-90% of reported cases [62]), have been rarely described, mainly within the red parts of the tattoos (79% of the 19 cases listed by Marchesi [62]), but also associated with blue, green and black pigments. The incubation period varies from a few weeks to 42 years. Pseudolymphomatous infiltrates, which are thought to be a delayed reaction to chronic antigen stimulation-albeit without conclusive patch-test, are not always confined to the tattooed area. A case of malignant transformation of a long-standing pseudolymphomatous tattoo reaction into a cutaneous lymphoma has been reported [57].

- **Pseudoepitheliomatous hyperplasia (PEH)** appears rarely as verrucous nodules or plaques, within weeks or months after tattooing. They are difficult to distinguish from tumours, hence skin biopsy is advisable, as they can also be linked to various infections [13].

The end stage of these chronic inflammatory tattoo reactions, if untreated, may take the clinical aspect of fibrosis, with scarring or even keloid formation, in what has been described as sclerodermatous or morphea-like pathologies, to be distinguished from the isomorphic phenomenon (see next paragraph) arising in patients prone to connective tissue diseases [57]. Thum Chee [49], cited 2 cases of pruritic morphea-like tattoo reaction developing in indurated multi-coloured tattoo (one of them restricted to the red area of the tattoo), without any systemic of scleroderma or morphea. Even though prior trauma (like vaccination) has been evoked in morphea etiopathogenesis, Thum Chee considered that the link between tattooing and morphea/scleroderma had not yet been demonstrated. Post-tattoo ocular involvement has also been reported by Ostheimer [63] (bilateral uveitis in all 7 patients with elevated and indurated black tattoos on various locations, e.g. arms, chest and abdomen), and by Kaatz [22] (concomitant retinal vasculitis and cystoid macular oedema).

3.1.3.2. Underlying Dermatoses reactivated by tattooing

"**Coincidental diseases**", regroup both the underlying dermatoses triggered/reactivated by tattooing ("concomitant diseases" such as sarcoidosis and other auto-immune pathologies), and tumours arising incidentally within a tattoo.

The isomorphic **phenomenon** has been originally reported by **Köbner** in 1872, who described a psoriasis-like eruption developing within a tattoo of a psoriatic patient, and may occur between 1 week and decades after the skin trauma (typically within 10-20 days). This flaring of known skin disease into the tattoo through "Köbnerisation", sometimes decades after tattoo application, is relatively frequent, especially in immunodepressed patients, but does not adhere to strict rules. This isomorphic response

may concern, further to psoriasis, various other chronic dermatoses such as lichen planus/sclerosus, cutaneous lupus erythematosus, atopic dermatitis, sarcoidosis, pyoderma gangrenosum, vitiligo, and cutaneous vasculitis.

Though these severe reactions are poorly understood [14], tattoo putative clients known to suffer from such chronic pathologies should be warned against tattooing, which might precipitate their underlying disease. Furthermore, tattooing might reactivate latent herpes infections.

The influence of tattooing on **sarcoidosis**, an autoimmune disease affecting 10 to 20 per 100000 persons (irrespectively if they are tattooed or not) [64], is a matter of a controversy [22], and remains as enigmatic as the etiology and pathogenesis of the disease itself [65]. This author is convinced that immunosensitivity towards specific tattoo pigments plays a role, especially in patients treated with interferon (four of such sarcoidal reactions have been reported by Simunovic [57]. Sarcoidosis has been labelled as one of the great dermatologic masqueraders. Ethnic susceptibility, together with environmental factors, have been suggested by Selim [66], as contributors to the etiology of the disease. He considered a challenge the correct diagnosis of sarcoidosis as its clinical presentation varies greatly.

Sarcoid reactions have been noticed on old scars, skin traumas sites and around embedded foreign material, including decorative and cosmetic tattoos. However, sarcoidosis belongs to category IV (poor or questionable trauma-induced processes), according to the Boyd-Nelder classification of the Köbner phenomenon. 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. Quoting Kluger [64], "*The tattoo is most likely the target of sarcoidosis, rather than its cause*".

Lesions consist mainly of asymptomatic, itchy or sometimes tender papules, nodules, plaques or infiltrations on the tattoos, with sometimes scaling, ulcers or blisters. Reviewing literature for sarcoidotic skin reaction to tattoos/PMU, Kluger [64] found 59 cases of sarcoidosis on tattoos, 8 on PMU and 8 cases of association of granulomatous tattoo reaction and uveitis. The 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. Moreover, a large male predominance was observed.. Granulomatous reaction to tattoos, even of the not sarcoidal pattern, may reveal or complicate systemic sarcoidosis. Cases of skin sarcoidosis restricted to one color of the tattoo might be sarcoidal hypersensitivity reaction to the tattoo pigment or the first and often unique symptom of a systemic sarcoidosis microscopically difficult to distinguish from foreign-body granuloma. Red and black tattoos were most often affected, but other colours (blue-in particular in case of systemic involvement, green and brown) were also reported. In the majority of patients with multi-coloured tattoos, skin reaction was confined to a single tattoo pigment, but several colours were simultaneously involved amongst 40% of cases. 84% of patients with multiple tattoos had more than one tattoos affected as well. Systemic involvement, defined as extra cutaneous manifestations of sarcoidosis, was found in 70% of cases, of which 69% had involvement of mediastinal lymph nodes and 46% parenchymal sarcoidosis. As there was no follow-up in most of the published cases, it is unknown whether the remaining 30% had developed systemic manifestations in the following years [64]. Lo Schiavo [67], estimated the rate of later generalisation of cutaneous sarcoidosis in a tattoo site at 74% of patients.

Thum Chee [49], mentions the development of psoriatic arthritis within a week of appearance of skin lesions. Generalized flare-up has been observed after tattooing, but a true link remains uncertain [12].

It is challenging to determine if a lichenoid eruption following a tattoo represents a generalized lichenoid tattoo reaction or a true **lichen** planus. Other anecdotal cases of lichen sclerosus and atrophicus, perforating granuloma annulare (commonly with red pigments), perforating collagenosis occurring in red tattoos, Darier's disease (genetic

Keratosis follicularis), erythema multiforme and scleroderma-like reaction restricted to the red parts of a tattoo have also been reported [12, 57, 61].

Thum Chee [49] reported a case of skin **lupus erythematosus** lesions developing 3 weeks after a black tattoo, and progressing beyond the tattooed areas. The term "cutaneous lupus erythematosus–like tattoo reaction" has been used for vacuolar interface dermatitis and perivascular inflammation involving an old tattoo in a patient lacking signs of systemic lupus erythematosus. Several cases of discoid lupus erythematosus–like lesions have been reported to occur in patients with systemic lupus erythematosus, on the red areas of the tattoo, sometimes 15 years after [12, 22, 43, 49].

Reviewing literature Thum Chee [49], reported only 4 cases of cutaneous **vasculitis** complicating a tattoo between 10 days to 28 years after the procedure, one of them on the red part of a tattoo (cited by Setlur [58]). Lesions appeared first on the tattoo and then extended further on the non-tattooed skin. As mentioned by Kluger [32], the role of ink in the pathogenesis of vasculitis is difficult to prove.

Pyoderma Gangrenosum (PG) is a rare complication of tattooing, particularly on the lower extremities, and has been described in only two patients, one of whom had an underlying blood cancer [57]. PG-like ulcers might be also elicited by bacterial infections.

A less commonly form, morphea, has also been described [44].

3.1.3.3. Tumours

The potential carcinogenic effects of tattoo inks remain unclear, both at skin and systemic levels. The tattoo inks injected in the dermis contain several chemicals, such as pigments, additives, plus impurities and degradation products, some with intrinsic carcinogenic properties (like polycyclic aromatic hydrocarbons and aromatic amines). Nevertheless, the causal link between the tattooing procedure and neoplasm formation has so far neither been established nor excluded due, on one hand, to the long latency of carcinogenesis and, on the other hand, to its multifactorial character.

Some theories suspect that trauma, scars or cutaneous chronic reaction to foreign material may elicit the development of tattoo-related skin tumours [59].

Kluger [68] extensively reviewed the literature over the 40 last years, and found only 50 cases of cutaneous tumours on tattoos: 23 cases of squamous-cell carcinoma (SCC) and keratoacanthoma (the distinction is often challenging), 11 cases of basal-cell carcinoma (BCC), and 16 cases of melanoma. Compared to the dozens of millions of tattooed individuals, and to the 2-3 millions of skin cancers per year [14, 26], the number of cutaneous neoplasms arising in tattoos seems negligible, making in the opinion of Kluger the association between the two events purely coincidental. As far as tattoo ink composition is concerned, Kluger [68] wrote that "*it is unknown so far, whether* polycyclic aromatic hydrocarbons *in black tattoo inks contribute to carcinogenic risk for individuals with tattoos*", adding that most of the investigations on detected carcinogenic chemicals are in-vitro studies, while it remains unclear whether some of these substances can cause health problems when tattooed in the skin.

Multiple malignant melanomas, BCCs, or SCCs occurring on a single tattoo have been never described. Recent findings showed that patients who develop skin neoplasms on tattoos are younger and have a shorter delay since tattoo placement. At the same time, skin cancer in general affects nowadays younger people than it used to be in the past, perhaps due to the fashion of sunbathing and use of UV lamps. And as simultaneously tattooing is getting more popular among youngsters as well, having a coincidental malignancy on a tattoo becomes more likely. Kluger added that the increase in reported cases of keratoacanthomas (KA) and pseudoepitheliomatous hyperplasia (PEH) on tattoos may reflect a true incidence hike or just a better recognition or bias in publishing

trendy complications. In the opinion of Kluger [40], previous concerns of epidermal carcinomas following lumbar puncture through lower back tattoos are outdated.

The majority of the published cases of melanoma and BCCs occurred on dark coloured tattoos, while SCCs, keratoacanthomas, and benign pseudoepitheliomatous hyperplasia were more frequent within red tattoos [68].

The tumour onset ranged from 1 month to 55 years following the tattoo.

Pseudoepitheliomatous Hyperplasia

Rapidly growing after tattooing (between 1 week and few months), albeit benign lesion, it presents as nodules, large verrucous plaques or ulcerated lesions, mostly confined to red areas. It can be associated with various infectious, inflammatory or neoplastic processes, and its clinical and histologic features are hard to differentiate from KA or verrucous carcinoma [57]. Kluger in his review reported 10 cases in the last 40 years [68].

Keratoacanthoma and Squamous Cell Carcinoma

Keratoacanthomas are considered by some physicians malignant SCCs, whereas others debate about its malignancy [68]. Biopsy does not always contribute to differentiate precisely between PEH, KA and SCC; but time lag after tattoo may help to distinguish KA, which grow usually within a week to a year and resolve spontaneously over some months [14], from SCC, whose first reported case occurred on a 21-year-old tattoo [12]. Red tattoo ink was associated with 9 out of 11 (82%) of the keratoacanthomas diagnosed in 8 patients [50]. According to Kazandjieva [69], there is not any specific proof for a causative link between tattoos and SCC.

Basal cell carcinoma

BCC has been rarely found to appear after trauma, for example in surgical scars [20]. In the case documented by Serup [14] the basal cell carcinoma originated in the adjacent non-tattooed skin and overgrew secondarily the tattoo.

Malignant melanoma

Both benign nevi and malignant melanoma can arise *de novo* in a tattooed area. While in-depth risk analyses did not reveal tattooing as a significant risk factor for the development of malignant melanoma [22], it can certainly delay its diagnosis and treatment.

Non-Hodgkin lymphoma

One case of B-cell lymphoma was reported in a patient with a long history of pseudolymphoma (a benign lymphocytic infiltration) on tattoos on both arms, the lymphoma developed on both tattooed and non-tattooed areas. Two additional reported cases of cutaneous lymphoma have been reconsidered as pseudo lymphoma [68].

Additionally, Kluger [68] cited some other anecdotal cases of rare skin malignant lesions, for which a true link with the tattooing event is highly speculative; these included two cases of dermatofibrosarcoma protuberans (Darier-Ferrand) occurring 1 and 2 years after tattooing, and a leiomyosarcoma which appeared 9 years after tattooing.

Baker [70] reported one case of dermatofibrosarcoma protuberans (uncommon, locally aggressive cutaneous tumour of intermediate grade malignancy) arising in a tattoo.

To conclude, the fact that a causal link between tattooing and cancers has not yet been established does not rule out the risk, but it seems negligible, probably a coincidence. Belgian and Danish authorities [51, 71] have drawn the same conclusions.

Monitoring and reporting side effects, together with epidemiological studies in the long run, is needed to demonstrate the causative nature of the connection between these two events, if any.

3.1.4. Medical diagnostic and treatment interference

Tattoo pigment deposition in the dermis may mask the pattern of dermatoses arising in the tattooed area, and in particular hamper dermatoscopic surveillance of pre-existing naevi with the risk of delaying the diagnostic of their potential malignant transformation into a melanoma.

These pigments stemming from dark tattoo inks may also lead to a false diagnosis of melanoma, and subsequent unnecessary stress linked to surgical excision. Similarly, dark pigments migrating to regional lymph nodes draining the tattooed area may mimic metastatic invasion of a sentinel lymph node by a melanoma; however, new immunohistochemical techniques are now able to differentiate the two types of pigmentation.

Metal (in particular iron)-containing inks may interfere with the quality of the diagnostic imaging techniques, such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) scan exams and give false-positive mammographies.

Rarely tingling and burning sensation during MRI exams has been reported, especially with red and black tattoos [22, 72]. The role of ferric oxides in this effect has been reported [73].

Lumbar tattoos may also complicate spinal anaesthesia, e.g. in obstetrics, but the potential risks of such a procedure are still under debate with different opinions expressed by various authors [40].

3.1.5. Contra-indications to tattooing

Some underlying clinical status may render the tattooing procedure problematic with regard to possible clinical complications, and, as such, should contra-indicate tattoo procedures.

The area to be tattooed should be free of pre-existing naevi and other pigmented lesions. The tattoo recipient should have no past history of melanoma or atypical mole syndrome.

Known allergies to nickel, latex, and other substances may be reactivated and hypersensitivity reactions triggered. Post-tattoo healing process may reveal problematic in patients suffering from eczema.

As for any other intervention individuals suffering from haemophilia or presenting other coagulation disorders (thrombopenia, von Willebrand disease, etc.), including those patients taking medications with possible haemorrhagic side-effects, should seek consent from their doctor before undergoing any tattoo procedure [57].

Pre-existing cardiac diseases, in particular valvulopathy, increase the risk of bacterial endocarditis with potential life-threatening consequences [31]. Antibiotic coverage is recommended prior these patients undergo a tattoo/PMU procedure.

In certain patients, predisposition to chronic autoimmune dermatoses (sarcoidosis, lupus erythematous, etc.) or treatment with interferon might trigger the skin disease to localise within a tattoo, sometimes many years after the application [57].

Years after the tattoo procedure, chronic skin disorders, such as psoriasis or lichen, might reactivate and induce a rash within the tattoo (Köbner phenomenon) [12]. Tattooing on the edge of a vitiligo lesion may trigger its extension [4]. Prior latent infection with herpes virus could precipitate the reawakening of the lesions.

There is no data supporting additional risks to the foetus or mother ascribed to tattooing during pregnancy. However, it is generally recommended to avoid tattoo application while pregnant or breast feeding [44].

Patients with known pre-existing Pyoderma Gangrenosum should be strongly advised against tattooing, particularly on the lower extremities [57].

3.2. Adverse health effects linked to tattoo/PMU removal

As the number of decorative tattoo and permanent make-up has been increasing during the last years, also the demand for their removal became greater. Actually, Karsai reported that the number of new tattoos has remained at a static rate while the number of removal requests is constantly growing [74], thus explaining the increasing number of tattoo studios offering such services. Motivations for tattoo removal include regrets (tattoo as a youthful folly or carried out under the influence of alcohol or drugs), aesthetic reason or medical problems [75]. Similarly to tattoo application, tattoo removal practice is not free from risks and adverse effects.

The early removal procedures consisted of destructive methods which entailed the mechanical stripping of layers of skin until the ink was no longer visible. Practices such as salabration and dermabrasion have been used for decades as the method of choice for tattoo removal. These destructive modalities often resulted in permanent scarring, serious inflammation, loss of normal skin pigment, residual tattoo and infections. Then surgical and chemical procedures (trichloroacetic acid and the so called glycolic acid mixture, made of lactic, tartaric, malic and glycolic acid) became of routinely use as well. Despite surgical excision replaces the tattoo with a surgical scar, it is still considered nowadays the best choice for people having strong allergic reaction to their tattoos. Chemical procedures do not completely remove the tattoo and have the disadvantages of being quite painful, and leading to depigmentation and hypertrophic scars. Nevertheless, such methods are still sporadically used nowadays, as they are cheap and may be sometimes managed at home.

Thermal procedures have also been used. Electrocautery, infrared coagulation, argon lasers, and CO_2 lasers are some examples. As already mentioned for mechanical methods, also these thermal procedures almost always leave a scar and, moreover, very often lead to incomplete tattoo removal.

Despite all their side effects and the lack of selectivity, argon and CO_2 lasers represented the first attempts of selective tattoo removal and foretold the modern age of Quality-switched (Q-switched or QS) ruby (694 nm), alexandrite (755 nm) and Nd:YAG (532 and 1064 nm) lasers which represent, since early 90s, the gold standard for tattoo removal [76, 77].

Although Q-switched lasers have made tremendous steps in advancing the safe and efficient removal of tattoos, both temporary and permanent side effects might still occur, especially when incorrect parameters such as pulse duration and light intensity are applied to the laser device [49, 76, 78-80].

In the following paragraphs the most frequent adverse effects reported in the literature linked to the use of Q-switched lasers are presented.

3.2.1. Thermally induced acute inflammation

Blistering is reported being one of the major transient effects of epidermal thermal damage induced by removal treatments. According to some authors [77, 81, 82], this side effect is expected in most cases and is linked both to incorrect parameters applied to the laser device and to an unexpectedly high level of absorption of laser energy by epidermal melanin. When the light intensity is too low or the pulse duration is too long (in the range of milliseconds), pigments in the skin are heated up rather than destroyed and the heat is conducted to the adjacent tissues causing injuries [78, 82]. Melanin plays a fundamental role as it competes for laser light absorption at certain wavelength (mostly the one of QS Ruby and the lowest wavelength of Nd:YAG). This may manifest acutely as blistering and skin sloughing and later as pigment disorders (namely hypopigmentation), especially in individuals with a darker skin type [81]. This is the reason why authors emphasise the importance of sun avoidance before the removal. In most cases, bulla formation is avoidable by strictly attaining to the post-treatment indications (elevate and ice the treated area) and, in any case, complete healing of the affected areas can be achieved following sterile aspiration, non-disruption of the roof of the blister, application of a petrolatum ointment, and dressing [83].

Local development of **crusting** is an additional effect caused by epidermal thermal stress [72, 74, 75, 78, 79, 81, 84]. As in the case of blistering phenomenon, crusting requires 7-10 day of appropriate post-intervention care that aims at optimising the cosmetic outcome. Despite the advent of modern Q-switched laser therapy drastically reduced the development of scars with respect to the earlier procedures, the formation of **permanent scars** is still possible when the type of laser and/or applied conditions are not correct and the damage is deeper. In case of particularly resistant tattoos (multi-coloured tattoo containing iron oxide or titanium dioxide), which require a more intense treatment for removal, it is more likely to develop permanent scars [72, 74]. Again in a study conducted by Wenzel [78], 10 out of 12 individuals treated with improper device or light parameters developed hypertrophic scars.

Another transient effect of laser removal is **erythema** formation and/or **pinpoint bleeding**. These effects are due to photo acoustic damage of dermal capillary walls as a result of the high peak of laser energy. This promotes extravasation of blood into the surrounding tissue. Erythema is reported healing after few days from the laser treatment with adequate cooling [82, 84]. The literature reports one case [78] of long lasting erythema associated to the use of a device operating in the millisecond domain (long pulsed).

Additional acute effects include scaling, induration and fibrosing. Transient textural changes may also be observed and are reported self-resolving in 1-2 months [84].

3.2.2. Allergic reactions

Similarly to what may happen during tattoo application, hypersensitivity reactions have been described following their laser removal. In this case it is not only the original dye that triggers a reaction, but also its degradation products that are considered as new antigens scattered by laser treatment [33, 44, 69, 76, 85].

After tattoo removal, local allergic reactions have been noticed mostly in red (e.g. presence of mercury), green (presence of chromium) and blue (presence of cobalt) parts; at the same time, photo allergic reactions have been described in the case of yellow cadmium based pigments [13]. Khunger and co-workers reported on local allergic reactions, observed in particular in the presence of red and yellow pigments and manifesting in the form of pruritic papules, nodules or scaly plaques. Red and yellow inks may be responsible of photo allergic reactions as well [86].

Unfortunately, many authors agree on the fact that a generalised allergic reaction could be potentially initiated by the systemic release of ink fragments taken up and

transported *via* the lymphatic system [69, 76, 77]. For this reason, patients who had developed allergic reaction at the time of tattoo placement should be particularly aware of the risk they come across removal.

Systemic allergic reactions may occur immediately after the treatment; however in 2007, Bernstein reported at least one case when an anaphylactic reaction occurred 1 hour after treatment of the tattoo. In order to avoid any allergic reaction, some practitioners suggest the use of oral corticosteroids and antihistamines before and during the laser session and one day after the procedure [69].

3.2.3. Pigmentary disorders

Pigmentary disorders are the most common side effects of non-ablative laser therapies, and numerous reports of paradoxical darkening, hyperpigmentation and hypopigmentation following a QS laser treatment are reported in the literature. Specifically, the main reason of **hypopigmentation** has been attributed to the presence of epidermal melanin, which is known to compete for laser light absorption especially at certain wavelengths. This interaction eventually leads to the destruction of melanocytes, according to the same mechanism that applies to tattoo pigments. As a chromophore, melanin is able to absorb energy throughout the whole range at which QS lasers operate with peaks of absorption lying in the ultraviolet range and decreasing at the longest wavelengths. Operating with Nd:YAG laser, at its highest wavelength (1064 nm), would minimise the risk of hypopigmentation, because absorption capacity of melanin at long wavelengths is minimum [74]. Nevertheless, some colours such as red, yellow and orange require 532 nm wavelength to be removed and side absorption by melanocytes with consequent hypopigmentation is unavoidable. The role of melanin as a competing chromophore explains why patients with darker skin types, or tanned, tend to be particularly at risk of unwanted pigmentary changes [77, 82]. Most of the time, the loss of melanin pigment is transient, but it may persist up to years or even become permanent especially after repeated treatments [13, 76, 82, 84]. The incidence of permanent hypopigmentation in different studies has been estimated to be up to 10% of the studied population [13, 74, 76]. Time of onset is reported being 4-6 weeks up to several months after treatment [77, 82].

Hyperpigmentation is considered a result of an increased UV sensitivity of the skin after laser irradiation. Again, it is related to the patient's skin type, with darker skin being more prone. The incidence is 5-10% of the population who underwent QS lasers, with higher occurrence in individuals subject to multiple laser treatment, and it is considered a transient effect [74, 76, 82, 84]. Because of this enhanced UV sensitivity, individuals who have received gold salts for diseases such as rheumatoid arthritis should be approached with caution because 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). In addition, individuals already subject to chrysiasis should avoid QS lasers in order not to worsen hyperpigmentation disorders [81].

An additional pigmentary disorder that is frequently observed after QS lasers treatment is a **paradoxical darkening** that takes place especially during the removal of multicolour tattoos. This phenomenon is strongly linked to the chemical composition of some colours. In particular, authors agree on identifying some metal oxides, present in pigments, as responsible of this side effect. Titanium dioxide, which is contained in white inks and is often used to add brilliance to other tattoo inks is the responsible of darkening when light colours are present [49, 72, 76, 77, 81]. The same complication can appear in tattoos containing iron pigments often used in flesh-toned colours for permanent make- up [72, 76, 77]. Thum Chee [49] explains the darkening encountered in the presence of these colours with the reduction of ferric oxide to jet black ferrous oxide. Kent [81] reports on a study involving 184 patients who underwent QS laser removal of non-black tattoos. 33 out of 184 individuals experienced a colour shifts,

ranging from mild greying to complete blackening of the white, flesh-coloured, red, brown, yellow and crimson parts of their tattoos. As already mentioned, patients should be informed that darkening of the tattoo can be permanent and additional laser sessions might be needed to completely remove the pigment [33, 49, 72, 77, 79, 81].

3.2.4. Concerns about unpredictable systemic risks

Up to date, the only evidence of systemic reactions found in the literature and linked to laser tattoo removal came from an internet survey launched in 2014 by Klein [75] where headache was reported by 6% of a population of 157 individuals, dizziness was described by 4%, vomiting by 1%, and fever by 1%. These systemic reactions persisted up to 5 weeks in 66% of participants, 6–9 weeks in 7% of people, and in 4% side effects persisted more than 10 weeks.

Nevertheless, some concerns have been expressed for the potential toxicity of the products arising from the photodecomposition of pigment during the laser session. Kent [81] focused the attention on the fact that laser induced cleavage of azo-containing tattoo pigments results in decomposition products known to be carcinogenic and cytotoxic when distribute throughout the body. The same concern has been expressed by several authors [68, 72, 80, 84], but so far these chemical changes have not been proven in vivo and there are no epidemiological clinical data supporting an alarming increase in skin cancers [13, 68]. Nevertheless, some in vitro studies revealed that UV and laser induced photochemical cleavage of commonly used tattoo pigments (Red 22, Red 9) yields 2-methyl-5-nitroaniline, a suspected carcinogenic compound, 2, 5-dichloroaniline and 4-nitro-toluene, which are known for being toxic [74, 80]. Yet, previous investigations on potential toxicity of 3,3''–dichlorobenzidine, also used in tattoo inks, revealed light-induced genotoxicity in some human cell lines [79].

3.2.5. Pre-treatment counselling: feasibility, expectations and outcomes

Authors agree on the need of a thorough pre-treatment counselling advising with regard to realistic expectations and possible side effects [33, 75, 77, 87]. Patients should be informed that, due to the possibility of developing pigmentary disorders, the procedure may not lead to the complete removal of the tattoo, especially, as widely discussed, in the presence of certain colours or skin type [33, 49, 72, 79, 81].

Patients should be also advised that several laser sessions are required for the complete removal of a tattoo. Williams [87] reports 4-6 sessions for removing an amateur tattoo and even more that 12 for a professional and multi-coloured one. Interval between treatments may range between 6 and 12 weeks, thus meaning that years may be required for the complete removal. In addition, and for the same reason, patients should be aware of the economic impact of removal operation. Given the number of removal sessions, it may result in a final cost much higher than the application itself.

Finally, a person who decides to undergo a removal treatment should know that the procedure might be painful. In a survey launched on the internet by Klein [75], 47% of the 157 participants stated that laser therapy was much more painful than tattooing and 33% stated that pain levels were similar. Pain persisted in 11.2% (59) cases after treatment. This is the reason why a number of authors agree on the need of using a topical anaesthetic before the treatment [77, 81, 82].

The initial consultation is not only important for the patient, but it is the moment for the physician to carry out a scrupulous skin examination in order to evaluate the suitability of the laser removal procedure. In the presence of hidden suspicious nevus or malignancy, laser treatment should be withheld until further investigations are carried out. Again, in the presence of dermatological reactions or skin infections, treatment should be postponed and the infections treated [74, 76, 77, 81, 88].

Some authors also highlight the problem arising in the presence of traumatic tattoos that may embed combustible material. In this case there is a concrete risk of re-ignition during the laser treatment. This event would lead to significant scarring [77, 81].

3.2.6. Future perspectives

Improper laser parameters are one of the main sources of adverse effects related to QS laser removal. For instance, lasers operating in the domain of milliseconds (10^{-3} seconds) are known heating up pigments rather than destroying them with consequent damage of adjacent tissues. In other words, when compared to the proper use of nanosecond (10^{-9} seconds) pulses, the pigment particles in the skin are heated up a million times longer than necessary. Therefore, excessive heat is conducted from the hot pigment particle to the adjacent dermis thus originating thermal damage.

Laser with shorter pulse duration are currently being tested. Pulses in the picoseconds (10^{-12} seconds) range have the advantage of targeting pigment particles more effectively, with more efficient delivering of energy minimising unwanted interaction with surrounding tissues. In a 2014 article, Freedman [89] reviewed the published data pertaining to the clinical reports of picosecond laser devices, including Nd:YAG, Titanium: Sapphire, a novel 758 nm/500 picosecond model, alexandrite and a picosecond infrared laser (PIRL). Comparing these new devices with analogue nanosecond lasers, authors were able to demonstrate that picosecond lasers generate greater clearance of black tattoos at lower energy and have a greater depth of penetration, when all other parameters are held constant.

In addition, a new tattoo ink easier to be removed was made available in the United States in 2009 [77, 81]. These new inks contain encapsulated bioresorbable dyes in polymethylmethacrylate beads in which additional pigments are also present with the aim of absorbing specific wavelengths and to facilitate the capsule rupture under laser irradiation thus making the removal easier. This procedure has the additional advantage of using pigments which may be too small in size to be used in a conventional tattoo ink, as they would be swept away by the body because of the small size.

A last possibility to facilitate the removal is working on the optical properties of the skin with the aim of facilitating the access of the laser light into the dermis. Reducing the light scattering caused by the presence of dermal collagen by using topical and injected solutions, such as glycerol, glucose and dimethylsulfoxide, should make the tattoo removal more efficient while decreasing side effects [77]. Nevertheless, it must be mentioned that, intradermal injection of chemicals resulted in tissue necrosis and scarring, making this option not really considerable [81].

3.3. Adverse health effects linked to henna-based temporary tattoos

This chapter has been included for completion purposes. The practice of decorating the skin with henna based preparations is wide spread; however, this is not a tattoo because it is not meant to be permanent and it does not involve needles. In fact, the henna is applied by brushes or special pens on the skin and not injected. Due to its non-invasive nature, the health risks associated to henna-based temporary tattoos are milder and less frequent with respect to permanent tattooing.

In the EU, henna is considered a cosmetic product and therefore shall fulfil the requirements of the EC Regulation 1223/2009 on cosmetic products [90].

Henna is a powder obtained from the dried leaves and stalk of a plant (*Lawsonia Inermis*). To create the henna preparation, a paste is made out of this powder, by adding water or oil and additional (often secret) ingredients to enhance the darkening effect. Natural henna is also known as "red henna", because of the typical reddish-brown

colour generated by the interaction between the pigment contained in the henna powder (lawsone, CI 75480, Natural Orange 6) and the skin keratin.

The practice of decorating the skin of hands and feet with henna-based dyes has been widely diffuse in Islamic and Hindu cultures in the Arab, African and Indian world for thousands of years. In the past decades, a revisited mode of henna application, the so-called temporary black henna tattoo has become fashionable in western cultures as well. It is usually applied to young people and children in holiday resort areas and in attraction parks, at festivals and fairs by street artisans. Black henna is the combination of red henna and PPD (p-phenylenediamine), which is used to accelerate the dyeing and drying process, to strengthen and darken the colour, to enhance the design pattern of the tattoo and to make the tattoo last longer (3 to 4 weeks).

According to the revised literature, most of reported side effects after henna tattooing are allergic reactions or sensitisation to one of its components.

As for red henna, its sensitising potential can be considered negligible. Moreover, despite the large number of people who have been exposed to natural henna at some time in life, immediate-type allergy to red henna preparations has been reported rarely [91, 92]. In the sporadic cases described, the actual allergen remained unknown and most of the studies cannot definitely exclude the presence of aromatic amines [92].

On the contrary, several cases of allergic reaction to black henna, in the form of localized or generalized contact dermatitis, hypertrophic or keloid scars, have been reported in the literature [49, 91, 92].

Induction of allergic reactions can take as long as 7 to 20 days, but it can be shorter (24 to 48 hours) if the patient has had previous exposure to the allergen. Normally, these types of reactions do not leave any permanent effect, as they completely heal if treated with the proper topical medicaments. In rare cases, permanent post-inflammatory dyschromic changes may occur.

Principal responsible for this type of adverse reactions is PPD, which is known to be a powerful antigen [49, 91-93]. Nevertheless, Calogiuri and colleagues reported the presence of other contaminants in henna preparations, such as thiurams and latex cross-reactive proteins, as well as nickel, cobalt and mercury, which may induce contact allergy as well.

At the same time, PPD has a very strong sensitising potential and may be responsible of the developing of threatening allergic reactions in response to a subsequent contact to the allergen. Kneilling [94] examined nine patients who developed severe allergic reactions in response to permanent black hair dye. Seven out of nine patients reported having temporary black henna tattoo 3–7 years prior to the use of the permanent hair dye, which resulted in a strong inflammation at the site of the tattoo. All of the seven patients resulted positive to patch test using 1.0%, 0.5% and 0.1% PPD.

According to the cosmetic regulation, PPD may only be used in hair colorants and only up to a maximum of 2% when applied to the hair. Therefore, the presence of PPD in so-called 'black henna' temporary tattoos is illegal in the EU.

3.4. Experience with the CoE ResAP (2008)1

A questionnaire developed for the national authorities was sent to the 28 Member States of the European Union plus the 4 EFTA countries (CH, IC, LI and NO) through the Consumer Safety Network. Fourteen Member States (BE, BG, CZ, DE, DK, ES, FI, FR, IT, NL, RO, SE, SI and SK) answered, though not all of them replied to each section of the questionnaire. The section on the experience with the CoE ResAP(2008)1 and the suggestions for updating its requirements was divided in five parts (in parenthesis the number of MS who replied): chemical (5), labelling (11), register of complaints/side effects and pre-marketing authorisation (11), hygiene/sterility (5) and other (10).

This chapter presents the outcome related to this section of the questionnaire, integrated with discussions held by the CSN-STPM. The whole set of answers is reported in Annex III.

3.4.1. Chemical requirements

The recommendations of the CoE ResAP(2008)1 with regards to chemical substances that should not be part of tattoo/PMU products are listed: in its Tables 1-3 [1]; in the Directive 95/45/EEC [95] on specific purity criteria concerning colours for use in foodstuffs; in Annexes II and IV (column g) to EC Reg. 1223/2009 on cosmetic products [90]; and in Annex VI (Table 3.1) to EC Reg. 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP regulation) [96], limited to the substances classified as carcinogenic, mutagenic and reprotoxic, CMRs, in categories 1A, 1B and 2.

Table 1 of the CoE ResAP(2008)1 reports a list of 27 aromatic amines which should neither be present in tattoos and PMU products nor released from azo-colorants in concentrations that are technically avoidable according to good manufacturing procedures.

Some Member States suggested modifications to this Table. In particular, Italy pointed out that, in order to help the implementation of these requirements, limit(s) should be established for the listed aromatic amines. This proposal was welcomed by the experts of the CSN-STPM. In addition, the Italian competent authority considered that aniline, 2-ethoxyaniline and N-isopropyl-N'-phenyl-1,4-phenylendiamine should be added. Also Spain and Denmark proposed to add aniline and the Danish competent authority suggested a limit of 10 ppm for this compound.

As shown in Table 3.1, actually the CoE ResAP(2008)1 already recommends not to use aniline in tattoo/PMU products, because it is listed in Annex II of the cosmetic regulation and because it is classified carcinogen and mutagen (category 2) in Annex VI, Table 3.1 of the CLP regulation. The inclusion of aniline in Table 1 of the CoE ResAP(2008)1, which takes into consideration just aromatic amines, could make this recommendation more visible for enforcement laboratories and manufacturers.

Table 3.1: Aromatic amines that could be evaluated for inclusion in Table 1 of the CoE ResAP(2008)1.

					EC Reg 1223/2009		EC Reg 1272/2008		
Substances	**CAS number**	**DK**	**ES**	**IT**	**Annex II**	**Reference number**	**Table 3.1**	**Index number**	**Classification (CMR, Skin/Eye Irrir./Sens.)**
aniline	62-53-3	X (10 ppm)	X	X	X (its salts and its halogenated and sulphonated derivatives	22	X	612-008-00-7	Carc. 2, Muta. 2, Eye Dam. 1, Skin Sens. 1
aromatic amines				set limits					
2-ethoxyaniline	94-70-2			X					
N-isopropyl-N'-phenyl-1,4-phenylenediamine	101-72-4			X					Skin Sens. 1

The CoE ResAP(2008)1 recommends not using in tattoo/PMU inks the 35 colorants listed in its Table 2. Germany, Italy and Spain, as well as stakeholders from CSN-STPM, proposed to add a number of colorants to this list (see Table 3.2). Actually, pigments green 7, blue 15, red 5 and 181 should not be present in hair dye products. Pigments yellow 1, yellow 3 and green 7 should already not be contained in tattoo products, as they are listed in Annex IV (with use limitations) of the cosmetic regulation. In addition, tattoo inks should not include solvent yellow 14 as it is both classified carcinogen and mutagen (category 2) and it is mentioned in Annex II of the cosmetic regulation.

Table 3.2: Colorants that could be evaluated for inclusion in Table 2 of the CoE ResAP(2008)1.

CI Generic Name	CAS number	CI number	Colorant class	DE	ES	IT	Annex II (ref. number)	Annex IV (column g) (ref. number)	Table 3.1 (index number)	Classification (CMR, Skin/Eye Irrir./Sens.)
Pigment Blue 15	147-14-8	74160	phthalocyanine			X	X (1367) (when used as a substance in hair dye products)			
Pigment Green 7	1328-53-6	74260	phthalocyanine			X	X (1369) (when used as a substance in hair dye products)	X (107) (not to be used in eye products)		
Pigment Red 5	6410-41-9	12490	monoazo		X	X	X (1347) (and its salts when used as a substance in hair dye products)			
Pigment Red 17	6655-84-1	12390	monoazo		X	X				
Pigment Red 181	2379-74-0	73360	indigoid		X	X	X (1365) (when used as a substance in hair dye products)			
Pigment Violet 1	1326-03-0	45170:2	xanthene		X	X				
Pigment Yellow 1	2512-29-0	11680	monoazo		X	X		X (4) (not to be used in products applied on mucous membranes)		
Pigment Yellow 2	6486-26-6	11730	monoazo							
Pigment Yellow 3	6486-23-3	11710	monoazo					X (5) (not to be used in products applied on mucous membranes)		
Pigment Yellow 5	4106-67-6	11660	monoazo							
Pigment Yellow 74	6358-31-2	11741	monoazo		X	X				
Solvent Yellow 14	842-07-9	12055	monoazo	X			X (1107)		X (611-056-00-6)	Carc. 2, Muta. 2, Skin Sens. 1

Table 3.3: Aromatic amines that could be formed from azo pigments with indication of their classification.

CI Generic Name	Aromatic amine	CAS number	CoE ResAP (2008)1 Table 1	EC Reg 1223/2009 Annex II (Ref number)	EC Reg 1272/2008 Table 3.1 (Index number) Classification (CMR, Skin/Eye Irrir./Sens.)
Pigment Red 17	5-nitro-o-toluidine	99-55-8	X	X (1195)	X (612-210-00-5) (Carc. 2)
	o-toluidine	95-53-4	X	X (32)	X (612-091-00-X) (Carc. 1B, Eye Irrit. 2)
Pigment Yellow 1	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)
Pigment Yellow 2	p-chloroaniline	106-47-8	X		X (612-137-00-9) (Carc. 1B, Skin Sens. 1)
Pigment Yellow 5	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)
Pigment Yellow 74	o-anisidine	90-04-0	X	X (708)	X (612-035-00-4) (Carc. 1B, Muta. 2)
Solvent Yellow 14	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)

It has to be noted that, out of the eight monoazo pigments that the experts from the CSN-STPM would like to be banned in tattoo/PMU inks, pigment red 17, yellow 1, yellow 2, yellow 5, yellow 74 and solvent yellow 14 could, by reductive cleavage of the azo

bond or by break of an amide link, form the carcinogenic aromatic amines reported in Table 3.3. According to the CoE ResAP(2008)1, these aromatic amines should not be present in these products. In addition, Cui [97] reported that pigment yellow 74 can, under light irradiation, decompose to o-acetoacetanisidide (CAS 92-15-9), 2-(hydroxyimine)-N-(2-methoxyphenyl)-3-oxobutanamide (CAS 42056-95-1) and N,N'-bis(2-methoxyphenyl)urea (CAS 1226-63-7), which could be further degraded to o-anisidine, classified carcinogen and/or mutagen in categories 1A, 1B or 2.

In a meeting of the CSN-STPM, a representative of TIME (Tattoo ink manufacturers in Europe) declared that for pigment green 7, which is in negative lists mentioned in the CoE ResAP(2008)1, nowadays there is not a better alternative.

The Norwegian representative considered that pigments that are not allowed in hair dyes or as colorants (i.e. that are not in the positive list of Annex IV to the cosmetic regulation) should also be banned in tattoo products.

As already discussed for aromatic amines, the inclusion of additional colorants in Table 2 of the CoE ResAP(2008)1, which should already not be present in tattoo/PMU inks, would most probably simplify the work of enforcement laboratories and manufacturers.

In addition, taking into account the fact that azo colorants have been proven to degrade, in the skin and under light irradiation, to the aromatic amines used in their production and that the analytical methods used to quantify the aromatic amines released by azo colorants are not vey reproducible, in order to improve the safety of inks the group considered more effective to ban all azo colorants that by reductive cleavage may form aromatic amines classified as CMRs.

A number of competent authorities also made suggestions for amendments of Table 3 of the CoE ResAP(2008)1, on maximum allowed concentrations for impurities in tattoo/PMU products; however, there was no consensus on the necessary modifications.

Concerning organic impurities, Denmark suggested to increase the limit from 0.005 to 0.2 ppm, Italy considered that it is necessary to set individual limits for the most toxic polycyclic aromatic hydrocarbons (PAHs) and The Netherlands would like to specify which PAHs should be measured, relatively to the cumulative limit of 0.5 ppm which applies to the sum of PAHs.

Speaking about elements, four Member States expressed the need to establish a limit for nickel (ES, IT, NL and SI), with Italy proposing the value of 0.5 ppm. Italy also suggested to decrease the limits for arsenic, cobalt, lead and antimony, as reported in Table 3.4; however, at the same time, Denmark proposed to increase the limit for lead. Finally, Italian competent authority considered important to label the product if it contains cobalt, would welcome the establishment of different limits for tattoo and PMU products and wondered if the limit for barium is based on recent toxicological data.

In a meeting of the CSN-STPM, a representative of TIME proposed 5 ppm as limit to be established for the content of nickel, while a Swedish expert suggested adding strontium on the basis of its presence in some inks.

In summary, there is a general consensus among experts for suggestions for revision of Tables from 1 to 3 of the CoE ResAP(2008)1, even if more in-deep discussions are needed, in particular on the establishment of new limit values.

Table 3.4: Suggestions for possible revision of Table 3 of the CoE ResAP(2008)1.

Substance	CAS number	CoE ResAP (2008)1 Table 3	DK	ES	IT	NL	SI
benzo[a]pyrene	50-32-8	0.005 ppm	↑ limit (0.2 ppm)				
PAHs		0.5 ppm			set individual limits for most toxic PAHs	Specify which PAHs has to be measured	
As		2 ppm			↓ limit (0.2 ppm)		
Co		25 ppm			↓ limit (5 ppm) add in the labelling "Contains cobalt; may cause an allergic reaction"		
Cu soluble		25 ppm			define what is intended for soluble Cu		
Ni		as low as technically achievable		set limit	set limit (0.5 ppm)	set limit	set limit
Pb		2 ppm	↑ limit (10 ppm)		↓ limit (1 ppm)		
Sb		2 ppm			↓ limit (1 ppm)		

Several national competent authorities would welcome the establishment of a positive list of colorants allowed to be used in tattoo/PMU products (BE, DE, IT, FI, NL, SE, SI, SK) and the harmonisation of analytical methods (BE, DE, DK, ES, IT, NL, SE, SI, SK). The preparation of a single list of chemicals that should not be present in tattoo/PMU inks was considered negatively by Germany and Sweden and positively by Belgium, France, Italy and Slovenia, even if France considered it difficult to achieve.

Other proposals mentioned by respondents were:

- to establish for chemicals (e.g. preservatives) in tattoo/PMU inks the same purity limits applicable to the drugs for injection in the body (BE);
- to establish guidance values for technically unavoidable amounts (DE);
- to establish a positive list for preservatives (NL);
- to come to a European consensus on the status of tattoo removal products (FR).

3.4.2. Labelling requirements

In this part of the questionnaire the national competent authorities were requested to indicate what changes in the labelling recommendations would improve the safety of tattoo/PMU inks compared to those currently mentioned by the CoE ResAP(2008)1.

Among the possible additional labelling requirements suggested in the questionnaire, there was a general consensus on the need to add the period of maximum durability after opening (PAO), the storage conditions, the product type (ink for tattoo or PMU) and health warnings. Seven countries were also in favour of having a compulsory quantitative composition label. On the contrary, Member States had different views 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.

Furthermore, Denmark and Italy proposed to add the batch number, Slovakia the symbol of minimum durability, while Italy was in favour of a label written in the national language of the country where the product is sold.

Table 3.5: Suggestions for possible additional labelling requirements.

Proposed modification	BE	DE	DK	ES	FI	FR	IT	NL	SE	SI	SK
PAO	Y	Y	Y	Y (with indication sterility assured for x applications)	Y	Y (present in national legislation)	Y	Y		Y (with indication of conditions to be satisfied)	Y (only for multiple-use packaging)
Quantitative composition label	Y	N	Y (not for < 1% unless skin sensitizer; use international nomenclature)	Y	Y	Y (present in national legislation)	Y	Y			
Production date	Y	N	indicate expiry date with the wording "May not be used after ..."	Y	Y		Y				N
Storage conditions	Y	Y (if specific conditions)	Y (if necessary)	Y	Y	Y (present in national legislation)	Y	Y		Y	Y
Product type	Y	Y		Y			Y		Y (to avoid injection of drawing inks)		
Distributor's address	Y	N	N	Y	Y	Y (present in national legislation)	Y	Y (preferably phone number)	N		N
Health warnings	Y	Y (useful in case of allergy)		Y	Y		Y (maybe in a separate document)			Y (about allergic reactions, phototoxicity, other health effects)	
Sterilisation method used	Y	N		N			Y				N
Batch number			Y		Y						
Label in the national language							Y				
Symbol of minimum durability											Y

3.4.3. Register of complains/side effects and pre-marketing requirements

A large majority of respondents (ten) considered useful the compulsory compilation of a register of complaints and side effects and only Slovenia was not favourable. French experts highlighted that this obligation already exists in France and some others suggested possible practical approaches.

On the contrary, opinions diverged on the proposal to set up a pre-marketing authorisation for tattoo/PMU inks; five Member States were in favour and four against. While Spain informed that this approach is already implemented in its territory, Belgium thought that the fulfilment of the requirements should be enough to guarantee the safety of these products, Germany considered the compulsory safety assessment carried out by manufacturers, importers or person responsible for the placing on the market the right solution and Sweden highlighted the role of public authorities in guiding companies to fulfil the requirements.

Table 3.6: Suggestions for possible additional safety requirements.

Proposed modification	BE	CZ	DE	ES	FI	FR	IT	NL	SE	SI	SK
Register of complains/side effects	Y	Y	Y	Y (with a questionnaire)	Y (notification similar to what foreseen by art. 23 of cosmetic regulation)	Y (present in national legislation)	Y	Y (side-effects to be included in an informed consent document)	Y (requirements for reporting side-effects should be discussed first)	N	Y (similar to cosmetics)
Pre-marketing authorisation of inks	N (respected requirements should be enough)		N (compulsory safety assessment made by manufacturers, importers or person responsible for the placing on the market)	Y (present in national legislation)		N	Y	Y	N (authorities should guide companies how to fulfil law)	Y	Y

3.4.4. Hygiene/sterility requirements

In the part related to hygiene/sterility requirements, the options available in the questionnaire were four: the specification of ink or tool sterilisation method, of premises'

disinfection method and the use of single dose containers. As reported in Table 3.7, five and four national competent authorities would be in favour of making compulsory the indication of the ink and tool sterilisation methods, respectively. Three and two respondents considered important to specify premises' disinfection methods and to use single dose containers, even though other highlighted that it is not practical for tattooists.

Slovakia proposed the establishment of good application practices for tattooists.

In a meeting of the CSN-STPM, a representative of TIME proposed to fix a maximum limit of 100 colony forming units (cfu) for a tattoo/PMU ink to be considered safe.

Table 3.7: Suggestions for possible additional hygiene/sterility requirements.

Proposed modification	DK	ES	FR	IT	SK
Specify ink sterilisation method	Y	Y	Y	Y (identification of the most effective method is needed)	Y
Specify tool sterilisation method		Y (already existing)	Y	Y (reference could be done to the sterilisation method used for medical devices)	Y
Specify premise disinfection method			Y		Y
Use single dose containers	Y		Y	Y (preferentially)	
Good application practices for tattooists					Y

3.4.5. Other proposals

Among the other proposals mentioned in the questionnaire, several Member States pointed out the need to establish Good Manufacturing Practices for tattoo/PMU inks, to carry out market surveillance on products sold on the web, to establish compulsory training for tattooists, to enhance the collaboration among manufacturers and authorities and to ban backyard tattooing (8, 6, 6, 5, 5 and 4 positive replies, respectively).

It is worth noticing that to set up compulsory training for tattooists, compliance with national legislations should be assured. For instance in Germany, a request should be presented to the Federal Ministry for Economic Affairs and Energy by the social partners.

Additional proposals put forward by respondents or discussed during CSN-STPM meetings were:

- to increase controls on imported products (BE);
- to set up more comprehensive and binding legislation (CZ);
- to set up working group to validate ink sterilisation methods (IT);
- to establish minimum age limit (IT);
- to make safety assessment of inks compulsory;
- to prepare guidelines for risk assessment of tattoo/PMU products;
- to develop harmonised hygiene guidelines;
- to ban illegal sales of "start-kits".

Table 3.8: Additional suggestions.

Additional requirements	BE	CZ	DE	ES	FI	FR	IT	SE	SI	SK
Control products sold on the web	Y (fakes and unsafe origin)		Y (market surveillance should include web sales)	Y	Y (difficult it can be done only at national level)		Y (to prevent the sale of fake inks)		Y	
Enhance collaboration manufacturers/authorities	Y			Y	Y		Y		Y (pre-authorisation)	
Ban backyard tattooing	Y			Y	Y		Y		Y	
Establish list of recognised tattooists	Y						Y (institution of national register of professional tattooists on the basis of an European standard)	Y (existing based on the notification to open the business)	Y	
Compulsory training for tattooists	Y		(need has to be presented to the Federal Ministry for Economic Affairs and Energy by the social partners), ES (existing regional certification)			Y (present in national legislation)	Y (harmonised at EU level)	Y	Y	
Set up Good Manufacturing Practices for inks	Y		Y	Y	Y	Y (present in national legislation)	Y		Y	Y (prepare EN standard)
Increase control on imported products	Y									
Set up more comprehensive and binding legislation		Y								
Set up working group to validate ink sterilisation methods							Y			
Establish minimum age limit							Y (forbidden under 14 years old, 14-18 with informed consent of parents)			

3.5. Risk perception and communication

This chapter presents the outcome related to the section of the questionnaire developed for the national authorities related to risk perception and communication, as well as a summary of what can be found in the literature on these issues.

3.5.1. Answers to questionnaire

Nine Member States informed that they had organised information campaigns in their countries, either at national (six) or at local level (three); while three of them reported that they had not. Various audiences were taken into consideration, including the general public, tattoo artists and studios, students, young people, prisoners, consumers, physicians and school teachers. The means used ranged from printed materials (reports, brochures, posters, newsletters, advertisements) to media coverage (newspapers and magazines, press releases, radio, TV), events held, such as conference and seminars, internet and social networks.

In the opinion of the majority of respondents and of experts of the CSN-STPM, additional information campaigns would help to improve the safety of tattoo/PMU and should be addressed to tattoo artists, potential clients and general public. Belgium and Slovenia highlighted the importance of targeting young students as well, to help them creating an educated opinion and making an informed choice.

Table 3.9: Information campaigns carried out.

Information campaigns carried out	BE	DE	DK	ES	FI	FR	IT	NL	SE	SI
National level	Y (report, dermatology newsletter, website)		Y	Y	Y			Y	Y (radio, reports, press release, advices)	
Local level		Y		Y			Y			
Targeted to general public	Y	Y		Y			Y			
Targeted to tattoo artists/studios				Y					Y (newsletter)	
Targeted to students							Y			Y
Targeted to prisoners							Y			
Targeted to young population			Y (18-35 years old)					Y (14-25 years old)		
Targeted to consumers									Y	
Targeted to physicians and school teachers										Y
Brochures		Y					Y		Y	Y (in preparation)
Posters		Y						Y		
Advertisements			Y (on homepage and bus stops)							
Newspapers/magazines	Y	Y	Y					Y	Y	
Radio	Y (interview with dermatologists)							Y		
TV	Y (interview with dermatologists)		Y					Y		
Events held		Y					Y			Y
Internet and social networks		Y	Y		Y			Y (Facebook)	Y	

Table 3.10: Possible additional information campaigns.

Possible additional information campaigns	BE	CZ	DE	ES	FR	IT	NL	SE	SI	SK
Targeted to tattoo artists	Y			Y	Y	Y	Y	Y	Y	Y
Targeted to potential clients	Y		Y	Y		Y		Y	Y	Y
Targeted to general public	Y	Y	Y	Y	Y	Y	Y		Y	Y
Targeted to students	Y (15-18 years old)								Y (in primary schools)	

Six national competent authorities (DE, ES, FR, NL, SE and SK) informed that they had no information regarding the risk perception of the general and/or the tattooed population. Italy considered that the risk perception is based on the awareness of prior aggravating medical conditions and of possible risks, among which those of infections and disease transmission. No one indicated, as important elements on which risk perception can be based on, the awareness of risks related to 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.

According to the replies received from Belgium, Italy and Slovenia, the main sources of information for people, on which risk perception is based on, are parents, friends, media and internet. None of the respondents indicated physicians as consultation source for potential clients to form an opinion and, strangely, the same happened for tattooists, which on the contrary are mentioned in the literature as being the ones mostly taken into consideration.

To the question on whether clients of parlours had to sign a compulsory prior informed consent, Italy replied yes, seven Member States replied no (CZ, DE, DK, FI, FR, NL and SE); even though in Finland, The Netherlands and Sweden it is recommended and in France compulsory information needs to be given to the clients. The information available or requested in the prior informed consent includes: an inquiry about client's health status, possible risks/complications, post-treatment instructions, what to do in case of problems and removal treatments, comprising risks.

Table 3.11: Risk perception in terms of awareness and sources of information.

Awareness of	BE	IT	SI
Prior aggravating medical conditions		Y	
Possible risks		Y	
Risks of infection and disease transmission		Y	Y
Sources of information			
Parents		Y	Y
Friends			Y
Media	Y	Y	Y
Internet	Y	Y	Y

Table 3.12: Information provided or requested in the prior informed consent.

	BE	ES	FI	IT	NL	SI
Inquiry about client's health status	Y	Y	Y		Y	
Possible risks/complications	Y	Y	Y	Y	Y	Y
Post-treatment instructions	Y		Y	Y	Y	Y
What to do in case of problems	Y (sometimes)		Y			
Removal treatments, including risks			Y			Y

3.5.2. Literature

Generally, considering the increasing prevalence of tattooing, particularly among youths, authors agree on the need of proper information related to tattoo/PMU-related risks.

For instance, Mudedla [98] highlighted the need to warn the public, tattoo artists, ink and pigment manufacturers and health care professionals about potential for non-tuberculous mycobacterium skin infections after tattooing. Carney [19] pointed out the necessity to organise information campaigns to raise awareness about the danger of transmitting blood borne infections, such as HCV, regardless of the venue of placement. To limit the risk of hepatitis transmission, Jafari [48] considered essential educational programs for tattoo parlour owners and tattoo artists, as well as regular and unscheduled inspection of tattoo parlours. In their opinion, information campaigns should be targeted to young people and prisoners, representing the population most likely to get tattoos and with the highest prevalence of hepatitis C, respectively. Furthermore, they considered tattoo artists should be obliged to keep records of their clients and to report any adverse effects related to tattoos to health authorities. Young people were identified as the most important target of information campaigns also by the Belgian Superior Health Council [71], who noted that not only adverse health effects linked to tattoos, but also to their removal should be explained. In their internet survey in German-speaking countries (sample 3411 tattooed participants), Klügl [18] reported that 37% of respondents declared to have been informed about the content and the safety of the tattoo colorants by their tattooists; however 41% were disinterested in the chemicals injected in their skin. Moreover, surprisingly about 33% of participants considered safe the injection of tattoo colorants in the human body, despite the fact that websites of public authorities, such as the German Federal Institute for Risk Assessment (BfR) and the US Food and Drug Administration (FDA), did not state this.

In the literature only few papers consider risk perception in relation to tattoo/PMU practices and usually these studies considered the risk perception related to body art practices, including also piercing.

As reported in Table 3.13, six studies were conducted in Italy [99-104] on young high school or university students, in various cities and regions, one in Canada [105] on high school students and one in Denmark [106] on a representative sample of Danish population. They were all based on anonymous questionnaires usually related to demographics, knowledge of health risks and personal experience with tattooing and body piercing.

The tattoo prevalence was in the range of 6.3-31.7%. When reported, the mean age at first tattoo was below 18 years old and the percentages of adolescents who got a tattoo before 15 and 18 years old were 32% in the Canadian survey and 48% in the Cegolon's paper, respectively. The prevalence of young people interested in getting a tattoo was in the range 25-57%.

36-90% of respondents declared to be aware of infectious risks related to body art practices (considering both piercing and tattooing), however the percentages of those able to identify hepatitis B and C viruses and HIV among the transmittable agents were much lower (3.5-60%) in particular for hepatitis, thus supporting the idea that information campaigns are needed.

In general, non-infectious risks associated to body art practices were less known that the infectious ones and the level of awareness ranged from 26 to 65%. Again, a more in-deep analysis of this knowledge in the Italian studies showed that only 2-5% of respondents were able to identify allergies, bleeding and cysts as non-infectious risks.

The tattooists or piercers were reported as being the main source of information on possible risks, followed by another person and the informed consent, which was signed by 7-31% of Italian respondents. Unpublished data from 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. Apart from the high school students in Naples, interviewed by Gallè [101, 102], in general a high percentage of students, both high school and university, referred to an authorised operator to get their body art practiced (66-90%) and more than 70% observed the use of sterile/disposable instruments.

Complications were reported in 7-23% of cases among the pupils having at least one body art modification. It has to be highlighted that in the survey conducted by Quaranta [103] a significant percentage (9%) of people who got their body art practiced by an authorised centre developed complications.

Table 3.13: Risk perception related to body art practices.

	2006, Deschesnes	2010, Cegolon	2010, Sidoti
Based on	anonymous questionnaire	anonymous questionnaire	anonymous questionnaire
Sample	2145 high school students	4277 secondary school students	1200 undergraduate university students
Country	Canada (Quebec)	Italy (Veneto region)	Italy
Tattoo prevalence	7.7%	6.3%	31.7%
Mean age at first tattoo	32.1% before 15 years old	48% before 18 years old	
Interested in getting a tattoo		47.2%	53.1% (M) - 39.4% (F)
Aware of health risks associated to body art practices			
Aware of infection risks related to body art practices		54.4%	36.5%
Able to identify hepatitis B and C viruses and HIV among the transmittable agents			
Able to identify tetanus among the transmittable agents			
Aware of non-infectious risks associated to body art practices			26%
Able to identify allergies, bleeding and cysts as non-infectious risks			
Informed about the risks before undergoing the practice			
Source of information - tattooist or piercer			
Source of information - another person			
Source of information - informed consent			
Signed informed consent			
Body art practiced by an authorised operator	90.4% for their first tattoo	63.5% considered it important	
Observed the use of sterile/disposable instruments			
Knowledge of hygienic norms		72.3%	
Complications			
Seek medical advice in case of infections		73.6% in case of complications	

	2011, Gallè		2011, Quaranta
Based on	anonymous questionnaire	anonymous questionnaire	anonymous questionnaire
Sample	9322 high school students	3610 university students	1598 university freshmen
Country	Italy (Naples)	Italy (Naples)	Italy (Bari and Naples)
Tattoo prevalence	11.3%	24.5%	10%
Mean age at first tattoo	14.8 years	17.6 years	17.5 years
Interested in getting a tattoo	42.5%	25.3%	
Aware of health risks associated to body art practices	24.7%	57.1%	
Aware of infection risks related to body art practices	79%	87%	90%
Able to identify hepatitis B and C viruses and HIV among the transmittable agents	3.5%	15%	34% - 38% - 60%
Able to identify tetanus among the transmittable agents			34%
Aware of non-infectious risks associated to body art practices	46%	59%	65%
Able to identify allergies, bleeding and cysts as non-infectious risks	2%	3%	
Informed about the risks before undergoing the practice			74%
Source of information - tattooist or piercer	main source	main source	52%
Source of information - another person			29%
Source of information - informed consent			19%
Signed informed consent	6.9%	15.3%	31%
Body art practiced by an authorised operator	27%	66.5%	
Observed the use of sterile/disposable instruments	27.9%	70.3%	
Knowledge of hygienic norms			
Complications	7%	7%	13% (9% of those treated in an authorised centre)
Seek medical advice in case of infections			

	2012, Gallè	2013, Majori	2013, DK YouGov
Based on	anonymous questionnaire	anonymous questionnaire	anonymous questionnaire
Sample	3132 university freshmen	2712 high school students	
Country	Italy (Bari)	Italy (Veneto region)	Denmark
Tattoo prevalence	19.8%	6.4%	20% (15-34 yeals old)
Mean age at first tattoo	17 years		37% before 20 years old
Interested in getting a tattoo	38.7%	57.4%	34% (15-34 yeals old)
Aware of health risks associated to body art practices			
Aware of infection risks related to body art practices	84.4%	81.6%	
Able to identify hepatitis B and C viruses and HIV among the transmittable agents	4.1%	50%	34% hepatitis, 29% HIV
Able to identify tetanus among the transmittable agents			
Aware of non-infectious risks associated to body art practices	59.2%		
Able to identify allergies, bleeding and cysts as non-infectious risks	5.4%		48% allergic reactions, 37% chronic swelling, 35% chronic inflammation, 33% photosensitivity, 19% cancer, 15% lump/node formations
Informed about the risks before undergoing the practice			
Source of information - tattooist or piercer	57.9%		45% no information, 11% chronic swelling, 11% allergy, 6% chronic inflammation, 4% lump/node formations, 2% cancer
Source of information - another person			
Source of information - informed consent			
Signed informed consent			
Body art practiced by an authorised operator	72.1%	88%	
Observed the use of sterile/disposable instruments	75.9%		
Knowledge of hygienic norms			
Complications	23.4% (58.7% non-infectious)		12% (7% ptotosensitivity, 3% chronic swelling, 1% hepatitis, 1% allergy, 1% lump/node formations, 1% chronic inflammation)
Seek medical advice in case of infections		30%	16% (in case of complications)

3.6. Data gaps and research needs

In this chapter, the answers of the ten national authorities who replied to the section of the questionnaire related to data gaps and research needs are reported, together with some suggestions found in the literature and raised during the discussions held in the meetings of the Consumer Safety Network Subgroup on Tattoos and Permanent Make-up.

Table 3.14: Data gaps and research needs.

	CZ	DE	DK	ES	FR	IT	NL	SE	SI	SK
Better knowledge of inks' chemical composition and purity, ingredients' conc.		Y			Y	Y	Y	Y	Y	
Better knowledge of inks' physical-chemical properties		Y			Y	Y	Y	Y	Y	
Data on normal usage of and exposure to tattoo inks		Y	Y (particularly amount applied)	Y	Y	Y	Y		Y	
Development and harmonization of analytical methods		Y	Y	Y	Y	Y (1-heavy metals, 2-AA, 3-PAH and BaP)	Y		Y	
Guidelines for risk assessment	Y	Y		Y	Y		Y	Y	Y	Y
Risk assessment of ingredients										
Absorption level, distribution, metabolism and excretion (ADME) of ingredients		Y		Y	Y		Y (top priority)		Y	
Derivation of No Adverse Effect Level (NOAEL)		Y			Y		Y		Y	
Phys-chem properties of ingredients										
Purity		Y			Y		Y	Y	Y	
Impurities		Y			Y		Y	Y	Y	
Auxiliary ingredients		Y			Y		Y		Y	
Stability		Y			Y		Y		Y	
Cleavage products		Y			Y		Y	Y	Y	
Toxicological data on ingredients										
Corrosion		Y			Y		Y		Y	
Irritation		Y			Y		Y		Y	
Phototoxicity		Y			Y		Y		Y	
Immunotoxicity		Y			Y		Y		Y	
Genotoxicity *in vitro*		Y			Y		Y		Y	
Photo-genotoxicity		Y			Y				Y	

A majority of the respondents considered that, to improve the safety of tattoo/PMU inks and practices, guidelines for risk assessment are needed, as well as the development and harmonisation of analytical methods, the collection of data on normal usage of and exposure to tattoo inks (surface of application, body area, colour, population group), a better knowledge of inks' physical-chemical properties (stability and shelf-life), chemical composition, purity, and ingredients' concentration. The lack of harmonised analytical methods had been already flagged in the report on the first Work Package of the project [2] and in the questionnaire, the Italian experts proposed the following priority list: 1) heavy metals; 2) aromatic amines; 3) polycyclic aromatic hydrocarbons and benzo(a)pyrene. The Danish authority highlighted the importance to collect data on the amount of inks applied for tattoos and PMU.

Considering the risk assessment of tattoo/PMU inks' ingredients, about half of the respondents identified the following data gaps and research needs: absorption level, distribution, metabolism and excretion (ADME) of ingredients, including pigments migration in the body and photo-degradation (top priority in the opinion of the Dutch authority); the derivation of No Adverse Effect Level (NOAEL); data on the purity level, impurities, auxiliaries, stability (to UV, laser, enzymes, bacteria) and cleavage products of ingredients; data on the following properties of ingredients: corrosion, irritation (skin, mucous membranes), phototoxicity, immunotoxicity (sensitisation, photo-sensitisation, etc.), *in vitro* genotoxicity, including test of cleavage products and photo-genotoxicity.

In addition, the German experts highlighted the urgent need of research on biokinetics of tattoo inks and their ingredients in the human body, opinion shared also by the Belgian authority, who referred also to nanoparticles [71]; while the Dutch experts mentioned the necessity to collect more information about adverse reactions linked to tattoo application and removal.

Kluger [68], in its paper on tattoos, inks and cancer concluded that, based on the literature review, the association between tattoos and skin tumours seems to be coincidental, as no direct cause/effect relationship could be established. At the same time, they noted the lack of large-scale studies of clinical and epidemiological factors and pointed out the necessity of *in-vivo* data on the skin concentrations of tattoo ingredients, impurities and by-products, both in the cancer area and in an unaffected area of the tattoo that contains the same colour. Similar opinions were expressed by Mataix [43] and the Belgian Superior Health Council [71] and by a number of experts of the CSN-STPM.

The need to investigate more the fate of tattoo ingredients in the skin and in the body in general, also under solar and laser light was mentioned by several authors (for example, [52, 71]) and experts during the meetings of the CSN-STPM.

4. Conclusion

The conclusions of the third Work Package of the EC project "Tattoos - Permanent Make-up" are described in the following paragraphs.

Adverse health effects linked to tattoo/PMU applications

As the popularity of tattoos and PMU has increased over the last decades, a wide range of health effects are nowadays encountered by physicians. The real incidence of tattoo reactions is currently unknown. The difficulty of precise counting stems also from the lack of differentiation between serious complications and mild discomfort "complaints", experienced by a highly variable proportion of tattooed individuals, up to 67% due to the subjectivity of the matter.

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

At short term, together with the inevitable wound healing process taking place already during the tattoo session, immediate complications may arise within days in the case of skin bacterial infection, or within weeks, for allergic reactions. In the long run persistent inflammatory reactions and delayed hypersensitivity with chronic dermatosis may appear, sometimes after years or decades.

Transmissible diseases through tattoo/PMU application involve mainly inoculation of bacteria or more rarely viruses. The frequency of cutaneous infections by pathogenic germs remains unknown, though it has been estimated at up to 5% of the tattoo-recipients, and even rarer in case of PMU applications, which usually take place in professional settings. Skin infections can generally be avoided by improving inks sterility and hygiene conditions of tattoo parlours.

The vast majority of tattoo/PMU complications are allergic reactions and poorly understood coincidental diseases implying autoimmunity, which are by definition unpredictable, except in susceptible patients, and which may show long latency (up to decades) after having placed the tattoo/PMU. So far, the risk of (skin) tattoo-induced tumours has been neither proved nor excluded. For both of these groups of diseases no straightforward causal relationship has been so far established with regard to ink composition and further studies, i.e. epidemiological screenings, would be needed to fill the data gaps.

Tattoos may interfere with medical procedures, such as PET and MRI. Sustained cutaneous reaction (“burn”) has been reported in patients going through Magnetic Resonance Imaging possibly due to the presence of ferromagnetic metallic compounds in tattoo pigments. Epidural anaesthesia could be complicated in case of tattoos in the spinal area.

Patients with prior cardiac, blood or autoimmune pathologies should be prevented from tattooing in order to avoid potential severe complications.

Adverse health effects linked to tattoo/PMU removal

Nowadays, the most commonly used technique for tattoo/PMU removal is based on the use of Q-switched lasers, which underwent significant technological improvements in the last decades. Despite this progress, temporary and permanent side effects still occur, especially when incorrect parameters are applied. Among these, acute aseptic inflammations, blistering, crusting, erythema and pinpoint bleeding have been described in the literature. At the same time, other risks such as allergic reactions and pigmentary disorders (hypo/hyperpigmentation and paradoxical darkening) have also been reported. The potential toxicity of the photo degradation products of ink ingredients and impurities, in particular of pigments, have been highlighted by several authors as possible cause of adverse reactions, also systemic, even though no clear cause/effect link has been proved so far. Correct information about possible side-effects and

impossibility to completely remove certain tattoos, because of colours and/or skin type, should be provided to the patients before initiating the removal treatment and possibly even before applying the tattoo.

Henna-based temporary tattoos: outline and side effects

Even though henna-based temporary tattoos are not made by injection, but the henna based preparation is applied on the skin surface, they may entail some risks, especially the ones made with black henna, such as contact dermatitis and hypertrophic/keloid scars. P-phenylenediamine, which is contained in black henna, is a powerful antigen potentially inducing immediate and/or delayed allergy type reactions.

Experience with the CoE ResAP(2008)1

The majority of the respondent national authorities considered that based on their experience the recommendations of the CoE ResAP(2008)1 should be updated to improve the level of safety of tattoo/PMU inks and practices. Practical suggestions regarding chemical, labelling, hygiene/sterility and other requirements were collected through the answers to a questionnaire and discussions during the meetings of the Consumer Safety Network Subgroup Tattoos and Permanent Make-up. Proposals ranged from the inclusion in the negative lists of additional substances, like aromatic amines, colorants and impurities, 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 of complications.

Additional proposals by Member States' authorities included the need of establishing Good Manufacturing Practices for tattoo/PMU inks, of controlling products sold on the internet, of establishing compulsory training for tattooists. Moreover, suggestions to enhance the collaboration among manufacturers and authorities and to ban "backyard" tattooing were also mentioned by several Member States.

Risk perception and communication

Concerning risk communication, among the respondents, nine Member States reported that information campaigns had been organised either at national or at local level in their countries. There was a general consensus on the benefit of additional information campaigns targeted to tattoo artists, potential clients and general public, with a particular emphasis on the young population. Similar conclusions can be found in the literature.

Currently the information on risk perception comes from the tattooist (possibly via an informed consent form), or is received through parents or friends, or read in mass media and internet. A number of surveys targeting students evidenced a general knowledge of infectious risks related to body art practices (considering both piercing and tattooing) in the range 36-90%, which decreased to 3.5-60% when more specific questions about transmittable agents were asked. Similarly, non-infectious risks associated to body art practices were indicated by 26-65% of students, with only 2-5% having a more precise knowledge of them.

Data gaps and research needs

The following data gaps and research needs were identified by the majority of experts:

- guidelines for risk assessment of tattoo/PMU products;
- harmonised analytical methods;
- data on normal usage of and exposure to tattoo inks;
- better knowledge of inks' physical-chemical properties, chemical composition, purity, and ingredients' concentration.

Experts also noted that to successfully carry out a toxicological assessment of tattoo/PMU inks, several data are missing, such as the ones on absorption level, distribution, metabolism and excretion (ADME) of ingredients, including pigments

migration in the body and photo-degradation, No Adverse Effect Level (NOAEL), as well as chemical and toxicological properties of ingredients.

Moreover, many authors suggested conducting prospective cohort studies in order to investigate the correlation between tattoos and skin carcinogenesis.

References

1. CoE Council of Europe, *Resolution (2008)1 on requirements and criteria for the safety of tattoos and permanent make-up*, 2008. p. 1-10, https://search.coe.int/cm/Pages/result_details.aspx?ObjectID=09000016805d3dc4.
2. Piccinini, P., et al., *Safety of tattoos and permanent make-up. Compilation of information on legislative framework and analytical methods*, 2015: JRC Report, EUR 27394 EN, doi:10.2788/542617. p. 1-446, http://bookshop.europa.eu/en/safety-of-tattoos-and-permanent-make-up-compilation-of-information-on-legislative-framework-and-analytical-methods-pbLBNA27394/.
3. 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/.
4. Kluger, N., *Contraindications for tattooing*, in *Tattooed Skin and Health, Curr. Probl. Dermatol.*2015, Serup J., Kluger N., Bäumler W. (eds). Basel, Karger. p. 76-87.
5. Harris Poll and S. Braverman, *One in five U.S. adults now has a tattoo.* February 23, n.22, 2012: p. 1-7. http://www.theharrispoll.com/health-and-life/One_in_Five_U_S__Adults_Now_Has_a_Tattoo.html.
6. Brady, B.G., et al., *Self-reported adverse tattoo reactions: a New York City Central Park study.* Contact Dermatitis, 2015. **73**(2): p. 91-9.
7. Papameletiou, D., et al., *Recommendations for regulatory action in the EU on the safety of tattoos, body piercing and of related practices in the EU*, 2003: JRC Final Report. p. 1-31.
8. CoE Council of Europe, *Resolution (2003)2 on tattoos and permanent make-up*, 2003. p. 1-8, https://search.coe.int/cm/Pages/result_details.aspx?ObjectId=09000016805df8e5.
9. Council_of_Europe, *Resolution (2008)1 on requirements and criteria for the safety of tattoos and permanent make-up*, 2008. p. https://wcd.coe.int/ViewDoc.jsp?id=1254065.
10. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.* J. Clin. Epidemiol., 2009. **62**(10): p. 1006-12.
11. Papameletiou, D., et al., *Risks and health effects from tattoos, body piercing and related ptractices*, 2003: JRC Report. p. 1-30.
12. Kluger, N., *Cutaneous complications related to permanent decorative tattooing.* Expert Rev Clin Immunol, 2010. **6**(3): p. 363-71.
13. Desai, N.A. and M.L. Smith, *Body art in adolescents: paint, piercings, and perils.* Adolesc Med State Art Rev, 2011. **22**(1): p. 97-118.
14. Serup, J., *The Spectrum of Clinical Complications of Tattoos In Europe.* Presentation at the Meeting of the Consumer Safety Network Sub-Group Tattoos and PMU, Ispra, Italy. 09.11.15, 2015.
15. Serup, J., Harrit N., Linnet J.T., Møhl B., Olsen O., Westh H. , *Tattoos – Health, Risks and Culture. With an introduction to the "seamless prevention" strategy.* Copenhagen: The Council on Health and Disease Prevention. 2015. 1-156. http://www.vidensraad.dk/sites/default/files/vidensraad_tatovering_engelsk_0.pdf.

16. Hutton Carlsen, K. and J. Serup, *Photosensitivity and photodynamic events in black, red and blue tattoos are common: A 'Beach Study'.* J Eur Acad Dermatol Venereol, 2014. **28**(2): p. 231-7.

17. Høgsberg, T., K.H. Carlsen, and J. Serup, *High prevalence of minor symptoms in tattoos among a young population tattooed with carbon black and organic pigments.* J. Eur. Acad. Dermatol. Venereol., 2013. **27**: p. 846-852.

18. Klügl, I., et al., *Incidence of health problems associated with tattooed skin: a nation-wide survey in German-speaking countries.* Dermatology, 2010. **221**(Copyright (C) 2015 U.S. National Library of Medicine.): p. 43-50.

19. Carney, K., et al., *Association of tattooing and hepatitis C virus infection: a multicenter case-control study.* Hepatology, 2013. **57**(6): p. 2117-23.

20. Wenzel, S.M., et al., *Adverse reactions after tattooing: review of the literature and comparison to results of a survey.* Dermatology, 2013. **226**(2): p. 138-47.

21. De Cuyper, C., *Cosmetic and Medical Applications of Tattooing*, in *Dermatologic Complications with Body Art, Tattoos, Piercings and Permanent Make-Up*2010, De Cuyper, C., Pérez-Cotapos, M.L. (Eds.). Heidelberg, Springer. p. 53-60.

22. Kaatz, M., P. Elsner, and A. Bauer, *Body-modifying concepts and dermatologic problems: tattooing and piercing.* Clin Dermatol, 2008. **26**(1): p. 35-44.

23. Laumann, A.E. and A.J. Derick, *Tattoos and body piercings in the United States: a national data set.* J Am Acad Dermatol, 2006. **55**(3): p. 413-21.

24. Antoszewski, B., et al., *Are body piercing and tattooing safe fashions?* Eur J Dermatol, 2006. **16**(5): p. 572-5.

25. Klügl, I., et al., *Incidence of health problems associated with tattooed skin: a nation-wide survey in German-speaking countries.* Dermatology, 2010. **221**(1): p. 43-50.

26. Serup, J., K. Hutton Carlsen, and M. Sepehri, *Tattoo complaints and complications: diagnosis and clinical spectrum*, in *Tattooed Skin and Health, Curr. Probl. Dermatol.*2015, Serup J., Kluger N., Bäumler W. (eds). Basel, Karger. p. 48-60.

27. Høgsberg, T., et al., *Microbial status and product labelling of 58 original tattoo inks.* J Eur Acad Dermatol Venereol, 2013. **27**(1): p. 73-80.

28. Health-Canada, *Market survey of tattoo dyes: microbial testing*, 2011: Activity Report June 20.

29. Baumgartner, A. and S. Gautsch, *Hygienic-microbiological quality of tattoo- and permanent make-up colours.* Journal fur Verbraucherschutz und Lebensmittelsicherheit, 2011. **6**(3): p. 319-325.

30. Armstrong, M.L., S. DeBoer, and F. Cetta, *Infective endocarditis after body art: a review of the literature and concerns.* J Adolesc Health, 2008. **43**(3): p. 217-25.

31. Tse, D., S. Khan, and S. Clarke, *Bacterial endocarditis complicating body art.* Int J Cardiol, 2009. **133**(1): p. e28-9.

32. Kluger, N., *Acute complications of tattooing presenting in the ED.* Am J Emerg Med, 2012. **30**(9): p. 2055-63.

33. Laux, P., et al., *A medical-toxicological view of tattooing.* The Lancet, 2016. **387**(10016): p. 395-402.

34. De Cuyper, C., *Complications of cosmetic tattoos*, in *Tattooed Skin and Health, Curr. Probl. Dermatol.*2015, Serup J., Kluger N., Bäumler W. (eds). Basel, Karger. p. 61-70.

35. Bedard, B., et al., *Tattoo-Associated Nontuberculous Mycobacterial Skin Infections — Multiple States, 2011–2012.* CDC MMWR Morb Mortal Wkly Rep, 2012. **61**(33): p. 653-656. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6133a3.htm?s_cid=mm6133a3_w.

36. Conaglen, P.D., et al., *Systematic review of tattoo-associated skin infection with rapidly growing mycobacteria and public health investigation of a cluster in Scotland, 2010.* Euro Surveill, 2013. **18**(32): p. 20553.

37. CDCP, C.f.D.C.a.P., *Tattoo-associated nontuberculous mycobacterial skin infections--multiple states, 2011-2012.* Morbidity and Mortality Weekly Report, 2012. **61**(33): p. 653–6.

38. Belgian_Superior_Health_Council, *In this scientific policy advisory report the Superior Health Council wants to reduce the complications and increase the safety of the products and the techniques of tattooing and of permanent and semi-permanent make-up.* 2015(N°8893).

39. CDCP, C.f.D.C.a.P., *Methicillin-resistant Staphylococcus aureus skin infections among tattoo recipients—Ohio, Kentucky, and Vermont, 2004–2005.* Morbidity and Mortality Weekly Report, 2006. **55**: p. 677–678.

40. Kluger, N., *Body art and pregnancy.* Eur J Obstet Gynecol Reprod Biol, 2010. **153**(1): p. 3-7.

41. Brajac, I., et al., *Delayed onset of warts over tattoo mark provoked by sunburn.* J Eur Acad Dermatol Venereol, 2005. **19**(2): p. 247-8.

42. Tohme, R.A. and S.D. Holmberg, *Transmission of hepatitis C virus infection through tattooing and piercing: a critical review.* Clin Infect Dis, 2012. **54**(8): p. 1167-78.

43. Mataix, J. and J.F. Silvestre, *Cutaneous adverse reactions to tattoos and piercings.* Actas Dermosifiliogr, 2009. **100**(8): p. 643-656.

44. Juhas, E. and J.C. English, 3rd, *Tattoo-associated complications.* J Pediatr Adolesc Gynecol, 2013. **26**(2): p. 125-9.

45. Mariano, A., et al., *Role of beauty treatment in the spread of parenterally transmitted hepatitis viruses in Italy.* J Med Virol, 2004. **74**(2): p. 216-20.

46. Urbanus, A.T., et al., *People with multiple tattoos and/or piercings are not at increased risk for HBV or HCV in The Netherlands.* PLoS One, 2011. **6**(9): p. 14.

47. Jafari, S., et al., *Tattooing and the risk of transmission of hepatitis C: a systematic review and meta-analysis.* Int J Infect Dis, 2010. **14**(11): p. e928-40.

48. Jafari, S., et al., *Tattooing and risk of hepatitis B: a systematic review and meta-analysis.* Can J Public Health, 2012. **103**(3): p. 207-12.

49. Thum Chee, K. and A. Biswas, *Inflammatory complications related to tattooing: a histopathological approach based on pattern analysis.* Am J Dermatopathol, 2015. **37**(1): p. 54-66.

50. Kaur, R.R., W. Kirby, and H. Maibach, *Cutaneous allergic reactions to tattoo ink.* J Cosmet Dermatol, 2009. **8**(4): p. 295-300.

51. DK EPA Danish Ministry of the Environment - Environment and Protection Agency (EPA) and E. Jacobsen, *Chemical Substances in Tattoo Ink - Survey of chemical substances in consumer products (Kortlægning af kemiske stoffer i forbrugerprodukter) no. 116*, 2012. p. 1-155, http://www2.mst.dk/Udgiv/publications/2012/03/978-87-92779-87-8.pdf.

52. Serup, J. and K. Hutton Carlsen, *Patch test study of 90 patients with tattoo reactions: negative outcome of allergy patch test to baseline batteries and culprit*

inks suggests allergen(s) are generated in the skin through haptenization. Contact Dermatitis, 2014. **71**(5): p. 255-63.

53. Kluger, N., et al., *Tattoos: natural history and histopathology of cutaneous reactions.* Ann Dermatol Venereol, 2011. **138**(2): p. 146-54.

54. Caucanas, M., et al., *Dermatological complications of temporary and indelible tattoos.* Ann Dermatol Venereol, 2011. **138**(2): p. 161-2.

55. Hutton Carlsen, K. and J. Serup, *Patients with tattoo reactions have reduced quality of life and suffer from itch: Dermatology Life Quality Index and Itch Severity Score measurements.* Skin Res Technol, 2015. **21**(1): p. 101-7.

56. Mortimer, N.J., T.A. Chave, and G.A. Johnston, *Red tattoo reactions.* Clin Exp Dermatol, 2003. **28**(5): p. 508-10.

57. Simunovic, C. and M.M. Shinohara, *Complications of decorative tattoos: recognition and management.* Am J Clin Dermatol, 2014. **15**(6): p. 525-36.

58. Setlur, J., *Cosmetic and reconstructive medical tattooing.* Curr Opin Otolaryngol Head Neck Surg, 2007. **15**(4): p. 253-7.

59. Sweeney, S.A., et al., *Perforating granulomatous dermatitis reaction to exogenous tattoo pigment: a case report and review of the literature.* Am J Dermatopathol, 2013. **35**(7): p. 754-6.

60. Kluger, N., *Cutaneous infections related to permanent tattooing.* Med Mal Infect, 2011. **41**(3): p. 115-22.

61. Wood, A., et al., *Necrobiotic granulomatous tattoo reaction: report of an unusual case showing features of both necrobiosis lipoidica and granuloma annulare patterns.* Am J Dermatopathol, 2014. **36**(8): p. 152-155.

62. Marchesi, A., et al., *Tattoo ink-related cutaneous pseudolymphoma: a rare but significant complication. Case report and review of the literature.* Aesthetic Plast Surg, 2014. **38**(2): p. 471-8.

63. Ostheimer, T.A., et al., *Tattoo-associated uveitis.* Am J Ophthalmol, 2014. **158**(3): p. 637-43.

64. Kluger, N., *Sarcoidosis on tattoos: a review of the literature from 1939 to 2011.* Sarcoidosis Vasc Diffuse Lung Dis, 2013. **30**(2): p. 86-102.

65. Ali, S.M., A.C. Gilliam, and R.T. Brodell, *Sarcoidosis appearing in a tattoo.* J Cutan Med Surg, 2008. **12**(1): p. 43-8.

66. Selim, A., et al., *Scar sarcoidosis: a case report and brief review.* Cutis, 2006. **78**(6): p. 418-22.

67. Lo Schiavo, A., et al., *Granulomatous dysimmune reactions (sarcoidosis, granuloma annulare, and others) on differently injured skin areas.* Clin Dermatol, 2014. **32**(5): p. 646-53.

68. Kluger, N. and V. Koljonen, *Tattoos, inks, and cancer.* Lancet Oncol, 2012. **13**(4): p. e161-8.

69. Kazandjieva, J. and N. Tsankov, *Tattoos: dermatological complications.* Clin Dermatol, 2007. **25**(4): p. 375-82.

70. Baker, P.A., O.D. G.J., and I.U. Khan, *Dermatofibrosarcoma protuberans arising in a decorative tattoo.* Sarcoma, 2005. **9**(1-2): p. 37-41.

71. CSS Conseil Supérieur de la Santé (BE), *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. [In this scientific policy advisory report the Superior Health*

Council wants to reduce the complications and increase the safety of the products and the techniques of tattooing and of permanent and semi-permanent make-up.], 2015: N°8893. p. 1-59, http://www.health.belgium.be/internet2Prd/groups/public/@public/@shc/documents/ie2divers/19101885.pdf.

72. Pérez-Cotapos S, M., C. De Cuyper, and L. Cossio, *Tattooing and Scarring: Technique and Complications*, in *Dermatologic Complications with Body Art, Tattoos, Piercings and Permanent Make-Up*2010, De Cuyper, C., Pérez-Cotapos S, M.L.(eds). Heidelberg, Springer. p. 29-41.
73. Ross, J.R. and M.J. Matava, *Tattoo-induced skin "burn" during magnetic resonance imaging in a professional football player: a case report.* Sports Health, 2011. **3**(5): p. 431-4.
74. Karsai, S., G. Krieger, and C. Raulin, *Tattoo removal by non-professionals--medical and forensic considerations.* J Eur Acad Dermatol Venereol, 2010. **24**(7): p. 756-62.
75. Klein, A., et al., *An Internet-based survey on characteristics of laser tattoo removal and associated side effects.* Lasers Med Sci, 2014. **29**(2): p. 729-38.
76. Eklund, Y. and T. Rubin Agneta, *Laser tattoo removal, precautions, and unwanted effects*, in *Tattooed Skin and Health, Curr. Probl. Dermatol.*2015, Serup J., Kluger N., Bäumler W. (eds). Basel, Karger. p. 88-96.
77. Bernstein, E.F., *Laser tattoo removal.* Semin Plast Surg, 2007. **21**(3): p. 175-92.
78. Wenzel, S., M. Landthaler, and W. Bäumler, *Recurring mistakes in tattoo removal. A case series.* Dermatology, 2009. **218**(2): p. 164-7.
79. Sweeney, S.M., *Tattoos: a review of tattoo practices and potential treatment options for removal.* Curr Opin Pediatr, 2006. **18**(4): p. 391-5.
80. Körner, R., et al., *Histopathology of body art revisited - analysis and discussion of 19 cases.* J Dtsch Dermatol Ges, 2013. **11**(11): p. 1073-80.
81. Kent, K.M. and E.M. Graber, *Laser tattoo removal: a review.* Dermatol. Surg., 2012. **38**: p. 1-13.
82. Handley, J.M., *Adverse events associated with nonablative cutaneous visible and infrared laser treatment.* J Am Acad Dermatol, 2006. **55**(3): p. 482-9.
83. Kirby, W., et al., *Treatment of large bulla formation after tattoo removal with a q-switched laser.* J Clin Aesthet Dermatol, 2010. **3**(1): p. 39-41.
84. Verhaeghe, E., *Techniques and Devices Used for Tattoo Removal*, in *Dermatologic Complications with Body Art, Tattoos, Piercings and Permanent Make-Up*2010, De Cuyper, C., Pérez-Cotapos S, M.L. (eds). Heidelberg, Springer. p. 91-105.
85. Aberer, W., J.E. Snauwaert, and U.-M. Render, *Allergic Reaction to Pigments and Metals*, in *Dermatologic Complications with Body Art, Tattoos, Piercings and Permanent Make-Up.* 2010, De Cuyper, C., Pérez-Cotapos, M.L. (Eds.) Heidelberg, Springer. p. 61-89.
86. Khunger, N., A. Molpariya, and A. Khunger, *Complications of Tattoos and Tattoo Removal: Stop and Think Before you ink.* J Cutan Aesthet Surg, 2015. **8**(1): p. 30-6.
87. Williams, N., *Quality-switched laser tattoo removal.* JAAPA, 2014. **27**(6): p. 53-6.
88. Pohl, L., K. Kaiser, and C. Raulin, *Pitfalls and recommendations in cases of laser removal of decorative tattoos with pigmented lesions: case report and review of the literature.* JAMA Dermatol, 2013. **149**(9): p. 1087-9.

89. Freedman, J.R., et al., *Picosecond lasers: the next generation of short-pulsed lasers.* Semin Cutan Med Surg, 2014. **33**(4): p. 164-8.

90. EC, *European Parliament and Council Regulation No 1223/2009 of 30 November 2009 on Cosmetic products.* Official Journal of the European Union, L 342/59, 22.12., 2009: p. 59-209. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009R1223&rid=1.

91. Kazandjieva, J., I. Grozdev, and N. Tsankov, *Temporary henna tattoos.* Clin Dermatol, 2007. **25**(4): p. 383-7.

92. de Groot, A.C., *Side-effects of henna and semi-permanent 'black henna' tattoos: a full review.* Contact Dermatitis, 2013. **69**(1): p. 1-25.

93. Calogiuri, G., et al., *Allergic reactions to henna-based temporary tattoos and their components.* Immunopharmacol Immunotoxicol, 2010. **32**(4): p. 700-4.

94. Kneilling, M., et al., *Para-phenylenediamine-specific lymphocyte activation test: a sensitive in vitro assay to detect para-phenylenediamine sensitization in patients with severe allergic reactions.* Exp. Dermatol., 2010. **19**(5): p. 435-441.

95. EC, *Commission Directive 95/45/EC of 26 July 1995 laying down specific purity criteria concerning colours for use in foodstuffs.* OJ L 226, 22.9., 1995: p. 1-41. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31995L0045&rid=62.

96. EC, *European Parliament and Council Regulation No 1272/2008 of 16 December 2008 on Classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.* OJ L 353, 31.12.2008, 1-1355, , 2008.

97. Cui, Y., et al., *Photodecomposition of Pigment Yellow 74, a pigment used in tattoo inks.* Photochem Photobiol, 2004. **80**(2): p. 175-84.

98. Mudedla, S., E.E. Avendano, and G. Raman, *Non-tuberculous mycobacterium skin infections after tattooing in healthy individuals: A systematic review of case reports.* Dermatol Online J, 2015. **21**.

99. Cegolon, L., C. Xodo, and G. Mastrangelo, *Characteristics of adolescents who expressed indifference or no interest towards body art.* BMC Public Health, 2010. **10**: p. 605.

100. Sidoti, E., G. Paolini, and G. Tringali, *Prevalence, knowledge, attitudes and practices towards body art in university students: body art as an indicator of risk taking behaviours?* IJPH, 2010. **7**(4): p. 386-394.

101. Gallè, F., et al., *Awareness of health risks related to body art practices among youth in Naples, Italy: a descriptive convenience sample study.* BMC Public Health, 2011. **11**: p. 625.

102. Gallè, F., et al., *Body art practices and health risks: young adults' knowledge in two regions of southern Italy.* Ann Ig, 2012. **24**(6): p. 535-42.

103. Quaranta, A., et al., *Body piercing and tattoos: a survey on young adults' knowledge of the risks and practices in body art.* BMC Public Health, 2011. **11**(774): p. 1471-2458.

104. Majori, S., et al., *Piercing and tattooing in high school students of Veneto region: prevalence and perception of infectious releated risk.* J Prev Med Hyg, 2013. **54**(1): p. 17-23.

105. Deschesnes, M., S. Demers, and P. Fines, *Prevalence and characteristics of body piercing and tattooing among high school students.* Can J Public Health, 2006. **97**(4): p. 325-9.

106. YouGov and What_the_world_thinks, *DK-Internet survey.* http://mst.dk/media/mst/67352/Unders%C3%B8gelsen%20er%20gennemf%C3%B8rt%20af%20analyseinstituttet%20YouGov.pdf, 2013.

107. Høgsberg, T., B.M. Thomsen, and J. Serup, *Histopathology and immune histochemistry of red tattoo reactions.* Skin Res Technol, 2015. **29**(10): p. 12213.

108. Fors, R., et al., *Lifestyle and nickel allergy in a Swedish adolescent population: effects of piercing, tattooing and orthodontic appliances.* Acta Derm Venereol, 2012. **92**(6): p. 664-8.

109. Wenzel, S.M., et al., *Permanent make-up colorants may cause severe skin reactions.* Contact Dermatitis, 2010. **63**(4): p. 223-7.

110. De Cuyper, C., *Permanent makeup: indications and complications.* Clin Dermatol, 2008. **26**(1): p. 30-4.

111. Teixeira, M., et al., *Contact allergy to para-phenylenediamine in a permanent eyelash dye.* Contact Dermatitis, 2006. **55**(2): p. 92-4.

112. Bhardwaj, S.S., R.T. Brodell, and J.S. Taylor, *Red tattoo reactions.* Contact Dermatitis, 2003. **48**(4): p. 236-7.

113. Huynh, T.N., D. Jackson Jeremy, and T. Brodell Robert, *Tattoo and vaccination sites: Possible nest for opportunistic infections, tumors, and dysimmune reactions.* Clin Dermatol, 2014. **32**(5): p. 678-84.

114. Bocca, B. and G. Forte, *The epidemiology of contact allergy to metals in the general population: prevalence and new evidences.* Open Chem. Biomed. Methods J., 2009. **2**: p. 26-34.

115. Forte, G., et al., *Quantification of sensitizing metals in tattooing pigments by SF-ICP-MS technique.* Open Chem. Biomed. Methods J., 2009. **2**: p. 42-47.

116. Gulati, S., A. Jain, and M. Sattari, *Tattooing: A potential novel risk factor for iliopsoas abscess.* World J Clin Cases, 2014. **2**(9): p. 459-62.

117. Falsey, R.R., et al., *Cutaneous inoculation of nontuberculous mycobacteria during professional tattooing: a case series and epidemiologic study.* Clin Infect Dis, 2013. **57**(6): p. e143-7.

118. Kennedy, B.S., et al., *Outbreak of Mycobacterium chelonae infection associated with tattoo ink.* N Engl J Med, 2012. **367**(11): p. 1020-4.

119. Hauri, U., et al., *Determination of carcinogenic aromatic amines in dyes, cosmetics, finger paints and inks for pens and tattoos with LC/MS.* Travaux de chimie alimentaire et d'hygièneMitteilungen aus Lebensmitteluntersuchung und Hygiene., 2005. **96**(5): p. 321-335.

120. Giulieri, S., et al., *Outbreak of Mycobacterium haemophilum infections after permanent makeup of the eyebrows.* Clin Infect Dis, 2011. **52**(4): p. 488-91.

121. Rodriguez-Blanco, I., et al., *Mycobacterium chelonae infection associated with tattoos.* Acta Derm Venereol, 2011. **91**(1): p. 61-2.

122. Bechara, C., et al., *Mycobacterium abscessus skin infection after tattooing: first case report and review of the literature.* Dermatology, 2010. **221**(1): p. 1-4.

123. Drage, L.A., et al., *An outbreak of Mycobacterium chelonae infections in tattoos.* J Am Acad Dermatol, 2010. **62**(3): p. 501-6.

124. Mortensen, S.K., et al., *Specific determination of 20 primary aromatic amines in aqueous food simulants by liquid chromatography-electrospray ionization-tandem mass spectrometry.* J Chromatogr A, 2005. **1091**(1-2): p. 40-50.

125. Porter, C.J., J.W. Simcock, and C.A. MacKinnon, *Necrotising fasciitis and cellulitis after traditional Samoan tattooing: case reports.* J Infect, 2005. **50**(2): p. 149-52.

126. Fowler, J. and D. Mahlen Steven, *Localized cutaneous infections in immunocompetent individuals due to rapidly growing mycobacteria.* Arch Pathol Lab Med, 2014. **138**(8): p. 1106-9.

127. Soran, A., et al., *A tattoo pigmented node and breast cancer.* Bratisl Lek Listy, 2014. **115**(5): p. 311-2.

128. dos Santos Gon, A., L. Minelli, and M.C. Meissner, *Keratoacanthoma in a tattoo.* Dermatol Online J, 2009. **15**(7): p. 9.

129. Kürle, S., K.W. Schulte, and B. Homey, *Accumulation of tattoo pigment in sentinel lymph nodes.* Hautarzt, 2009. **60**(10): p. 781-3.

130. Lee, J.-S., et al., *Basal cell carcinoma arising in a tattooed eyebrow.* Ann Dermatol, 2009. **21**(3): p. 281-4.

131. Goldenberg, G., et al., *Eruptive squamous cell carcinomas, keratoacanthoma type, arising in a multicolor tattoo.* J Cutan Pathol, 2008. **35**(1): p. 62-4.

132. Birnie, A.J., K. Kulkarni, and S. Varma, *Basal cell carcinoma arising in a tattoo.* Clin Exp Dermatol, 2006. **31**(6): p. 820-1.

List of abbreviations and definitions

Abbreviations

AA	Aromatic Amines
ADME	Absorption, Distribution, Metabolism and Excretion
BCC	Basal Cell Carcinoma
BfR	German Federal Institute for Risk Assessment
CoE	Council of Europe
CMR	carcinogenic, mutagenic and reprotoxic
CSN	Consumer Safety Network
EFTA	European Free Trade Association
EC	European Commission
EU	European Union
GMP	Good Manufacturing Practices
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
KA	Keratoacanthoma
MCV	Molluscum Contagiosum Virus
MRI	Magnetic Resonance Imaging
MRSA	Methicillin-Resistant Staphylococcus Aureus
MS	Member States
NDELA	N-nitrosodiethanolamine
NOAEL	No Adverse Effect Level
NTM	Non Tuberculosis Mycobacteriae
PAA	Primary Aromatic Amines
PAH	Polycyclic Aromatic Hydrocarbons
PAO	Period of maximum durability After Opening
PEH	Pseudoepitheliomatous Hyperplasia
PET	Positron Emission Tomography
PIRL	picosecond infrared laser
PG	Pyoderma Gangrenosum
PMU	Permanent Make-Up
PPD	Para-phenylendiamine
ResAP	Resolution (Council of Europe)
STPM	Subgroup Tattoos and Permanent Make-up
QS laser	Quality Switched laser
SCC	Squamous Cell Carcinoma

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 tumour 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) [57].

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 [65] 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” [14].

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 [14].

Uveitis: eye inflammation affecting the middle layer of tissue in the eye wall (uvea).Uveitis 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)

List of figures

List of tables

Annex I

Meeting of the Consumer Safety Network Subgroup Tattoos and Permanent Make-up (9th November 2015)

Minutes of the meeting of the Consumer Safety Network Subgroup Tattoos and Permanent Make-up (Ispra (VA), Italy – 9th November 2015)

The agenda and list of participants are reported in Tables A and B, respectively.

Welcome and adoption of the agenda

Mrs Piccinini, chair of the meeting and project responsible, EC DG JRC IHCP, welcomed the country delegates and stakeholders. She reminded all present the aims and different Work Packages of the project. After each participant's introduction, the agenda of the meeting was approved as written, with the addition of a presentation from Mr. Michel, TIME, in case the schedule would allow it under data gaps and research needs.
Mrs Blass Rico, EC DG JUST, informed about the EC decision of not going ahead with an emergency measure for tattoo/PMU inks under Article 13 of the General Product Safety Directive (GPSD) 2001/95/EC. She explained that the Commission has decided to address the chemical safety of tattoo inks under the chemical legislation and stressed the high expectations from the output of this project, which is still very important and will be considered for any future actions. She acknowledged the work of this group and thanked all for their support, reminding that the final conclusions from the project shall be very well supported and solid.

Adoption of the minutes

The minutes of the meeting of the Consumer Safety Network Sub-group Tattoos and Permanent Make-up, held on 20th April 2015, were adopted without any modification.

The spectrum of clinical complications of tattoos in Europe (Jørgen SERUP, Bispebjerg University Hospital, DK)

Mr Serup summarised the various types of health concerns linked to tattoos/PMU in a pyramide scheme containing in decreasing order of severity and increasing order of frequency: 1) disablement, death; 2) medical complications; 3) the complaints (for which generally people do not see a doctor); and 4) the absence of any problem, which represents the majority (+/- regrets). An impressive photo gallery of complications coming from his professional experience very well illustrated the various range and grade of tattoo complications that have been observed and treated.
In studies [16, 17] of a tattooed sample of 298 people, the prevalence of mild tattoo symptoms or complaints reached 42% (with 44% concerning photosensitivity). Mr Serup reported similar medical complications based on his recent statistical data from the "Tattoo Clinic": 405 patients with 493 tattoo complications between October 2008 - June 2015. The diagnoses showed the hereunder distribution:

- 12% infections
- 57% non infectious
- 9% psycho-social
- 16% miscellaneous
- 6% techniques and treatment failures

Mr Serup concluded by noting that the majority of the complications (40.5%) were multiple and by mentioning that, in his opinion, tattoo inks cause not more than 9-15% of the observed problems. He also put forward the question of determining to what extent a possible regulation could change the pyramid distribution levels.

Literature - Adverse health effects linked to tattoo/PMU Practices (Sazan PAKALIN, EC DG JRC)

Mr Pakalin summarised the data published in the literature from 2004 on by briefly introducing the methodology followed and by describing the following complications.
Infections: these types of complications depend on human and technical factors (hygiene), the bacterial infections are mainly local, they include skin infections and non-tuberculous mycobacterial infections.

Allergy: allergic reactions are the most common reaction to tattoo pigments and occur predominantly with red inks; they can provoke acute inflammation (heals within 1-3 weeks), delayed hypersensitivity reactions and eczema or allergic contact dermatitis.
Coincidental diseases: this group includes reactivation of underlying dermatoses within a tattoo (isomorphic phenomenon), sarcoidosis (autoimmune disease) and cancers/malignancy risks possibly due to the potential carcinogenicity of some ink contaminants (AA, PAH, heavy metals), and photo degradation products of ingredients, such as pigments. It was highlighted that the casual link between tattooing and the development of malignant tumours has not been proven.
Mr Pakalin also mentioned the possible disruption of diagnosis and medical procedures by tattoo applications and the possible adverse health effects of tattoo removal.

Questionnaires - Adverse health effects linked to tattoo/PMU practices (Laura CONTOR, EC DG JRC)

Mrs Laura Contor described the two questionnaires developed for competent authorities and dermatologists and reported back on the responses. 5 Member States answered to the health effects section of the questionnaires and 19 dermatologists reported on the health complications. Among these, 15 dermatologists see less than 15 patients/year showing tattoo complications and 4 examine up to 150. This low number of replies limits the interpretation of the results of the exercise.
The outcome showed that some common pre-conditions affecting complications include metal allergy and atopic or contact dermatitis. The top three skin symptoms ranked as being frequent/common and severe were reported as being skin ulceration, swelling and pain. Removals were reported as involving pain as common reported effect. The respondents also agreed that adverse effects were more frequently encountered in black and red colours.

Questionnaires - Proposals to improve the safety of tattoo/PMU practices (Paola PICCININI, EC DG JRC)

Mrs. Piccinini reviewed the questionnaire responses of the competent authorities regarding the experience with the CoE ResAP(2008)1. 14 replies were received. To improve the safety of tattoo/PMU inks and practices, some modifications of the recommendations laid down in the CoE ResAP(2008)1were considered necessary. Member states proposed some modifications to the negative lists of chemicals in the CoE ResAP(2008)1.
These changes covered aromatic amines (AA), such as adding aniline, 2-ethoxyaniline and N-isopropyl-N'-phenyl-1,4-phenylendiamine, and introducing concentration limits for AA. A number of pigments were suggested to be added to the negative list of colorants. Proposals for establishing a limit value for nickel and modifying limits for benzo[a]pyrene, Ni, As, Co, Pb and Sb were also put forward. Regarding labelling requirements, a number of respondents agreed on adding the period of durability after opening (PAO), the quantitative composition of inks and the storage conditions. A register of complaints was felt necessary, as well as compulsory training for tattooists.

Questionnaires – Data gaps and research needs (Paola PICCININI, EC DG JRC)

Among the proposals provided in the questionnaires, Mrs Piccinini highlighted the most cited data gaps: data on normal usage of and exposure to tattoo inks, guidelines for risk assessment of tattoo/PMU products, data needed to carry out the risk assessment and development and harmonisation of analytical methods.

Literature and questionnaires – Risk communication and perception (Paola PICCININI, EC DG JRC)

Mrs Piccinini reviewed the questionnaires responses on risk communication and perception. Nine countries informed that they had organised information campaigns, either at national or local level, using means such as brochures, newspapers/magazines and internet/social networks to communicate with tattoo artists, potential clients, the

general public, young people, students, physicians and school teachers. Respondents agreed on the fact that additional information campaigns would be beneficial.
In the opinion of national authorities and several authors in the literature, risk perception seems to be based on the information received by the tattooist, another person (either parents or friends), the informed consent, or what is available in the media and internet. In addition, some papers estimated the level of knowledge of possible health risks among students. In general, infectious risks were better known that non-infectious ones, even though the level of knowledge was in many cases only superficial. These evidences support the need of further additional information campaigns.

Discussions on health effects

Cancer

Discussions took place around the levels of evidence for skin cancer and/or systemic cancer. Mr Fiala (ANEC) recommended being cautious before stating there is evidence that tattoos do not cause cancer. Ms. De Cuyper, Belgium Superior Health Council, noted that 50 cases of skin cancer related to tattoos were reported, but no data exists regarding systemic cancer. Mr Serup highlighted that in the last century black pigments, probably containing PAH, were used and no problems were evidenced. Mrs Blume, BfR (DE), commented that carcinogenic substances in tattoo inks might induce cancer inside the body if they become systematically available; that it could be difficult, however, to demonstrate a causal link between a given tattoo ink ingredient and internal cancer, because the human body is exposed to a variety of carcinogenic substances throughout lifetime. Mr Pakalin noted that some substances do not have a safe threshold.

Hepatitis

Mr Renzoni, Superior Health Institute (IT), mentioned that Italy shows the highest prevalence of hepatitis in the Mediterranean area. In an epidemiological study performed by the Italian Surveillance System (SEIEVA), between 2010-2014, in the age group of 15 to 54 years old, 10.3% of patients newly infected with HCV, and 4.8% of those infected with HBV had placed a tattoo within 6 months prior to the hepatitis onset.
The report indicates a strong association, albeit no formal causal relationship, between the two events. Mr Bergström, Sweden Registered Tattoo artists, informed that in Sweden public health inspectors had identified 40 cases of hepatitis related to tattoo practices during the last 3-4 years, all from home tattooing, probably due to low hygiene conditions. Mr Serup noted that it might be worth to have a specialist in infectious diseases examine this matter further.

Colours

According to Mrs De Cuyper, the health effects related to the red colour were under reported in the literature. Mr Michel, TIME (DE), considered that nowadays the complications related to the red colour are not due to the presence of mercury as in the past, but to some organic pigment, especially photo reactive pigments.

Regulations

Mrs Bjerregaard Lerche, Danish EPA, supported by Mr Fiala, commented that two worlds co-existed: the clinical world with the physicians and the regulatory world with a more preventive approach where regulations are based on effects in animals. Both need to be considered and mentioned in this description; at present the clinical side is very big while the other approach is not so well covered. According to Mrs. De Cuyper, it is needed to divide the issues in 1) procedures (infections) and materials (sterility) to be addressed by the CEN guidelines and 2) toxicity, carcinogenicity, allergy to be addressed by this CSN subgroup to identify the problematic ingredients and impurities that could be taken into account by regulatory action to eliminate the risky substances.

Data collection

This tattoo health effect field is new for dermatologists and clinicians, no prior education exists, and no solid diagnosis can be made due to the lack of knowledge and limited experience. Mr Serup stated that the replies to the questionnaires collected and the literature review are not enough to reflect the real picture. In his opinion, infections by staphylococcus are far more common than the Köbner phenomenon or the mycobacteria.

Mrs. De Cuyper added that usually minor symptoms are dealt with by the client himself, the pharmacist, the tattooist or the general practitioners. The number of consulted dermatologists does not provide a reliable picture of all complications.
Mr Baeumler, University of Regensburg (DE), believed that the data acquisition was the problem, more information is needed from dermatologists and physicians and data from more than 1000 patients should be collected to have reliable statistics. Focus should be put on infections, allergies and foreign body reactions and the identification of the right questions would be challenging. Currently, not enough reliable information is available and there is the need of a reliable reporting system.
Mr Serup agreed with the existence of data gaps and lack of knowledge and considered important to focus on clinical problems more than on ink composition. He would be in favour of a registry where doctors would be obliged to report tattoo complications like what already exists in Sweden regarding cancer and occupational diseases. He considered that this is a Member States task and that the RAPEX system does not collect adverse health reactions but actions taken by the Member States on dangerous inks on the market.
The registry of adverse reactions should be made mandatory to be effective according to Mrs Lerche. Mrs Verdier, French National Safety Agency of medicine and health products, complemented this information explaining the vigilance system put in place in France since 2008. A notification form is filled in when adverse health effects are observed, however, despite this obligation adverse health effects are usually under reported and the register does not allow any client-ink traceability. So far, 37 side-effects were reported and many questions about the process or the removals were raised.
Mr Bäumler believed that the reporting system should concentrate on a short list of most common problems and focus on hospitals/dermatologists that would volunteer to complete an on-line questionnaire for input in a data base, thus forming a reporting network. The advantages would be the voluntary/dedicated basis of the exercise, the reduction of under-reporting, and a professional outcome with a medical diagnosis, avoiding self-reporting and biased reports.
In Mr Bäumler's opinion, it will probably take some years before a reliable information collection system on adverse health effects could be put in place, therefore he considered that, in parallel, attention should be paid to what can be addressed already, i.e. black inks without PAH, ban the red pigment 22 that causes most of the adverse effects among the 20-25 red pigments available, ensure hygiene and sterility measures.
German and Danish experts agreed that there are enough data and information to act, as shown by the Member States where there are national legislation on tattoo inks; that the focus should be on further collaboration and each part involved in the tattoo activities assuming their responsibility towards safety.

Allergy

Mr Serup proposed a possible study using the skin sample collection he has gathered from the allergic patients. The skin samples could be tested for the identification of inks ingredients that could be linked to the triggering of the allergic reaction. Mr Serup asked the possibilities for EU funding of such study. The limitation of this proposal, highlighted by Mrs Lerche, was that allergies are very-much individual-dependant. Nevertheless, Mrs Lerche supported the need for further data on released substances after cleavage and on removal products, as well as investigation of the biopsies in allergic skins.

Discussions on safety improvements

Chemicals

Experts were in favour of specifying concentration limits for the aromatic amines that should not be contained in tattoo/PMU products according to the CoE ResAP(2008)1 and some proposed to include additional AAs in the negative lists. Similarly, various pigments were mentioned as possible candidates for the negative list. In the opinion of the manufacturers' representatives, pigment green 7 should not be prohibited as there are not better substitutes available. It was pointed out that some of the candidates for the negative lists should already not be used in tattoo/PMU products as they are classified as CMRs in the CLP regulation or they are listed either in Annexes II or IV

(column g) of the cosmetic regulation. It was generally agreed that any change in the list of substances or on the recommended limits should be based on solid data and duly justified.
When the proposal for a positive list of colorants was discussed, Mr Renzoni noted that such a list requires preparing accurate risk assessment dossiers.

Adverse effect/complaint registers

Experts agreed on the usefulness of a register of complaints. Mrs Kisacova, Public Health Authority of the Slovak Republic, believed that this register would improve the public and tattooist knowledge.

Pre-marketing

In the questionnaires, pre-marketing authorisation of inks was supported by 5/9 countries. Germany considered that compulsory safety assessment should be made by manufacturers, importers or the person responsible for placing the product on the market. For the manufacturers and tattooists associations, it is very important to ensure that the ingredients reported on the bottle are reliable and complete.

Hygiene practices

The participants were briefed about the activities of the European Committee for Standardization (CEN)/Technical committee 435 on tattooing services, which is preparing guidelines on hygiene for tattooists (including tools) and clients. The document, to be completed in 2016, will address topics such as sterilisation of tools, disinfection of premises, possible vaccination of tattooists, informed consent form, training programmes, age limits, etc. Tattooists associations, together with dermatologists and other stakeholders are involved in the exercise.
The validation of the sterilisation method for inks was considered; however it was highlighted that it would be difficult as it depends on the packaging, product, etc. Mr Michel (TIME) agreed to share a proposal they developed to avoid contamination. Mr Renzoni considered that it is necessary to identify an effective sterilisation method, as the results of microbiological analyses performed show that sealed inks, marketed as sterile, are actually contaminated. Hence, Italy proposed to set up a working group to validate ink sterilisation methods.

Discussions on regulations options

Mrs Piccinini reminded all participants that the aims of this meeting are to come up with recommendations to improve the safety of tattoo/PMU inks and practices based on the lessons learned and experience from the MS. How the conclusions and recommendations would be taken up by the legislator is beyond the remit of this group. The project should establish the state of play, identify the problems and provide suggestions to improve the safety. Mrs Blass Rico reminded that the recommendations in the CoE ResAPs as benchmark used by the Member States to draft their national legislations have been revised by the experts. A representative of the Council of Europe is member of the group although Council of Europe activities are of course beyond the scope of this project. The CoE representative in the meeting acknowledged the usefulness of the discussions and informed that at the next meeting of the Steering Committee on Consumer Safety Products (February 2016) a point to consider the new data made available by this project could be included on the agenda.
Mrs Blass Rico explained that some circumstances have evolved since the project was originally designed in principle linked to a possible emergency measure. A detailed impact assessment is needed for any new legislative proposal: including what is the problem and its size, data on the health costs, what is the prevalence in the population, what are the costs for the manufacturers, etc.
She stressed that pragmatic recommendations and concrete proposals from this project are still very relevant to improve the safety of tattoo and PMU inks.
Germany, Denmark and Belgium experts considered that an EU harmonised measure was needed.
Mr Bergström (Tattoo artists) stressed that the main safety problems are linked to the existence of "black market" of tattoo artists who do not respect hygiene and good practices. The project should recommend addressing the "illegal" practice at EU level. Mr

Michel agreed that national laws will not be sufficient to tackle the problem of home scratchers. He also stressed the difficulties for manufacturers to comply with different national regulations in each country.
Mr Fiala noted that a key outcome of this project could be a recommendation to establish limits, to identify the key PAHs, to gather basic information on toxicity of colorants, to harmonise the classification of sensitisation and, as a next step, establish a positive list. Building on this, Mr Michel – supported by Mrs Hrzenjak, National Laboratory of Health Environment and Food (SI) and Mr Serup – added the need to clarify which limits should be addressed and with which analytical methods.
Mr Bäumler mentioned that the real challenge is to identify the problem, determine its size and increase the awareness. Mr Serup added that manufacturers will not be able to solve the data weaknesses; in the meantime, if the absence of regulation the illegal market will increase. The focus should be to produce solid figures with good research.
During the meeting the majority of participants voiced support for the preparation of a stand-alone legislation on tattoo inks in the EU.

Discussion on data gaps and recommendations

Analytical methods for limit setting

As suggestions were made to modify or set more limits, Mrs Piccinini reminded the lack of analytical methods developed for tattoo inks. Mrs Josefa Barrero, EC DG JRC, added that the limit values needed also to be harmonised and agreed upon.

Guidelines for risk assessment

Mrs Amela Saracevic, Council of Europe (FR), informed the participants that the CoE has finalised a document on guidelines for risk assessment that should be ready during the first quarter of 2016.

Risk perception

The public, in particular the young population, need to be aware of the risks of taking a tattoo and the possible consequences of opting for a backyard tattooist compared to a professional working under good hygienic conditions.

Informed consent

Mr Serup stressed the need for informing the customer in writing, preferably the day before the procedure and including the data regarding possible interfering pre-conditions. Mrs Meisner noted that this step would also protect the tattooist. In addition, according to Mr Serup and Mr Bergström, not only the customers should be registered but also the inks used, to allow tracing back in case of adverse health effects.

Training of tattooists

Mr Bergström considers that most of the infections occur outside the parlour after the tattoo is performed; if both the tattooist and the client are aware of aftercare rules half of the infections would be avoided. The group agreed on the need for training for tattooists at EU and /or national level on hygiene, cross-contamination, storage, inks, adverse effects, skin/body elements but not the artistic/aesthetic part. This is being addressed by the CEN/TC 435.

Follow-up

Participants were invited to:

- send in writing further suggestions regarding recommendations
- comment on presentations, missing points
- identify relevant items to be addressed
- as soon as available, review the report on WP2: State of play and trends in tattoo practices – (a) statistics about practices, (b) ink ingredients & their fate and (c) RAPEX notifications & market surveillance.

The 1st draft of WP3 was expected by the end of 2015: (a) adverse health effects linked to tattoo/PMU applications and removals, (b) assessment and update of the ResAP (2008)1, (c) risk perception and communication and (d) data gaps and research needs.

Next meeting

The final meeting of the project would be held during the first quarter of 2016.

Table A: Agenda of the meeting of the CSN-STPM held on 9th November 2015 at the DG JRC in Ispra (VA), Italy.

CSN Subgroup Tattoos and Permanent Make-up 9 November 2015	
09:00-09:10	**Welcome and adoption of the agenda**
09:10-09:15	**Adoption of the minutes of the CSN-STPM meeting of 15.04.2015**
09:15-09:45	**The spectrum of clinical complications of tattoos in Europe** Jørgen SERUP (Bispebjerg University Hospital)
09:45-10:15	**Literature - Adverse health effects linked to tattoo/PMU practices** Sazan PAKALIN (EC DG JRC)
10:15-10:45	**Questionnaires - Adverse health effects linked to tattoo/ PMU practices** Laura CONTOR (EC DG JRC)
10:45-11:00	Coffee break
11:00-12:30	**Discussion**
12:30-13:30	Lunch at Piccola Mensa
13:30-13:45	**Questionnaires - Proposals to improve the safety of tattoo/PMU practices** Paola PICCININI (EC DG JRC)
13:45-15:00	**Discussion**
15:00-15:15	**Questionnaires – Data gaps and research needs** Paola PICCININI (EC DG JRC)
15:15-15:45	**Discussion**
15:45-16:00	Coffee break
16:00-16:15	**Literature and questionnaires – Risk communication and perception** Paola PICCININI (EC DG JRC)
16:15-16:45	**Discussion**
16:45-17:00	**Conclusions and follow-up**

Table B: List of participants (meeting of the CSN-STPM on 9th November 2015).

Country	National Expert	Affiliation
Belgium	DE CUYPER Christa	Belgian Superior Health Council
Denmark	LERCHE Dorte B.	Danish Environmental Protection Agency
France	VERDIER Cécile	Agence Nationale de sécurité du Médicament et des produits de santé
Germany	BLUME Annegret MEISNER Anke	Bundesinstitut für Risikobewertung Federal Ministry of Food and Agriculture
Italy	RENZONI Alberto	Istituto Superiore di Sanità
Netherlands	DE VRIES-HLAVACOVA Mariana JANSSEN Pjcm	Nederlandse Voedsel- en Warenautoriteit Netherlands National Institute for Public Health and the Environment
Slovak Republic	KISACOVA Janka	Public Health Authority of the Slovak Republic
Slovenia	HRŽENJAK Vesna	National laboratory of health- environment and food
Spain	VIDAL Areses	Agencia Española de Medicamentos y Productos Sanitarios
Sweden	CRONA Magnus	Medical Product Agency
Switzerland	HOHL Christopher	Kantonales Laboratoirum Basel-Stadt
United Kingdom	AXFORD Ian	LGC LTD
Country	**Stakeholders**	**Affiliation**
Austria	FIALA Franz	ASI Consumer Council
Denmark	SERUP Jørgen	Bispebjerg University Hospital
France	SARACEVIC Amela	European Directorate for the Quality of Medicines & HealthCare- Council of Europe
Germany	BAUMLER Wolfgang KEMNER Sina MICHEL Ralf WERNER Alexander	University of Regensburg Tattoo Ink Manufacturers in Europe (TIME) Tattoo Ink Manufacturers in Europe (TIME) H-A-N Haus der Angewandten Naturwissenschaften GmbH
Italy	GIUSEPPIN Eliseo	Associazione tatuatori.it
Italy	ZOPPETTI Marco	Associazione tatuatori.it
Sweden	BERGSTROM Jens	Sweeden Registered Tattoo artists (SRT)
European Commission	**Directorate General**	**Institute and Unit**
BARRERO Josefa BIANCHI Ivana	Joint Research Centre	Institue for Health and Consumer Protection, Chemical Assessment and Testing Unit (Dir I.1)
BLASS RICO Ana Maria	EC DG Justice and Consumers	Dir. E Product and Service Safety
CONTOR Laura PAKALIN Sazan PICCININI Paola	Joint Research Centre	Institue for Health and Consumer Protection, Chemical Assessment and Testing Unit (Dir I.1)

Annex II

Questionnaires

Table A: Questionnaires on adverse health effects for dermatologists.

1. COMPLICATIONS FOLLOWING TATTOO/PMU APPLICATION

1.1 Are you a dermatologist interested in complications linked to tattoos/PMU and do you perform tattoo removals

1.2 How many patients do you see in a year and how many of them have tattoo complications

1.3 What was the interval between the tattoo/PMU application and the onset of symptoms: infectious and non-infectious complications (1 week - > 1 year)

1.4 - 1.5 Amongst all your patients having consulted for tattoo/PMU complications, how frequently did you observe the following cases and how severe were these symptoms:

SKIN
- □ Bleeding
- □ Swelling
- □ Itching
- □ Pain

SKIN
- □ Burning
- □ Crusts
- □ Redness
- □ Skin ulceration

SKIN
- □ Skin ulceration
- □ Wounds
- □ Sun-related lesion (photosensitivity)
- □ Scar tissue
- □ Numbness

SYSTEMIC
- □ Fever
- □ Dizziness
- □ Headache
- □ Nausea
- □ Behavioral changes

1.6 Amongst all your patients having consulted for tattoo/PMU complications, what proportion had previous known allergies and/or skin diseases' history

ATOPIC OR CONTACT DERMATITIS HISTORY
- □ allergy to metals (e.g. nickel, cobalt, chromate)
- □ allergy to para-phenylendiamine (PPD)
- □ allergy to latex

ATOPIC OR CONTACT DERMATITIS HISTORY
- □ allergy to preservatives
- □ allergy to medical drugs

OTHER SKIN DISEASES
- □ urticaria
- □ wart (verruca)
- □ vitiligo

1.7 - 1.8 Amongst all your patients having consulted for tattoo complications, how frequently did you establish the following diagnosis and what was the main histopathologic diagnosis

ALLERGIC SKIN REACTIONS
- □ Contact dermatitis
- □ Plaque elevation
- □ Hyperkeratosis
- □ Ulceration/necrosis
- □ General rash (in allergy to nickel or preservatives)

NON-ALLERGIC INFLAMMATORY REACTIONS
- □ Papulo-nodular inflammatory reactions (typical in black tattoos)
- □ Nodules and granulomas including cutaneous sarcoidosis
- □ tattoo general sarcoidosis

CUTANEOUS INFECTIONS
- □ Bacterial (streptococcus, staphylococcus, pseudomonas, mycobacterium,...)
- □ Viral (herpes papilloma, molluscum etc
- □ Fungal: (Candida albicans, Cutaneous Tinea infection, zygomycosis, sporotrichosis, …)

REGIONAL INFECTIONS
- □ Erysipelas
- □ Abscess

SYSTEMIC INFECTIONS
- □ hepatitis B/C
- □ AIDS
- □ septicaemia

OTHERS
- □ Hypo/hyper pigmentation
- □ Photosensitivity
- □ Urticaria
- □ Lymphoedema and lymph node reaction

TATTOO RELATED TUMOURS
- □ Benign tumours
1. Hyperplastic scar or keloid
2. Keratoacanthoma
3. Other tissue reactions

- □ Malignancies
1. Basal cell carcinoma
2. Squamous cell carcinoma
3. Melanoma
4. Lymphoma

HISTOPATHOLOGICAL DIAGNOSIS
- □ Inflammation only
- □ Lichenoid reaction
- □ Granulomatous reaction
- □ Sarcoid reaction or sarcoidosis
- □ Pseudolymphoma
- □ Pseudoepitheliomatous hyperplasia
- □ Other histologic diagnosis (specify)

2. COMPLICATIONS FOLLOWING TATTOO/PMU REMOVAL

2.1 How many patients do you see in a year and how many of them have tattoo/PMU removal complications

2.2 How frequent are the following health issues (acute/chronic) amongst your patients having undertaken tattoos/PMU removals

ACUTE SYMPTOMS (<1 MONTH)
- ☐ pain
- ☐ blistering
- ☐ pinpoint bleeding
- ☐ crusting
- ☐ urticarial
- ☐ other (specify)

DELAYED SYMPTOMS (>1 MONTH)
- ☐ (photo) allergic reactions
- ☐ scars
- ☐ hyper- and hypopigmentation
- ☐ ink retention and darkening
- ☐ other (specify)

2.3 What was the technique/instrumentation used for the removal

3. CORRELATIONS BETWEEN HEALTH COMPLICATIONS AND CERTAIN TATTOO CHARACTERISTICS/PARAMETERS

3.1 Amongst the patients that consulted you for medical complications, how frequent were the number of tattoos/patient: 1, 2, 3, 4, 5 or >5

3.2 What was the prevalence of the tattoo' sizes: Total tattooed area (cm²)

- ☐ <150
- ☐ 151 – 300
- ☐ 301 – 900
- ☐ >900

3.3 How frequent were the different gender/age characteristics of these patients

3.4 What was the frequency of the various colours of their tattoos/PMU

- ☐ black
- ☐ red
- ☐ orange
- ☐ violet/purple
- ☐ henna colours
- ☐ blue/green/turquoise
- ☐ brown
- ☐ white
- ☐ yellow
- ☐ multi-coloured

3.5 Which localisations of the tattoo/PMU applications were most frequent

- ☐ Legs
- ☐ Arms
- ☐ Trunk
- ☐ Head/neck
- ☐ Genitals
- ☐ Multiple locations

3.6 How frequent were the various tattoo/PMU procedures having provoked the health complications

- ☐ Performed by registered/official tattooist
- ☐ Perfomed by amateur/scratcher tattooist
- ☐ Performed by cosmetic professional
- ☐ Henna application
- ☐ Traumatic tattoo
- ☐ Iatrogenic tattoo (e.g. nipple reconstruction)

4 OTHER INFORMATION THAT COULD BE RELEVANT FOR THE PURPOSE OF THIS SURVEY

Table B: Questionnaires for National Authorities.

1. HEALTH EFFECTS			
1.1 How frequent are the different health issues amongst people having undertaken tattoos/PMU procedures in your country			
Skin Acute side-effects (<1 month) □ infections □ allergic reactions □ edema □ itching □ numbness □ wound healing problems	Skin Persistent side-effects (> 1 month) □ eczema □ psoriasis □ scars □ scleroderma □ photosensitivity □ granulomas □ tumours	Systemic Acute side-effects (<1 month) □ fever □ infections □ dizziness □ headache □ nausea □ behavioural changes	Systemic Persistent side-effects (> 1 month) □ infections □ hepatitis □ AIDS □ psychic problems
1.2 How frequent are the different health issues amongst people having undertaken tattoos/PMU removals in your country			
Immediate skin reactions (< 1 month) □ pain □ blistering □ pinpoint bleeding	Immediate skin reactions (< 1 month) □ crusting □ urticarial	Delayed symptoms (> 1 month) □ (photo) allergic reactions □ local □ systemic	Delayed symptoms (> 1 month) □ scars □ hyper- and hypopigmentation □ ink retention and darkening
1.3 Were the following factors correlated to higher frequency of medical complications			
□ number of tattoos (single vs multiple) □ size of the tattoo □ gender differences (men vs women)	□ customer's age at the time of tattooing (adults vs under18 years old)	□ colour of the tattoo □ localisation of the tattoo (limbs, trunk, head/neck, genitals)	□ localisation of the tattoo (limbs, trunk, head/neck, genitals) □ type of tattooist (professional, scratcher,…)

2. EXPERIENCE WITH THE COUNCIL OF EUROPE RESOLUTION (2008)1			
2.1 Chemicals **Do you have suggestions on what changes in the chemical recommendations would improve the safety of tattoo and PMU inks compared to those currently listed in the CoE ResAP(2008)1**			
CoE ResAP(2008)1 □ CoE ResAP(2008)1, Table 1 □ CoE ResAP(2008)1, Table 2 □ CoE ResAP(2008)1, Table 3	□ Requirements for further organic impurities for colorants used in foodstuffs and cosmetic products as set out in Directive 95/45/EEC □ Ingredients mentioned in Annex II to EC Regulation 1223/2009 on Cosmetics	□ Colorants specified in Annex IV, column g of EC Regulation 1223/2009 on Cosmetics □ CMR substances classified under categories 1A, 1B and 2 in Table 3.1 of Annex VI to EC Regulation 1272/2008 on Classification, Labelling and Packaging	Other proposals on chemical requirements □ Establish positive lists of colorants □ Single lists of chemicals (e.g. colorants, aromatic amines, impurities) instead of cross references lists □ Harmonise analytical methods for testing hazardous chemicals
2.2 Labelling **Do you have suggestions on what changes in the labelling recommendations would improve the safety of tattoo and PMU inks compared to those currently mentioned by the CoE ResAP(2008)1**			
□ PAO (period of durability after opening) □ Quantitative composition of inks (decreasing order of concentration for each ingredient)	□ Date of production □ Conditions of storage □ Type of product: tattoo colour / permanent make-up ink	□ Address of distributor □ Health warnings □ Sterilization method	
2.3 Safety assessment			
2.3.1 Do you think a register of complaints/side effects would improve the safety of tattoo/PMU inks			
2.3.3 How should the safety assessment be performed			
2.3.4 In your opinion would a pre-marketing authorisation for tattoo/PMU inks be necessary to improve the safety			
2.4 Hygiene/sterility **Do you have suggestions on what changes in hygiene/sterility recommendations would improve the safety of tattoo and PMU inks**			
□ Specify the sterilisation method for inks	□ Specify the sterilisation method for tattooing tools	□ Specify the sterilisation method for parlour premises	□ Use of single dose containers vs multidose packaging
2.5 Other suggestions			
□ Control products sold on web □ Enhance collaboration between manufacturers and authorities	□ Ban backyard tattooing □ Establish a list of recognised tattooists	□ Compulsory training for tattooists □ Set up Good Manufacture Practices for inks	

3. RISK COMMUNICATION AND PERCEPTION

3.1 Did you carry out any information campaigns on tattoo/PMU practices in your country

Audience	**Audience**	**Means used**	**Media coverage:**
□ National □ Local	□ Targeted: - tattoo artists/studios - students - military staff - sports clubs - music concerts participants	Printed material: - Brochures - Posters - Advertisements - Commercials - Mix	- Newspapers/Magazines - Radio - Television **Events held** **Internet and social networks**

3.2 Do you think an (additional) information campaign would help to improve the safety of tattoo/PMU

□ Addressed to tattoo artists □ Addressed to potential clients	□ Media campaigns for general public □ Addressed to tattoo artists	□ Addressed to potential clients □ Media campaigns for general public

3.3 Do you have any information as to how the risk on tattoo/PMU procedures is perceived by the general public, or by the tattooed population

□ Awareness of prior aggravating medical condition □ Awareness of possible risks □ Awareness of risks of infection and disease transmission	□ Risks related to the choice of tattooists (professional or not) □ Safety of premises and tools (sterility and hygiene) □ Permanency and risks associated to removal options	What main sources of information was their perception based on: □ Parents □ Friends □ Media	What main sources of information was their perception based on: □ Internet □ Tattooists □ Physicians

3.4 In your country, do the clients of tattoo parlours have to sign a prior informed consent

□ Inquiry about client's health status □ Information on risks, possible complications □ Post-treatment instructions	□ Knowledge on what to do in case of problems □ Information on removal treatments, including their risks

4. DATA GAPS IDENTIFICATION			
4.1 In your opinion what are the data gaps that deserve further research or technical development in order to improve the safety of tattoo/PMU inks and practices			
□ Better knowledge of inks' chemical composition and purity, ingredients' concentration □ Better knowledge of inks physical-chemical properties (stability, shelf-life) □ Data on normal usage of and exposure to tattoo inks (surface of application, body area, colour, population group)	□ Guidelines for risk assessment □ Risk assessment of ingredients: - Data on physical-chemical properties of ingredients (purity, impurities, auxiliary ingredients, stability, cleavage products)	□ Risk assessment of ingredients: - Toxicological data on ingredients (corrosion, irritation, phototoxicity, immunotoxicity, genotoxicity in vitro including test of cleavage products, photo-genotoxicity - Absorption level, distribution, metabolism and excretion (ADME) of ingredients, including pigments migration in the body and photo-degradation - Derivation of No Adverse Effect Level (NOAEL)	□ Development and harmonization of analytical methods for tattoo/PMU inks (please indicate priority)

Annex III

Replies to questionnaires
National Authorities

Table A: Frequency of health issues amongst people having undertaken tattoo/PMU.

HEALTH EFFECTS/TATTOO APPLICATION Q 1.1

	Local															Systemic														
	Acute side-effects							Persistent side-effects								Acute side-effects								Persistent side-effects					
	infections	allergic reactions	edema	itching	numbness	wound healing problems	other	frequency	eczema	psoriasis	scars	scleroderma	photosensitivity	granulomas	tumours	other	frequency	fever	infections	dizziness	headache	nausea	behavioural changes	other	frequency	infections	hepatitis	AIDS	psychic problems	other	frequency
BE	R	R	F	C	E	R		na	E	E	R	N	C	E	N		na	E	E	R	R	R	E		na	E	na	na	na		No data if viral infections are tattoo related
BG																															Only studios are controlled, not able to answer.
CZ																															na
DK																															No systematic official registration of negative effects from tattoos.
ES								N									N								N						N
FI								R									R								N/E						N/E
FR	X	X						F	X								C									X					F
IT																															No register of complaints/side effects thus no data available on frequency.
NL	F	C	E	F	R	E			R	R	C	N	R	C	R			E	E	N	N	N	N			E	N	N	E		
RO																															na
SE																											R				No requirements in legislation to report side-effects coupled to tattooing.
SK																															No information in this area. Only market surveillance for Tattoos notified through RAPEX - according national law.

Frequency: **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent **na**: not available

Table B: Frequency of health issues amongst people having undertaken tattoo/PMU removal.

HEALTH EFFECTS/TATTOO REMOVAL Q 1.2

MS	Immediate skin reactions							Delayed symptoms						
	pain	blistering	pinpoint bleeding	crusting	urticarial	other	frequency	local (photo) allergic reactions	systemic (photo) allergic reactions	scars	hyper- and hypopigmentation	ink retention and darkening	other	frequency
BE	C	R	C	R	E		All symptoms are considered as acceptable after laser tattoo removal	R	E	C	C	C/R		
CZ							na							na
DK														No systematic official registration of negative effects from tattoos or removal from tattoo.
ES	X						N			X			Keloid	R
FI							na			In two cases reported scars and skin burns after applying do-it-yourself-removalcream (Verruxin)				na
FR														No information. More and more questions regarding the status of tattoo removal products (and laser). Real problem because not under the scope of French legislation on tattoos. Real need for a harmonization and a common European status for these products.
NL	F	N	E	C	N			E	E	E	C	C	E	
SE							na							na
SK							na							na

Frequency: **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent **na**: not available

Table C: Correlation between health issues and tattoo characteristics.

HEALTH EFFECTS/CORRELATION Q 1.3									
MS	**Are the following factors correlated to higher frequency of medical complications?**								
	Number of tattoos	**Size of the tattoo**	**Gender differences**	**Customer's age**	**Colour of the tattoo**	**Localisation of the tattoo**	**Type of tattooist**	**Other**	**Frequency**
BE	Yes	Yes	na	na	Yes RED	Yes Exposed areas	Yes Poor quality tattoos and scarring	Little tattooing under the age of 18!	
CZ									na
FI	na	X	na	na	na	na	na		
FR					Yes			Strong suspicions concerning bad practices of tattooist	
NL			Women; propably because women are currently more frequently tattood		Red (following black, blue, yellow)	Possibly sunlight-exposed areas.	na	Sunlight exposure	
SE									na
SK									na

na: not available

Table D: Experience with the Council of Europe Resolution (2008)1 – Chemicals.

EXPERIENCE WITH THE COUNCIL OF EUROPE RESOLUTION (2008/1) Q 2.1a

Chemicals						
MS	**CoE ResAP(2008)1, Table 1**		**CoE ResAP(2008)1, Table 2**		**CoE ResAP(2008)1, Table 3**	
	Suggestion	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**
DE			Add Solvent Yellow 14			
DK	yes + aniline and limit value of 10 ppm				The limit values are unnecessarily restrictive (low). For lead we suggest 10 ppm and for Bap 0,2 ppm.	
ES	Revision	Update: Add aniline	Revision	Evaluate the following dyes, already mentioned for their possible toxicity: 45170.2 CI, CI 11741, CI 12390. CI 73360, CI 12490, CI 11680.	Revision	Update: Nickel content limit.
FI	Should be taken into account		Should be taken into account		Should be taken into account	
IT	Determination of further dangerous aromatic amines: qualitative screening revealed that other aromatic amines were not carcinogenic but toxic (aniline CAS n° [62-53-3], 2-etoxianiline CAS n° [94-70-2] and IPPD CAS n° [101-72-4]) were found in certain samples. Extension of aromatic amines list in Resolution ResAP Introduction of concentration limits for AA in table 1 as provided for Benzo(a)Pyrene in table 3	Table 1 is not complete for different aspects	The use of the following colorants, in addition to the 35 listed in the CoE ResAP (2008)1, should be avoided: Pigment Violet 1; Pigment Yellow 74; Pigment Red 17; Pigment Red 181; Pigment Blue 15; Pigment Green 7; Pigment Red 5; Pigment Yellow 1.	Nowadays there aren't enough evidences for the effective hazard of these colorants listed in the suggestion box. The introduction of these colorants should be done after a verification study	• "Copper (Cu) soluble" to be defined. • Fix a maximum allowed concentration for Ni •Base actual limit on toxicological study • Amend concentration limits for: As: 0.2 ppm; Co: 5.0 ppm (labelling: 'Contains cobalt; may cause an allergic reaction'); Pb: 1.0 ppm; Sb: 1.0 ppm; Ni: 0.5 ppm • As use & quantities different, tattoo colours and PMU inks limits should be differentiated. • Clarify list of single PAH classification for hazard or cancer risk, as provided for BaP (Benzo(a)pyrene).	Some unclear aspects in ResAP lead to controversy and are a problem for producers, importers, retailers and control authorities. General PAHs index does not clarify mixtures composition that need to be classified in terms of hazards and cancer risk.
NL					Nickel PAH Barium	• Nickel's allowed concentration to be clarified as different countries and labs give their own interpretation of this item. When Fe oxides used as pigments, Ni concentration higher. • Specify which PAH have to be chosen. • Barium – in art. 2 BaSO4 specified; not in accordance with Ba requirement of 50 mg/kg.
SI					Nickel (Ni)	Setting maximum allowed concentration based on risk assessment and technical ability

EXPERIENCE WITH THE COUNCIL OF EUROPE RESOLUTION (2008/1) Q 2.1b

MS	Chemicals							
	Requirements for further organic impurities for colorants used in foodstuffs and cosmetic products as set out in Directive 95/45/EEC		Ingredients mentioned in Annex II to EC Regulation 1223/2009 on Cosmetics		Colorants specified in Annex IV, column g of EC Regulation 1223/2009 on Cosmetics		CMR substances classified under categories 1A, 1B and 2 in Table 3.1 of Annex VI to EC Regulation 1272/2008 on Classification, Labelling and Packaging	
	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale
DE							Yes	
DK							Yes	
ES							Include updated website CMR substances in list	To facilitate knowledge and consultation of manufacturers and authorities.
FI			Should be banned in tattoo colours	Is continuously changing. Same level of safety should be required when chemicals are injected into the skin as with chemicals on the skin.		Not relevant as risk is assessed only for skin contact and not inside skin.	Should be banned	The CLP-classification as a CMR substance triggers a lot of consequences in other legislations and should be taken into account in restrictions on tattoo inks
FR	Yes							
IT	Yes				Yes			
NL	(Yes)							

EXPRIENCE WITH THE COUNCIL OF EUROPE RESOLUTION (2008)1 Q 2.1c

MS	Chemicals			
	Establish positive lists of colorants		Single lists of chemicals (e.g. colorants, aromatic amines, impurities) instead of cross references lists	
	Suggestion	Rationale	Suggestion	Rationale
BE	Yes	Safety garantee	Yes	Easier
DE	Yes	Best way to ensure consumer protection; negative lists cannot be exhaustive.	No	Cross references lists mirror the actual state of regulation; otherwise changes in other areas would have to be regularly incorporated into tattoo regulation.
FI	Not easy to establish. Would be good to establish but needs time and ressources	Wide number of ingredients can be carcinogenic according to the WHO		
FR			Yes	Positive lists ideal and more understandable for operators. But needs updating according to other regulations evolution. Given lack of human resources, this option is impossible to follow.
IT	Italy would favourably consider positive lists of colorants, but there are positive elements and negative elements to be taken into account (see Rationale column).	A positive list of colorants means that each substance is associated with a very accurate risk assessment dossier that would be stable over time. But random tests would be needed to check the composition of inks. It is easier that substances not properly investigated, could result to further study toxic or carcinogenic. So the negative list should be periodically updated. Negative lists speed up controls: check label to assess ink composition and absence of banned components. Negative lists allows producer to avoid components that should not be present in the ink formulation.	Yes	
NL	The Netherlands is in favour of an exhaustive list of substances proved safe for this use under specified conditions	List should be supported by safety assessments from competent bodies and harmonised at the European level.		
SE	A EU-COM scientific committé performs the examination of colorants and safe colorants are listed on a positive list	• Easier for companies to check the ingredient list/documentation to make sure their tattoo colors only contain permitted colorants. • The companies would have to invest less time choosing colorants and evaluating their safety, however they must ensure that their tattoo color do not exceed limitations for contaminants found in table 3 Resap2008.	No. Instead we suggest a single positive list of colorants in tattoo legislation instead of reference to appendix IV colorants in regulation (EU) nr 1223/2009 on cosmetics	Companies can easily check forbidden colorants in table 2 Resap2008. But with the current cross reference to appendix IV regulation (EU) nr 1223/2009, such company could be tempted to choose those colorants and think that they are automatically safe to use in tattoo colours. But these colorants are evaluated for cosmetic use and not for injection through the skin. Furthermore, there are no requirements that substances listed in this appendix IV should be re-evaluated once they have been put in such annexes.
SI	Yes	Positive list of colorants based on risk assessment provides more safety	Yes	Would be easier
SK	positive list of colorants	Positive list of colorants better to increase consumer safety		

EXPERIENCE WITH THE COUNCIL OF EUROPE RESOLUTION (2008/1) Q 2.1d

MS	Chemicals			
	Harmonise analytical methods for testing hazardous chemicals		Other	
	Suggestion	Rationale	Suggestion	Rationale
BE	Absolutely		All products forbidden in cosmetics should be banned from tattoo inks and all products (ea preservatives) in tattoo inks should have the same limits of concentration as drugs used for injection in the body	It is logical that products injected in the body should be as safe as food or products in contact with the skin
DE	Yes	Better comparability of results.	Guidance values for technically unavoidable amounts.	Guidance for manufacturers and market surveillance authorities.
DK	Yes		We recommend a safety assessment	
ES	Agree	Need to have harmonized analytical methods to compare results.		
FR			Establishing a European consensus on the status of tattoo removal products.	
IT	More information strongly needed for Table 3 elements: • sample preparation (maximum allowed concentrations for product as such or dry substance; or analysis of part or entire amount of an element present in sample) • can the microwave-assisted acid digestion be applied • How to make extraction for “Copper (Cu) soluble” • PAH and BaP • AA (because the concentration of sodium dithionite (the reductive agent) could influence the AA cleavage from the pigment).	The described unclear aspects in the ResAP are a great problem for producers, importers, retailers and control authorities		
NL	The method of NVWA		According the resolution 2008(1) preservatives should only be used after a safety assessment. Therefore a positive list of conservatives is	
SE	There would be optimal for the analysis of the hazardous chemicals in tattoo inks (powders and solutions) if there are harmonized methods, aimed for this group of product. Further, methods for the determination of the impurities (eg primary aromatic amines, residual organic solvents, softeners like phthalate, heavy metals) of the tattoo inks that are relevant for the safe use of tattoo inks should, if possible, also be harmonized.	The analytical methods that are commonly used for the qualitative and quantitative determination of the hazardous chemicals, mainly aromatic amines, in tattoo inks (eg EN 14362, part 1 , 2 and 3) are aimed for azo colorant in textiles, while the determination of PAHs are often carried out by the ZEK 01.2-08 method GC-MS, which is harmonized by GS - "Geprüfte Sicherheit" mark bodies.		
SI	Yes	Comparability		
SK	Harmonise analytical methods for testing tattoos and PMU	Harmonisation of methods will be helpful for market control activities		

Table E: Experience with the Council of Europe Resolution (2008)1 – Labelling.

LABELLING Q 2.2a

MS	PAO (period of durability after opening)		Quantitative composition of inks (decreasing order of concentration for each ingredient)		Date of production		Storage conditions	
	Suggestion	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**
BE	As for cosmetics		Yes		Yes		Yes	
DE	Yes	Sterility is difficult to maintain after opening; PAO indicates period of safe use after opening.	No	Qualitative composition should be given to inform consumers (as suggested by ResAP 2008).	No	Date of minimum durability suffices (as suggested by ResAP 2008).	Yes	If specific storage conditions are necessary.
DK	Yes		Yes List to begin with "Ingredients"; listed in descending order according to weight when added to ink; concentration < 1% not listed (unless classified as skin sensitiser); use international nomenclature (INCI, EINECS or ELINCS) - if substance not found then ISO or IUPAC names; for dyes use Colour Index (CI) Constitution Numbers and the container's nominal amount (nominal mass or nominal volume)		Yes Wording "May not be used after ..." should be placed before the expiry date clearly stating either 'month and year' or 'day, month and year'.		If necessary, the conditions under which the shelf life can be maintained may be stated.	
ES	In addition to the PAO, include the following sentence: "the sterility of the contents is guaranteed for X applications"	For more safety.	Yes	For added safety and information for users and authorities.	yes		Yes	
FI	Yes		Yes		Yes		Yes	
FR	Present in national legislation		Present in national legislation				Present in national legislation	
IT	Yes		Yes		Yes		Yes	
NL	Yes		Datasheet with concentration of all relevant parameters				Yes	
SI	Yes	Should be supplemented by an indication of conditions which must be satisfied to guarantee the stated PAO					Yes	To provide safe storage after opening
SK	PAO for non-single-use packaging	Irrelevant for single-use packaging			Not required	It depends of form of labelling date of durability, please see Other	Required	It is required for safety of products

LABELLING Q 2.2b

MS	Type of product: tattoo colour/PMU ink		Address of distributor		Health warnings		Sterilization method		Other	
	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale
BE	Yes		Yes		Yes		Yes			
DE	Yes	Consumer information. However, technical differences are small.	No	Name and address of manufacturer, importer or person responsible for placing on the market should be given (as suggested by ResAP (2008)1)	Yes	Useful in case of allergy, if known	No	Guaranteed sterility (as suggested by ResAP 2008).		
DK			The manufacturer's and the importer's (if for resale) company name and address.						The batch number of manufacture or reference to identify the tattoo ink.	
ES	Yes		Yes Address of distributor in the EU and manufacturer if a third country.		Yes			It is not necessary to indicate the manufacturing method		
FI			Yes		Yes				Identification of the manufacturer and a batch number	
FR			Present in national legislation							
IT	The products could be labelled differently	Considering the different use and injected quantities, the products could be separated in two different categories	Address of the person responsible for placing the product on the market		They may be included in a separate document		The declaration of sterility should specify the sterilization method and be accompanied by technical/ analytical documents	It is a useful tool for surveillance authorities	The label should be written in the language of the country in which it is marketed	The label must be easily understood by the final client.
NL			Preferably phone number							
SE	Such labeling requirements could help avoid the usage of inks that is not supposed to be injected like drawing inks	Sweden has noticed that drawing inks are sometimes used by tattooist's for injection even though such colors should not be injected because it endangers consumers health	The Swedish legislation on tattoo colors requires name and address of the manufacturer if outside Sweden	Name and address of the manufacturer is useful during market surveillance (if help is needed from authorities abroad) and when performing Rapex-notification			The Swedish legislation says that a tattoo color is considered sterile if it fulfils European Pharmacopeia about sterility		The Swedish legislation requires that the tattooist gives the following information (printed form or electronically using e-mail) to the consumer immediately after being tattooed: • Name of the tattoo colour • Ingredient list • Batch-number • Name and address of distributor or manufacturer in Sweden + name and address of foreign manufacturer	If doctors / patient / consumers know which colours had been used for injection, they could inform authorities or doctors in the case of side-effects that would then help researchers studying health effects.
SI					Yes	About possible allergic reactions, phototoxicity, other health effects (infection, keloid,..)				
SK			Not required				Not required	Information only relevant for specialists. No list of sterilisation methods for tattoos and PMU.	Date of minimum durability- can be used symbol (sand-glass) which is used for cosmetics and medicines.	For simplification

Table F: Experience with the Council of Europe Resolution (2008)1 – Safety assessment.

	SAFETY ASSESSMENT Q 2.3		
MS	**A register of complaints/side effects would improve the safety of tattoo/PMU inks?**	**How should the safety assessment be performed?**	**Would a pre-marketing authorisation for tattoo/PMU inks be necessary to improve the safety?**
BE	1.It would give a better view on the number of side effects and offer more info for researcher to focus on specific problems. 2. It would give the authorities a better view on the weak points in tattoo parlors, border control, distribution etc		If the requirements are clear and sufficient to guarantee safety and if they are respected by the producers premarketing authorisation is not necessary
CZ	Yes It should be based on the resolution resap(2008)1		
DE	Yes A "tattoovigilance" system would be helpful to track undesirable effects and take appropriate measures.	For each ingredient (helpful, if effect can be traced back to a specific ingredient) and for the final product	A pre-marketing authorisation would guarantee a high level of consumer protection. However, there are still data gaps that need to be filled. A compulsory safety assessment to be commissioned by manufacturers, importers or persons responsible for the placing on the market and performed by qualified persons is a step towards safer products.
ES	Through a form that that could be filled by dermatologists, users, professionals or those responsible for the placing on the market.	Final product	Yes In Spain a process of authorization is required prior to marketing, which includes an evaluation of the safety of products and of labels.
FI	Similar kind of notifications as in Article 23 of the Cosmetics Regulation (SUE notifications)	Final product	NA
FR	Yes Vigilance of tattoo products not specifically addressed by the CoE ResAp 2008. France has established a national vigilance system of tattoo products in 2008 to monitor the risk of side effects from the use of tattoo products that are available on the market.	In the French notification form, it is requested to indicate the composition of the colorants in the product.	No The spirit of the resolution of the Council of Europe and the French legislation, is that the responsibility to place tattoo products on the market is supported by the responsible person.
IT	Yes A register of complaints/side effects is a useful tool to acquire information about the extent and the frequency of complications and side effects. It could be correlated with the inks used, to provide traceability.	Each and final ingredients. The simultaneous presence of more ingredients may give an amplified or a different effect compared to the single ingredient one.	Yes It would improve the safety: the long contact time of the ink in the body could be considered similar to that of implantable devices.
NL	• Stimulation from the consumer side for 'good work practices' • Side effects/complaints should be included in an 'informed consent' form people should sign before taking a tattoo.	Final product	Yes It will probably improve the transparency
SE	• Requirements for reporting side-effects should be discussed before a discussion about a register. • Side-effects could be caused by for example hygiene issues or a harmful tattoo colour. • Even if the tattoo colour fulfils the legislation the consumer might react to the tattoo colour getting a side-effect. • Even if the side-effect is reported it is not easy for the authority to decide what have caused the side effect. • In Sweden also different authorities control the tattoo colours and the hygiene at the tattooist.	Final product	No Authorities should guide companies on how to fulfil the legislation. An pre-marketing approval of tattoo colours would demand a lot of resources, but such authorisation could be financed through fees from the companies.
SI	No But a register of complaints/side effects would improve public and tattoo artist awareness about health risks.	Both (if a register would be set)	Yes If a tattoo/PMU ink is not safe, it is not placed on the market
SK	Reports about serious undesirable effect of inks (e.g. the same way like SUE of cosmetics, can be used IC SMS system (The internet-supported information and communication system for the pan-European market surveillance)	Final product	Yes

Table G: Experience with the Council of Europe Resolution (2008)1 – Hygiene/sterility.

MS	HYGIENE Q 2.4					
	Do you have any suggestion on how to improve safety of tattoo/PMU inks?					
	NO	YES				
		Inks	Tools	Studio	Dose	Other
BE						1.Materials should be sterile. The sterilisation method should be adapted to the material. (ea ink and tools will be sterilised in a different way) 2. single dose units (although the best guarantee for sterility) are utopy and not practical for tattooist; Sterile products and limited duration of use (PAO) is more realistic.
DE					Or multi use containers with a design that ensures that the contents will not be contaminated during the period of use.	
DK		Yes			Yes	
ES		Yes	Yes		In Spain the use of single-dose containers is recommended to ensure the sterility of each application. Multidose containers are accepted for a maxiumum content of 30ml , guaranteeing the sterility of each application.	In Spain tattoo/PMU parlors are regulated by the regional authority. In particular, methods of disinfection and sterilization of instruments are listed .
FI	No					
FR		Yes	Yes	Yes	Yes	
IT		It is necessary to identify the most effective sterilizing method for inks.	It could be referred to the harmonized standards concerning the validation of sterilization methods applicable to medical devices.	Regarding "parlor premises" it should be more appropriate referring to sanitization and disinfection.	preferentially single use, if technically possible.	
SE		The Swedish legislation says that a tattoo color is seen sterile if it fulfils European Pharmacopeia about sterility				
SI	hygiene and sterility recommendations are good, but use of single dose containers should be enhanced because of difficulties in keeping ink sterility after opening					
SK		Yes	Yes	Yes		e.g. Good Application Practices for tattoo artists

Table H: Experience with the Council of Europe Resolution (2008)1 – Other suggestions.

OTHER SUGGESTIONS Q 2.5a														
MS	**Control web sales**		**Collaboration**		**Ban backyard**		**List of recognised**		**Compulsory training for tattooists**		**Set GMP for inks**		**Other**	
	Suggestion	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**	**Suggestion**	**Rationale**
BE	Absolutely	Fakes and unsafe origin	Yes		Yes		Yes		Yes		Yes		Border control	Import in one EU country means free transport allover EU
CZ														More comprehensive and binding
DE	Yes	Market surveillance should include web sales.								In Germany the need for dual vocational training must be presented to the Federal Ministry for Economic Affairs	Yes	Production conditions are essential for safe products.		
ES	Yes	To improve safety	Yes	In Spain there is a close collaboration with manufacturers to register tattoo inks and permanent	Yes	They should be banned as they do not guarantee the proper sanitary conditions			Yes	A certificate issued by regional authorities is required in Spain	Yes	To improve manufacturing conditions		
FI	Difficult due to the limits of jurisdictions and powers of the authorities. Can be done on national level only.		Yes		Qualified yes - Finland already has legislation on safety of the consumer services. Though surveillance of homemade tattoos is nearly impossible.		na		na		Yes			

OTHER SUGGESTIONS Q 2.5b

MS	Control web sales		Collaboration		Ban backyard		List of recognised tattooists		Compulsory training for tattooists		Set GMP for inks		Other	
	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale	Suggestion	Rationale
FR										In France, the regulation indicates that tattoo artists should attend training in hygiene and sanitary. An order of the Minister of Health determines the categories of institutions and organizations authorized by the State representative in the region to deliver this training, and the contents thereof and diplomas accepted by the equity method.	Yes	In France, there is an order regarding the GMP for tattoo products (Arrêté du 15 septembre 2010)		
IT	Harmonisation of surveillance procedures within the EU in order to prevent the sale of fake inks	Problems related with the presence of fake inks of unknown origin on the market.	Yes		See next item		Definition of a uniform professional profile for tattooists. Institution of a national register of licensed tattooists on the basis of an European standard	Protect clients, preventing illegal tattooist and backyard tattoing	Harmonize tattooist training, with the aim to guarantee the same performance and reliability all over EU.	Ensure a minimum level of skill. Ensure uniform criteria for the definition of the professional requirements for tattooists.	Yes		Sterilisation: As the scientific literature on the subject is insufficient, Italy proposes a working group to validate ink sterilization methods and procedures. It is necessary to identify an effective sterilization method.There is no common regulation about age limits. An age limit should be seriously considered at European level. It should be forbidden to perform tattoos under the age of 14. Performing tattoos under the age of eighteen would be possible only with the informed consent of the parents or guardian.	Microbiological analysis show that some sealed inks, marketed as sterile on the label, are contaminated. These results elicit doubts about che effectiveness of the sterilization procedures. Minors do not have a full awareness of the risks.
SE							In Sweden tattoists/PMU-artists have to notify their business to the local authorities. Lists of such companies may be extracted from our 290 local authorities		Sweden think obligatory training regarding hygiene is a good suggestion					
SI	Yes	A the moment there are no control measures for web sales Most problematic tattoo inks and permanent make-up colorants are probably sold via web sites	Yes	Pre - autorisation	Yes	Most health problems are probably associated with backyard tattooing Better control of hygiene and sterility	Yes	Better control	Yes	Better knowledge of tattooists about safe practices	Yes	Good manufacture practices would improve the safety of tattoo and PMU inks		
SK											prepare EN standard			

Annex IV

Replies to questionnaires
Dermatologists

Table A: Complication following tattoo/PMU application.

COMPLICATIONS Q 1.1-1.3

MS	Interest in tattoos/PMU complications	Removals performed	Number of tattoo complications	Number patients/year	Interval between application and onset of symptoms									
					Infectious complications					Non-infectious complications				
					<1w	1w-1m	1m-1y	>1y	Uncertain	<1w	1w-1m	1m-1y	>1y	Uncertain
BE-1	yes	yes	50	6000	<1%	<1%	<1%			10%	10%	20-30%	>30%	
BE-2	yes	no	1	5000										
BE-3	yes	yes	10	2700		50%			50%		30%	30%	30%	
BE-4	yes	yes	2	200										
DE-1	yes	no	10	1200		80%						80%		
DE-2	yes	no	2-6	6000	50%	50%					50%	50%		
DE-3	yes	yes	0	30-50										
DE-4	yes	no	3	6000	70%	30%						50%	50%	
DE-5	yes	yes	15/300	6000		35%	20%		45%	10%	15%	25%	20%	30%
DK-1	yes	no	1-2	10000					X				X	
DK-2	yes		0-1	1200					X					X
DK-3	yes	yes	5	50								X		
DK-4	yes	yes	2-5	50	50%	50%						100%		
DK-5	yes	yes	150+	5000	90%	10%				5%	25%	40%	25%	5%
FI-1	yes	no	na	na	80-90%	10-20%				10%		90%		
NL-1	yes	no	4-5	?		50%	50%				10%	70%	20%	
NL-2	no	no	2	3500									100%	
NL-3	yes	no	75	7500							30%	60%	10%	
SE-1	yes	no	4	2000								50%	50%	

COMPLICATIONS Q 1.4-1.5

Frequency and severity of symptoms observed

Skin

MS	Bleeding		Swelling		Itching		Pain		Burning		Crusts		Redness		Skin ulceration		Wounds		Sun-related lesion		Scar tissue		Numbness	
	F	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**
BE-1	E	L	C	M	F	S	E	M	R	L	R	L	C	M	E	M	F		F		R		E	
BE-2	N		N		N		N		N		N		N		N		N		N		N		N	
BE-3	N		F	M	R	L	E	L	E	L	C	L	C	L	N		N		N		N		N	
BE-4	R	L	C	L	E	L	C	M	C	M	C	L	C	L	R	L	E	L	R	L	R	L	R	L
DE-1	R	L	C	L	C	L	C	L	C	L	C	L	C	L	R	L	E	L	E		C	L	R	L
DE-2	N		F	M	E	M	E	M	E	M	E	M	F	M	E		E		N		E	M	E	M
DE-3																								
DE-4	N		C	M	R	M	E	M	R	M	R	M	R	M	R	M	R	M	R	M	C	M	E	M
DE-5	R	L	F	S	F	S	F	S	F	S	F	M	F	S	C	L	C	M	R	L	C	L	C	L
DK-1	N		C	M	C		N		N		R		C	M	E		E		E		C	M	N	
DK-2	N		C	M	na		na		na		N		C	M	N		N		na		N		na	
DK-3	E	L	C	MS	C	MS	C	M	C	M	C	M	C	M	R	L	C	L	R	M	E	L	N	
DK-4	E	L	F	S	C	S	C	S	C	S	C	M	C	S	R	M	N		E	M	R	M	R	S
DK-5	N		F	M	F	S	C	M	R	L	R	M	F	M	R	S	R	S	F	M	R	M	F	M
FI-1	E	L	F	M	F	M	E	L	E	L	E	L	F	M	E	S	E		C	M	N	L	N	L
NL-1	N		E	L	C	M	R	M	C	M	C	L	N	L	R	L	E	M	R	L	C	L	C	L
NL-2	N		R	M	R	S	N		R	M	R	M	R	M					R	L	E	S		
NL-3	E	L	F	M	F	S	R	S	R	L	C	L	C	L	E	S	C	M	R	L	R	M	E	L
SE-1			R	M	R	S							R	M					E	M	R	M		

MS	Skin – Other: Hypopigmentation		Skin – Other: acute dermatitis		Skin – Other: scaling hyperkeratosis		Skin – Other: Pseudoepitheliomatous hyperplasia		Systemic: Fever		Systemic: Dizziness		Systemic: Headache		Systemic: Nausea		Systemic: Behavioral changes		Systemic – Other: urticaria	Systemic – Other: allergic rash	Systemic – Other: local lymph nod		Systemic – Other: Malaise		Systemic – Other: flu itch
	F	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**G**	**F**	**F**	**F**	**G**	**F**	**G**	**F**
BE-1									E	L	N		N		N		N								
BE-2									N		N		N		N		N								
BE-3									N	N	N	N	N	N	N	N	N								
BE-4	R	L							N		N		N		N		N								
DE-1									N		N		N		N		N								
DE-2			C	S					N		N		N		N		N								
DE-3																									
DE-4									N		N		N		N		N								
DE-5									R	L	R	L	E	L	N	L	E	L							
DK-1									N		N		N		N		N								
DK-2									N		N		N		N		N								
DK-3									N		N		N		N		N								
DK-4									E	L	N		N		N										
DK-5					F	C			R	S	E	M	E	M	E	M	E	L	R	R					
FI-1									N		N		N		N		N				E	L			
NL-1					N				N	L	E	L	R	L	N	L	N	L							
NL-2									E	M													E	M	E
NL-3									N		N		N		N		N								
SE-1							E	S																	

Frequency (F): **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent. Grade (G): **L**=light **M**=moderate **S**=severe. **na**: not applicable

COMPLICATIONS 1.6

MS	Previous known allergies/skin diseases																
	Allergy								Other diseases								
	Atopic or contact dermatitis	Allergy to metals	Allergy to para-phenylen diamine	Allergy to latex	Allergy to preservatives	Allergy to medical drugs	Other	Pollen	Other skin diseases	Urticaria	Wart	Vitiligo	Other	Sarcoidosis	Eczema	NA	
BE-1	R	C	N	N	N	E	R			N	N	N					
BE-2	N	N	N	N	N	N	N			N	N	N	N				
BE-3	R									E							
BE-4	E		N	N	N	N	N		E	E	N	N	N				
DE-1	F	F	F	R	R	R		C		N	R	E					
DE-2	C	C	E	N	N	E	E			N	R	N					
DE-3																	
DE-4																	
DE-5	C	R	E	E	E	E			E	E	E	E					
DK-1	X	C	N	N	N	N	N		N	N	N	N					
DK-2																	
DK-3																	
DK-4	R	E	R	N	N	N	N			E	R	N					
DK-5	C	C	E	E	R	E	R			R	R	N		R			
FI-1												E				X	
NL-1	R	R	E	R	E	E	R			R	E	E					
NL-2	N	N	N	N	N	N	N		N	N	N	N	N				
NL-3		R	N	N	R	N		C		N	NA	R			R		
SE-1		R	R	E						R	R					50% of cases	

Frequency: **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent

COMPLICATIONS Q 1.7-1.8

Frequency of diagnosis and main histopathologic diagnosis

MS	Allergic skin reactions							Non-allergic inflammatory reactions							Cutaneous infections				Regional infections			Systemic infections				Benign tumours			Malignancies									Others				Histopathological diagnosis							
						Other						Other							other																													Other	
	Contact dermatitis	Plaque elevation	Hyperkeratosis	Ulceration/necrosis	General rash	React on products after treatment	Urticaria	Papulo-nodular inflammatory reactions	Nodules and granulomas including cutaneous sarcoidosis	general sarcoidosis	non-allergic immune activation	pain syndrome	lymphopathies	blow-out	bacterial	virus	fungal	other	erysipelas	abscess	local infection in tattoo	hepatitis B/C	AIDS	septicaemia	other	Hyperplastic scar or keloid	Keratoacanthoma	Other	Basal cell carcinoma	Squamous cell carcinoma	Melanoma	Lymphoma	Other	Hypo/hyper pigmentation	Photosensitivity	Urticaria	Lymphoedema and lymph node reaction	Other	Inflammation only	Lichenoid reaction	Granulomatous reaction	Sarcoid reaction or sarcoidosis	Pseudolymphoma	Pseudoepitheliomatous hyperplasia	interfase dermatitis	
BE-1	E	R	N	N	E			R	E	N					E	N	N		E	E		N	N	E		R	N	N						C	C	N	E			R	C	N	E	C		
BE-2	N	N	N	N	N		N	N	N	E					N	N	N		N	N	N	N	N	N	N	E			N	N	N	N		E	N	N	N	N			N	N	N			
BE-3	C	N	N	N	N		N	N	E	N				N	C	E	E	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	E	N	N	N	N	N	N	N	N	N	N	N	
BE-4	E	N	N	N	E	E		N	N	N				N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	R	E	E	N	N	E	N	N	N	N	N	N		N
DE-1	C	C	N	N	N			N	N	N				N	R	N	N		N	E		N	N	N		E	E	N	N	N	N	N	N	N	E	N	N		R	N	R	N	N	N		
DE-2	F	C	E	N	N			E							E	E						N	N	N			E	N	E	N	N	N			E	N	N	E								
DE-3																																														
DE-4	R	F	F	N	R			R	N	N					R	N	N																													
DE-5	C	E	N	R	N			C	C	N					C	N	N		C	C		N	N	N			C	N	N	N	N	N	N	F	R	N	E		C	N	C	N	N	N		
DK-1	C	N	N	N	N			C	R	N				N	R	N	N		N	N	N	N	N	N		X	C	N	N	N	N	N	N	R	R	N	N	N		N	C	C	N	N	N		
DK-2	N										F				N	N	N		N	N		N	N	N		N	N		N	N	N			N	N	N	N								
DK-3	N	C	C	E				E	N	N					N	N	N		N	N	N	N	N	N	N	N	E	N		N	N	N			E	R	R	N		R	R	E	N	N	N		
DK-4	C	C	C	C	N			R	N						R	R	R		R	R		R	N	N			C	E		N	N	N	N		C	R	R	C		R	C	C	N	R	C		
DK-5	R	F	C	R	R		R	F	R	R		R	R		C	R	N		R	R	C	E	N	R		R	R		N	N	N	N	N		R	C	R	R		C	E	R	R	E	E	C	
FI-1	-	C	C	E	N			R	R	R					R	E	E	N	N	N	N	N	N	N		E	N	E			N	E	N		N	C	N	E		C	C	C	R	C	C		
NL-1	E	R	E	E				C	C	C					R	E	E					N	N	N		C	R		N	N	N	N			R	C	E	N		C		C		R	R		
NL-2	R								R						N	N	N		N	N		N	N	N		N	N		N	N	N	N	N		N	N	N	N	N			R					
NL-3	C	F	E	E	N			E	E	N				X	C	N	N		N	N		N	N	N			C	N	N		E	N	N	N		N	E	N	N		R	F	F	E	C	E		
SE-3	R	R														R										R	E		E							E						R	R			R		

Frequency: **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent

Table B: Complication following tattoo/PMU removal.

2. COMPLICATIONS FOLLOWING A TATTOO/PMU REMOVAL Q 2.1-2.3

MS	Number of complications linked to tattoo removals	Number patients/year	Acute symptons						Delayed symptons					Technique/instrument used
			Pain	Blistering	Pin-point bleeding	Crusting	Urtical	Other / Infection	(photo) allergic reactions	Scars	hyper- and hypopigmentation	ink retention and darkening	Other	
BE-1	20	6000	C	E	R	E			E	R	C	E		QS Lasers (ND-Yag 1064,532, Alexandrite 755)
BE-2	0	5000												
BE-3	20	2700	E	E	E	E	N	N	N	N	N	N		Q Switched 1064/532 nm
BE-4	2	200	R	E	E	E	E	N	R	E	R	E		Trivantage Alexandriet 1064/755 2mm/3mm
DE-1	na	na	na	na	na	na	na		na	na	na	na		
DE-2	na	na	na	na	na	na	na		na	na	na	na		
DE-3	0	30-50	C	E	R	CR	E		0	0	0	0		Revlite si cynosure (ND:YAG laser)
DE-4	na	na	na	na	na	na	na		na	na	na	na		Rubin Laser
DE-5	5/300	6000	F	R	C	C	N		N	R	R	E	N	ERB YAG - LASER
DK-1	0	10000												
DK-2	0	0												
DK-3	5	5	na	N	N	N			N	F	F			
DK-4	2-3	600	F	C	R	R	E		E	C	C	E		ND:YAG laser
DK-5	3	20	F	F	C	C	R	R	N	F	F	C		Some Q-switched Yag but most complications come from low cost lasers. In the hospital only apply Q-switched Yag.
FI-1	0	0												
NL-1	?	?	C	R	C	C	R		E	R	R	E		na
NL-2														
NL-3	5	7500	C	N	N	N	N		N	C	N	N		
SE-1	0	2000												

Frequency: **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent. **na**: not available

Table C: Correlation between health complications and tattoo characteristics.

3. CORRELATIONS BETWEEN HEALTH COMPLICATIONS AND CERTAIN TATTOO CHARACTERISTICS/PARAMETERS Q 3.1-3.6

MS	Number of tattoos							Tattoo size					Gender/age							Colours										Localisation							Procedure						
	1	2	3	4	5	>5	na	small=<150 cm2	medium=151-300 cm2	large=301-900 cm2	extra large=>900 cm2	na	women	young	adult	men	young	adult	na	black	red	orange	violet/purple	henna colors	blue/green/turquoise	brown	white	yellow	multi-coloured	na	legs	arms	trunk	head/neck	genitals	multiple locations	na	Professional tattooist	Amateur tattooist	Professional cosmetic	Henna application	Traumatic tattoo	Medical	na
BE-1	E	R	C						C		E			E	F		E	F		F	C	C			F			R	R	C		C	F	C		E	F		F		F		C			
BE-2								F	R	E	N			E	C		E	C		F	F	E	C	E	R	R	R	C		C	C	R	N	C										
BE-3	F	C	E	N	N	N		F	F	R	E			E	F		E	F		F	R	N	E	E	E	N	N	N	R	R	C	F	E	N	E		F	F	F	R	R	E	E
BE-4							X					X							X	F	R	E	R	R	R	E	N	R	R	R	F	R	E	N	R									X
DE-1		C							C						C			C		C	C	E	N	E	E	E	N	E	R			C				C	C	E	E	E	N		
DE-2																																													
DE-3							X	F	F	F	R			E	F		R	F		F	C	E	C	E	F	E	E	R	F	F	F	F	R	E	R									X
DE-4															F			F		F																									
DE-5	F	F	F	C	R	R		F	F	C	R		F	R	F	F	R	F		F	F	R	F	F	C	R	E	C	C	F	F	F	R	E	F		R	F	F	F	C	R	
DK-1	C								C					N	C		N	C		C	C	C	C	N	C	N	N	C	C	R	C	C	R	E	C		C	R	R	E	R	R	
DK-2							X					X							X											X	C	C	C												X
DK-3	R	C	R					C	C					N	C	N	C			C	R	R		R								R	C			X								
DK-4	R	R	C	C	F			R	C	C	C		F	R	C	C	R	C		R	F	C	F	E	R	R			C		F	F	R	N	F		F	C	N	F	E	N	
DK-5	R	C	C	C	C	R		C	C	R	R		F	C	F	F	C	F		F	F	R	R	R	F	R	F	F	F		F	F	F	F	E	F		F	R	R	C	R	C	
FI-1							X	F	N	N	N		C		C	C		C		F	F	R	C	N	R		N	N	F							X	F	R						
NL-1																				C	C		E	E	E	E	E	E									C	E	C	C	E	E	
NL-2	1					1		1			1				1			1		F	C		N	C	R	C	N	R	C		C	C	C	R	N	C								X
NL-3	C	C	C	R	E	E		F	C	E	N		F	E	F	C	E	F		F	F	E	E	E	C	E	E	R	F		E	F	R	E	N	F		F	C	R	N	N	N	
SE-1		C						C	R						C				C	R	C	C		R				C	R		R	R	C				R			R				

Frequency: **N**= never, **E**= exceptional, **R**= rare, **C**= common, **F**= frequent

Annex V

Adverse health effects
Supplementary information

Table A: Adverse health effects: allergy/inflammation.

Reference	Country of study	Sample size	Study covered years	Age range (Years)	Time of onset after tattooing	Colour/Location/ Gender	Incidence rate	Minor symptoms <3 months
2015, Hutton-Carlsen	DK	40 (34 Females, 6 Males)	Sept-Nov 2012	Mean age: 33				
2015, Høgsberg	DK	19	2009-2011	18-52	Average 3 months	Red nuances (red, pink, purple, bordeaux)		
2012, Fors	SE		2000-2004	15-23				
2010, Klügl	DE	3411 (Internet survey)	July 2007-March 2008		Immediately to 4 weeks after tattooing		67.5% transitory skin problems; "moderate" in 10% of cases and "intense" to "very intense" in 1.8%. 4 weeks after tattooing, 9% still had health problems, 6% persistent skin effects: oedema, itching, papules and scarring; 6.6% systemic reactions:dizziness,headache, nausea or fever; 1.3% reported burning and itching of tattooed skin when exposed to sun. 3% stated psychic problems and light sensitivity of tattoo	Bleeding, crusts, itching edema and pain, followed by burning sensation, blister formation
2010, Wenzel	DE				6 weeks to several months	Pigment Red 181 (CI73360). Female, PMU		
2009, Mataix	Multi				Delayed allergic reactions:weeks-years after tattooing (difficult to classify); they may last years despite treatment			Acute inflammation lasting for 1 to 2 weeks.
2008, Ali Saba	US	1		31	10 years after tattooing (incubation period=3-20 years)			
2008, De Cuyper	Multi						Rare	Swelling and crusting may persist for a few days; swelling or burning when undergoing MRI
2007, Kazandjieva	BG	234					Overall prevalence of skin complications = 2.1% (5 of 234 cases), including infections and allergic/granulomatous complications	Immediate (after few hours) inflammatory reaction always appears; transient symptoms at the site of tattoo (swelling, heating,skin irritation) in small n° of patients (< 10) after magnetic resonance imaging
2006, Teixeira		1		30	1 day	PMU: black eyelash and eyebrow dye		
2003, Bhardwaj	US	1		38		Red (Patchy red 904A)		

[55], [107], [108], [18], [109], [43], [65], [110], [69], [111], [112]

Reference	LIC+ECZ (linked to SRC & Granuloma)	SRC+FBD (linked to Granuloma)	Systemic sarcoidosis	Pseudolymphomatous reactions	Contact Dermatitis	Plaque Elevation	Ulceration/ Necrosis	Papulo-nodular inflammatory Reactions (non specific)	Anaphylactic reaction	Fibro-Scleroderma (scars)	Reactivation of Underlying Dermatoses	Dermatofibroma	Other
2015, Hutton-Carlsen													Quality of life evaluation according to the Itch Severity Scale (ISS) and the Dermatology Life Quality Index (DLQI). The ISS has been used to evaluate patients with pruritus, genital pruritus and nephrogenic pruritus as well as atopic dermatitis, psoriasis and urticaria, which revealed ISS scores from 7.4-13.4. Patients with tattoo reactions revealed an average ISS score of 7.2. The DLQI has also been utilized on patients with hand eczema, pruritus and neurodermatitis with scores from 8-13.3. Tattooed patients DLQI score was 7.4
2015, Høgsberg	6 cases; The granulomatous pattern has been found on a background of interface dermatitis				14/19 cases of interface dermatitis.		1/19 cases					13/19 cases	14/19 Patients were patch tested with European standard because suspected to be allergic. 5/14 resuted allergic towards potassium dichromate, fragrance mix, hydrocyisohexyl-3-cyclohexene-carbon-xaldehyd, sorbic acid, cobalt chloride and nickel sulphate. 11/19 were patch tested with a textile series consisting of 42 dispersed dyes. Two reacted with reactions to red and orange dyes. 13/19 patients were patch tested with a selection of eight problematic stock tattoo ink products. One patient reacted against the red and yellow inks.
2014, Huynh	Granulomatous, lychenoid and pseudolymphomatous reactions represent the most common dysimmune reaction and may be the direct result of the tattooing practice.												
2013, Juhas	Reported	Reported	Reported	Reported				Reported	Reported	Less common	Koebner phenomenon in preexisting psoriasis, systemic lupusand sarcoidosis	Following trauma or coincidence	Vasculitis
2012, Fors					The study is <u>not directly related</u> to adverse effect of tattooing practice. It tries to correlate the effect of lifestyle (for instance the presence of a tattoo) with nickel allergy by patch testing some volunteers. Conclusion is that in comparison with not tattooed people, tattooed boys showed a 3-fold and girls almost 2-fold increase in Nikel allergy by patch test.								
2010, Klügl						0.7% (n=3411) complained of "elevated skin"		0.4% (n=3411) complained of "skin papules"					
2010, Wenzel					3/4 resulted positive to prick test of both PMU colorant and CI 73360 (red). 1 patient declined prick test. Patch test negative in all cases.								

LIC+ECZ: Lichenoid and eczematous reaction. SRC+FBD: Cutaneous Sarcoidosis and Foreign body reaction

[55], [107], [113], [44], [108], [18], [109]

Reference	LIC+ECZ (linked to SRC & Granuloma)	SRC+FBD (linked to Granuloma)	Systemic sarcoidosis	Granuloma	Pseudolymphomatous reactions	Contact Dermatitis	Photoallergy	Plaque Elevation	Papulo-nodular inflammatory Reactions (non specific)	Fibro-Scleroderma (scars)	Reactivation of Underlying Dermatoses	Other
2009, Bocca				Granulomatous reaction can be induced by pigments containing Al and Ti		Reported a case of skin hypersensitivity caused by the presence of Co in the blue ink used for tattoo; Hg contained in some tattoo red dyes is reported to produce a delayed hypersensitivity reaction						
2009, Forte				Granulomatous reaction can be induced by pigments containing Al and Ti. Sarcoid granulomas developed in a black area of a tattoo; patch test positive to Ni, Co, Cd. Analysis of pigment revealed the presence of Ni and Co. Acute dermatitis overlaying a granuloma has been reported at the site of a violet tattoo.					Eryhemathous papules scattered within a black area			
2009, Mataix	Lichenoid reactions are the most common type of tattoo reaction, with lesions that are clinically and histologically similar to lichen planus.	Granulomatous reactions reported in association with chromium, mercury, cobalt,and magnesium; Less common, sarcoid granulomas may be non specific but can also be an early manifestation of systemic sarcoidosis.			Indurated, erythematous, violaceous nodules confined to the tattoo, mainly described for red pigment tattoo but also for green and blue pigments.	Eczematous lesions confined to the tattooed area, with occasional secondary spread; patch test inconclusive;	UV-induced erythematous oedema most often caused by yellow and red Cd-containing pigments.				Koebner phenomenon in association with sarcoidosis, pyoderma gangrenosum, and cutaneous lupus erythematosus.	
2008, Ali Saba		Intermittent swelling, blistering, burning, confined to brown areas of tattoo; edematous papules with surrounding erythema	Known hilar lymphadenopathy									
2008, De Cuyper	Foreign body epitheloid granuloma after cosmetic eyebrow tattooing.	Frequent								Eyelid necrosis, loss of eyelashes, and secondary cicatricial ectropion, hypertrophic scars, and keloids		
2007, Kazandjieva	Lichenoid reactions more often to the red pigment.	Single cases (Days to months)		Single cases (Days to months)	Always in the red areas of the tattoo	Single cases (Days to weeks)	Single cases: After sun exposure and cadmium in sufficient amount in tattoo dye (yellow)				Single cases: Psoriasis (10 d-30 y)	Lichen planus, Lupus erythematosus chronicus discoides (always in the red areas of the tattoo)
2006, Teixeira						Positive patch results to: *p*-phenylendiamine both at 0,1 and 1%, Disperse red 17, disperse red 1, disperse orange 3, disperse orange 1 and dye as it has been used. Allergy manifested as intense itching, erythema, swelling and exudation.						Important: the permanent eyelash used contained p-phenylendiamine.
2003, Bhardwaj						Patch test positive for "Patchy Red 904A" both on normal skin and on scar tissue after tattoo removal		Swelling and itching confined to the red areas				

[114], [115], [43], [65], [110], [69], [111], [112]

Table B: Correlations among tattoo characteristics and adverse health effects.

	COLOUR							LOCATION			GENDER	
Reference	BLK	COLOR	RED	OR	VL	BG	WH	Extremities	Trunk	Head	F	M
2015, Hutton-Carlsen								35	5	1	34	6
2015, Høgsberg								18 (arms=6, legs=11, foot=1)	1		12	7
2013, Juhas		Anaphylactic reaction	Pseudolymphomatous lichenoid and granulomatous reactions	Pseudolymphomatous reactions		Pseudolymphomatous reactions						
2010, Klügl		Slightly more short-term skin or systemic reactions									Crusts, itching, edema and systemic health problems directly after tattooing slightly more frequent in females. After 4 weeks,health problems were graded as more severe by females; 7.3% (n=3411) reported persistent skin problems. Solar sensitization and psychic problems more frequent in young people (not gender related)	4.2 % (n=3411) reported persistent skin problems. Solar sensitization and psychic problems more frequent in young people (not gender related)
2009, Bocca			Cinnabar and Vermilion contain Hg which is known to produce delayed hypersensitivity		Al and Ti were detected by microscopic examination of excised tumor in the violet areas of a tattoo.	Co containing tattoo ink caused skin hypersensitivity						
2009, Forte	Sarcoid granulomas developed in a black area of a tattoo; patch test positive to Ni, Co, Cd. Analysis of pigment revealed the presence of Ni and Co; erythema tous papules originating from "India Ink"		Cinnabar and Vermilion contain Hg which is known to produce delayed hypersensitivity. In the preent work Cr is the predominant metal in ink composition wile other metals reported giving strong allergic reaction (Hg, Ni and Cd) did not reach µg/g level.		Al and Ti were detected by microscopic examination of excised tumor in the violet areas of a tattoo. Large amount of Mn was fount in the biopsy specimen of a granuloma at the site of a violet tattoo. In the present work Mn was not analysed, but analysis of violet ink revealed high contents of Cr and Ni	Co contained as component or impurity is reported to cause urticaria; Ti (linked to granulomatous reactions) found in a commercial available blue ink: Co, when present in blue dyes, is reported being cause of deep granulomas and urticarial syntomps. Green may contain Cr which is deemed to cause eczemathous reactions. Hg and Cr have been found at high concentration in the present work.	From Ti or ZnO. In the present work, Ni was the prevailing metal followed by Cd. Traces of Cr and Co were observed.It could potentially contain other metallic derivatives. µg/g concentartion was never reached.				
2009, Mataix			Red inks, particularly if containing Hg, are the most common causes of delayed allergic reactions.									
2008, De Cuyper			Red inks, containing Hg, cause lichenoid reactions.									
2007, Kazandjieva	case of sarcoid granulomas developing in blue-black tattoo reported					Case of sarcoid granulomas developing in blue-black tattoo reported						

[55], [107], [44], [18], [114], [115], [43], [110], [69]

Table C: Adverse health effects: infections.

Reference	Country of study	Sample size	Study covered years	Age range (Years)	Time of onset after tattooing	Colour/Location/Gender	Tattoo Application
2015, Mudedla	Multi	114	2003 -2013		Within 4 to 6 weeks (majority of cases), up to 6 months after tattoo		
2014, Gulati	US	1		48		Female, tattoo on the back	Home made tattoo
2013, Falsey		3	Jan-Mar 2012		First papules appeared 7-21 day after tattoo placement. New papules developed in the subsequent 1-4 months		
2012, Kennedy	Rochester, NY. US	19	Oct-Dec 2011	18-48	Within 3 weeks	Premixed grey ink	
2012, Morbidity and Mortality weekly report (CDC)	US: New York (refers to 2012, Kennedy), Washington. Iowa and Colorado	Washington, cluster 1: 27 Washington, cluster 2: 4 Iowa:2 Colorado: 1	2011-2012			Washington, cluster 1: Black Washington, cluster 2: Grey Iowa:Back Colorado: Black	
2012, Tohme	Multi		1994-2011				
2011, Giulieri	CH	12	2009-2010	56	Range 2-7 weeks	Female, with PMU	
2011, Rodriguez-Blanco	ES	5 (plus 2 suspected but not analysed)	Sept 2008-April 2009	18-23	3 to 30 days	Grey	
2011, Urbanus	NL	375 tattoed persons among total 434 interviwed.		23-37			
2010, Bechara	FR (Brazilian man) +internet review	1 + review (36 patients)		51	10 days after tattoo (review: 1 w.- 3 months)		
2010, Drage	US	6	Oct 2007-May 2008	20-49	1-2 weeks	Grey (by water dilution of black ink)	
2010, Klügl	DE	3411 (survey)					
2010, Pérez-Cotapos							Depends on the hygienic conditions under which the procedure was carried out, and the expertise of the tattooist
2008, De Cuyper					LASER/PMU		
2007, Kazandjieva	BG	234					Overall prevalence of skin complic. = 2.1% (5 / 234 cases), including infections and allergic/granulom.reactions
2006, Morbidity and Mortality weekly report (CDC)	US	34 primary cases, 10 secondary cases. The persons with secondary cases were exposed to persons with primary cases by direct contact because they were living in the same house or had close personal contact.	Jun 2004- Aug 2005	15-42	4-22 days among all 34 primary cases	73% male, 27% female. Outbreaks was reported in three different states: Kentucky, Ohio and Vermont	During interviews, 13 unlicenced tattooist were identified. 7 tattoist were located and interviewed. Adherence to some infection control measures were not practiced.
2005, Porter	NZ	2		45 and 29 years old	within 2 days		Both cases of Samoan tattoing, performed in unlicensed premises by temporary tattooist

[98], [116], [117], [118], [119], [42], [120], [121], [46], [122], [123], [18], [72], [110], [69], [124], [125]

Reference	% contaminated inks	Bacterial				Viral	
		Incidence rates	Pyogenic	NTM	Other	Hepatitis B and C	Other
2015, Mudedla		unknown		Unspecific erythematous papules, pustules, and nodules, predominantly within the borders of tattoos, generally the gray part; *Chelonae* most common cause; contamination occurs through unsterile instrumentation or tap water used for diluting tattoo ink.			
2014, Fowler				This paper cites a number of reports of cutaneous Mycobacterium Chelonae infections in immunocompetent hosts due to subcutaneous inoculation with contaminated tattoo ink			
2014, Gulati	Same ink and equipment were used by her husband who also developed IPA due to Staphylococcus aureus.		Iliopsoas abscess due to Staphylococcus aureus				
2014, Huynh					A predominance of warts among a variety of opportunistic infections may result from a local immune disregulation (rather than from direct inoculation or coincidence) caused by tattooing practice.		
2013, Falsey	2 different inks (A and B), from 2 different companies (A and B) arose concerns. Company A reported receiving 35 complaints of unusual skin reactions to brand A ink. Company A had identified a single batch of ink that was associated with these complaints and voluntarily issued a recall. Company B declined to provide ingredients or sources of inks, and denied receiving any complaints. Nevertheless, no NTM was recovered from brand A ink samples; brand B ink samples obtained from the tattoo artist grew M. chelonae indistinguishable from patient 1's	An health alert was sent out and an investigation was initiated. 2 tattoo artists involved were contacted and interviewed. This investigation revealed 2 unlinked clusters of NTM infections. Cluster A comprised 27 infections, all tattooed by the same artist by using the same bottle of brand A black ink. Three of these infections were confirmed by biopsy and culture; the remaining infection swere suspected. Cluster B comprised 4 infections (2 confirmed through biopsy and culture), all of whom were tattooed by using the same bottle of brand B gray wash ink. No infections were identified among either artist's clients tattooed with previous or subsequent bottles of ink.		Tissue culture grew nontuberculous mycobacteria (NTM) in all cases. Speciation from patient 1 revealed Mycobacterium chelonae; speciation in patients 2 and 3 revealed Mycobacterium abscesuss			
2012, Kennedy	Premixed grey ink from 1 company	14 confirmed 4 probable 1 suspected		chelonae, giving the pathologic evidence as papules, pustules			
2012, Morbidity and Mortality weekly report (CDC)	Total of 3 companies. Washington cl 2 and Iowa cases used ink from the same company.	Washington, cl 1: 3 confirmed and 24 possible Washington, cl 2: 2 confirmed and 2 possible Iowa: 2 confirmed Colorado: 1 confirmed		Washington, cl 1: Abscessus Washington, cl 2: Chelonae Iowa: Chelonae Colorado: Chelonae Always giving the pathologic evidence as papules, pustules			
2012, Tohme (included in 2013,Carney)						No evidence for an increased risk of HCV infection in professional parlors.	
2011, Giulieri	All procedures were performed by the same artist. Microbiological investigation of oil and cold sterilising agents were negative. Direct examination of 18 inks resulted negative. Nevetheless 6/18 samples, broad-spectrum PCR resulted positive for Mycobacterium haemophilum			Index patient presented with skin lesion of the eyebrow and ipsilateral lymphadenitis. Mycobacterium haemophilum was identified by sequencing. 11 additional patients with lesion of the eyebrow and ipsilateral lymphadenitis were identified. 10/12 had microbiological diagnosis of M. Haemphilum. For the remaining 2 diagnosiswas based on clinical presentation.			
2011, Rodriguez-Blanco				Chelonae giving the pathologic evidence as skin lesions			
2011, Urbanus						375 people bearing at least one tattoo (median number 5, median body surface 18%) have been tested for anti-HBc and HCV. The study population included both tattoo related variables (number of tattoos, % of body tattoed, being a tattoo artist, have had a tattoo in a HBV endemic country) and tattoo-unrelated variables (HBV vaccination, being born in HBV endemic country, residence, snorting drugs). NONE OF THE TATTOO-RELATED VARIABLES WERE SIGNIFICANTLY ASSOCIATED WITH HBV. As for HCV, only 1 participant resulted infected. The participant was a tattoo artist who received a tattoo more than 100 times and reported several other risk factors, including needel-stick accidents.	375 people bearing at least one tattoo (median number 5, median body surface 18%)

[98], [126], [116], [113], [117], [118], [37], [42], [120], [121], [46]

Reference	% contaminated inks	Bacterial				Viral			Fungal	Septicaemia
		Incidence rates	Pyogenic	NTM	Other	Hepatitis B and C	AIDS	Other		
2010, Bechara		RGM rarely documented after tattoo, but in progression; M.*abscessus* :1st case published		*M.abscessus:* erythematous papulo-pustula, limited to the colored parts of tattoo;symptoms:pruritus, tenderness						
2010, Drage	Grey ink used by the same artist at a single establishment	5 confirmed 1 suspected		chelonae, giving the pathologic evidence as papules, pustules						
2010, Klügl		0,50%	Bacterial skin infections (pus-filled skin areas)							
2010, Pérez-Cotapos		Bacterial infections are more common following piercing than tattooing procedures. The most frequent are local bacterial infections at the site of the procedure.			1) Often Streptococcus pyogenes and Staphylococcus aureus 2) Severe secondary infections have been reported such as erysipelas, cellulitis, sepsis, and spinal abcesses, either due to Streptococcus pyogenes , Staphylococcus aureus , or Pseudomonas species 3) outbreak of Mycobacterium chelonae infection in 6 patients tattooed by same tattooist			Different types of viral infections can be transmitted. Papiloma virusinduced warts , Mollusca contagiosa, herpes simplex , blood-transmitted diseases such as hepatitis and HIV		
2009, Mataix		Incidence diicult to determine	Relatively common			Epidemiologically, the risk factor of HIV/ hepatitis C virus e transmission through tattoo is not statistically relevant.			Isolated cases of skin infection caused by the human papilloma virus and molluscum contagiosum		Increase in systemic infections due to bacteria that gain access to the body via tattoos.
2008, De Cuyper		Bacterial superinfection is rare				Through nonsterile equipment and needles				
2007, Kazandjieva			Impetigo, Acne varioliformis, Ecthyma: Usually located in tattooed area (First few days)		Historical: Tetanus, Chancroid,Tuberculosis cutis, Lepra, Syphilis (onset from weeks to years)	Reported	Reported	Only few cases: Verruca, Molluscum contagiosum (Incubation: weeks to months)	Single cases: Zygomycoses (After years), Tinea cutis glabrae (After weeks)	Toxic shock syndrome
2006, Morbidity and Mortality weekly report (CDC)			A primary case of tattoo-associated Methicillin-resistant Staphylococcus aureus (MRSA) skin infection was defined as a skin infection consistent with staphylococcal infection (e.g., boil, folliculitis, erythema, or abscess) that occurred near or at the site of a recent tattoo in a person from whom a culture from that site yielded MRSA. A secondary case was defined as a skin infection consistent with staphylococcal disease that occurred in a person who had not received a recent tattoo but had been in close contact with an MRSA patient who had received a tattoo. A total of 34 primary cases and 10 secondary cases were identified in the three states.							
2005, Porter	Samoan tattoo equipement was analised in one case and grew various quantities of mixed Gram + organisms.Most extensive growth came from ink and yellow pigment.		Streptococcus pyogenes and Staphylococcus aureus were grew in both cases. In one case Preudomonas aeruginosa was grew as well. Tissue cultures also grew Corynebacterium species and Klebisella oxtoca in the second case.		Bacterial infection caused skin necrosis septic shock that led to death in one case.					Septic shock registered in both cases

[122], [123], [18], [72], [43], [110], [69], [124], [125]

Table D: Adverse health effects: tumours.

Reference	Country of study	Sample size	Study covered years	Age range (Years)	Time of onset after tattooing	Colour/Location/Gender
2015, Høgsberg	DK	19	2009-2011	18-52	Average 3 months	Red nuances (red, pink, purple, bordeaux)
2014, Soran	US	1		73		
2010, Klugl	DE	3411 (survey)				
2009, Dos Santos Gon	BR	1		60	4 months	woman
2009, Kürle	DE	1		22		Female. Tattoos on the right ankle, right groin and coccyx.
2009, Lee	KR	1 (plus 7 already reported in the past)		60 (other cases from 28 to 74)	3 years (other cases from 1 to 46 years)	Black PMU on left eyebrow. Woman
2008, Goldenberg	US	1		38	1 month	
2007, Kazandjieva	BG	234				
2006, Birnie				28	6 years	Black,/central back/Female
2005, Baker	UK	1		35	7 years	

[107], [127], [18], [128], [129], [130], [131], [69], [132], [70]

Reference	Benign tumours			Malignancies					Lymph nodes
	Frequency	Keratocanthoma (KA)	Pseudolymphoma (PSL)	Frequency	Basal cell carcinoma (BCC)	Squamous cell carcinoma (SCC)	Melanoma (MEL)	Other	
2015, Høgsberg			6 cases: pseudolymphomatous infiltration pattern has been found on a background of interface dermatitis						
2014, Huynh					BCC, SCC and MEL may result from the local dysimmune reactions triggered by tattooing				
2014, Soran								Tattooing causes difficulties in assessing a sentinel lymph node biopsy specimen because the pigment can mimic metastatic disease and thus provide a challenge for surgeons and pathologists. Sentynel limph node biopsy was performed to stage a ductal carcinoma in situ (NOT NECESSARILY RELATED TO THE PRESENCE OF THE TATTOO). Intra-operatively four colored nodes were harvested, labeled and sent separately for histopathology. The first and third nodes were hot with technetium 99 and contained blue dye staining, the second node was blue in color and the fourth axillary SLN was palpable only. The pathology report of the lymph nodes revealed that all axillary SLN were free of tumor. In addition, the second axillary SLN which was grossly blue/black in color haextracellular anthracotic pigmentation and pigment-laden macrophages.	
2010, Klugl				0.1% (all male, n=3411)					

[107], [113], [127], [18]

Reference	Benign tumours				Malignancies				Lymph nodes
	Frequency	Keratocanthoma (KA)	Pseudolymphoma (PSL)	Other tissue reactions	Frequency	Basal cell carcinoma (BCC)	Squamous cell carcinoma (SCC)	Melanoma (MEL)	
2009, Dos Santos Gon		Keratocanthoma confirmed by histological analysis							
2009, Kürle								Noticed at first as brownish-black skin lesion noticed in the region of the right thigh, then confirmed by hisological analysis.	Black pigmented lymph node found negative at histological analysis.
2009, Lee	8 cases reported in the literature over 33 years					Confirmed by histopatologic findings			
2009, Mateix	Purely coincidental	5 cases cited				7 cases cited	3 cases cited	12 cases cited	
2008, Goldenberg							The case reports a superficially invasive squamous cell carcinoma, keratocanthoma type (in the form of erythematous hyperkerathotic papules)		
2007, Kazandjieva						5 cases reported	Single cases (no proof for a link with tattoo)	6 cases reported	
2006, Birnie						Basal cell carcinoma of no special type confirmed by hystology, manifesting as asymptomatic nodule			
2005, Baker	This is reported as the first case of dermatofibrosarcoma protuberans occurring in a decorative tattoo			Dermatofobrosarcoma protuberans has an intermediate grade of malignancy. It is reported being locally aggressive and rarely methastatic. In this case it manifested as cutaneous nodule.					

[128], [129], [130], [43], [131], [69], [132], [70]

LB-NA-27672-EN-N

JRC Mission

As the Commission's in-house science service, the Joint Research Centre's mission is to provide EU policies with independent, evidence-based scientific and technical support throughout the whole policy cycle.

Working in close cooperation with policy Directorates-General, the JRC addresses key societal challenges while stimulating innovation through developing new methods, tools and standards, and sharing its know-how with the Member States, the scientific community and international partners.

Serving society
Stimulating innovation
Supporting legislation

Publications Office

doi:10.2788/177900

ISBN 978-92-79-54234-3