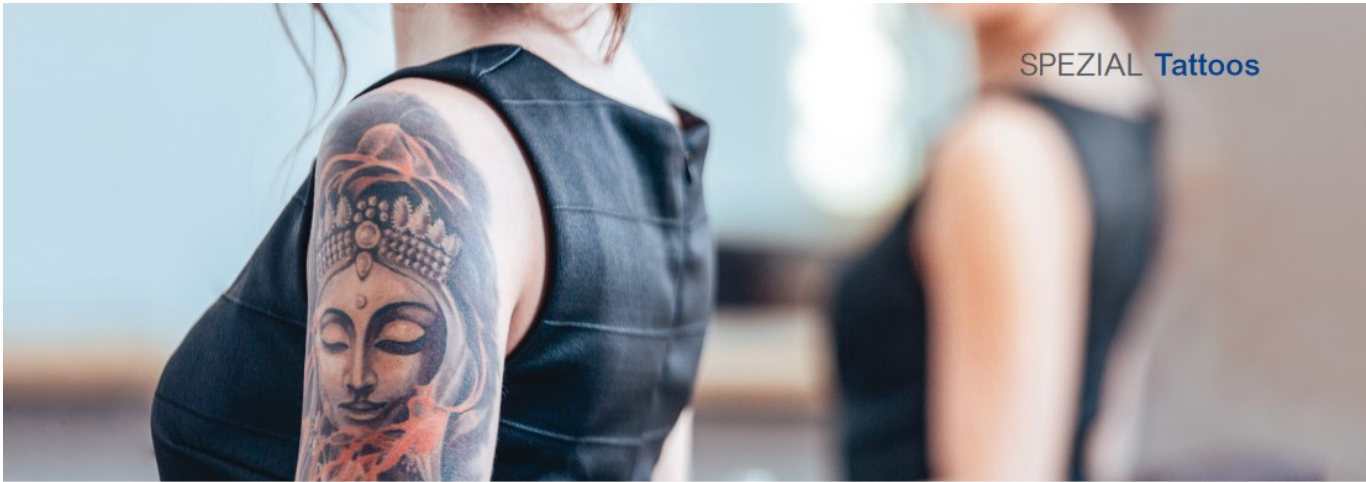




Requirements for the risk assessment of tattoo inks: chances and challenges

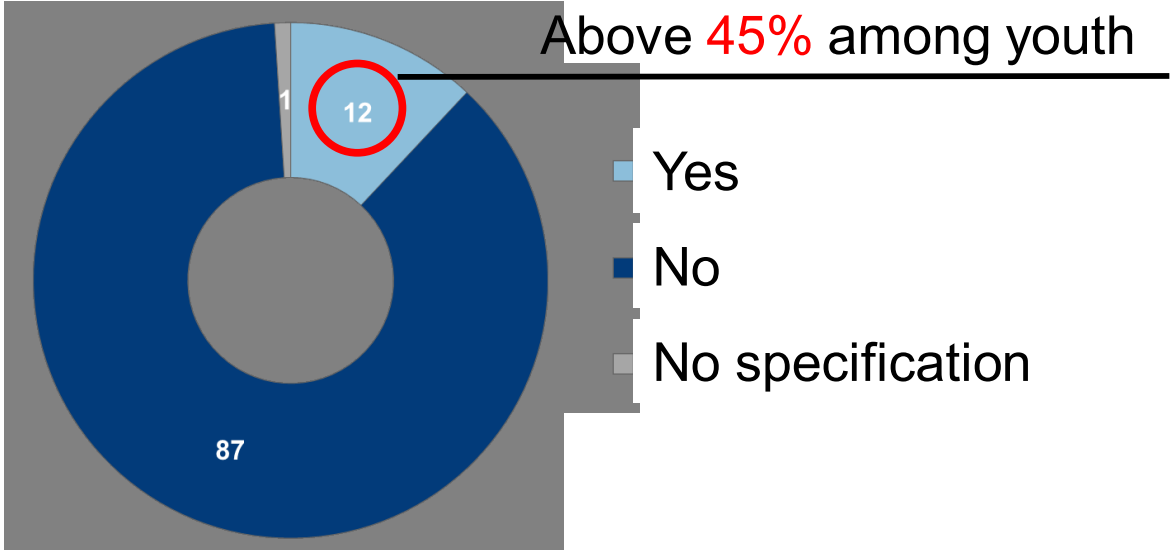
Dr. Michael Giulbudagian, Dr. Peter Laux
BfR - 2nd International Conference on Tattoo Safety

BfR - Consumer Monitor

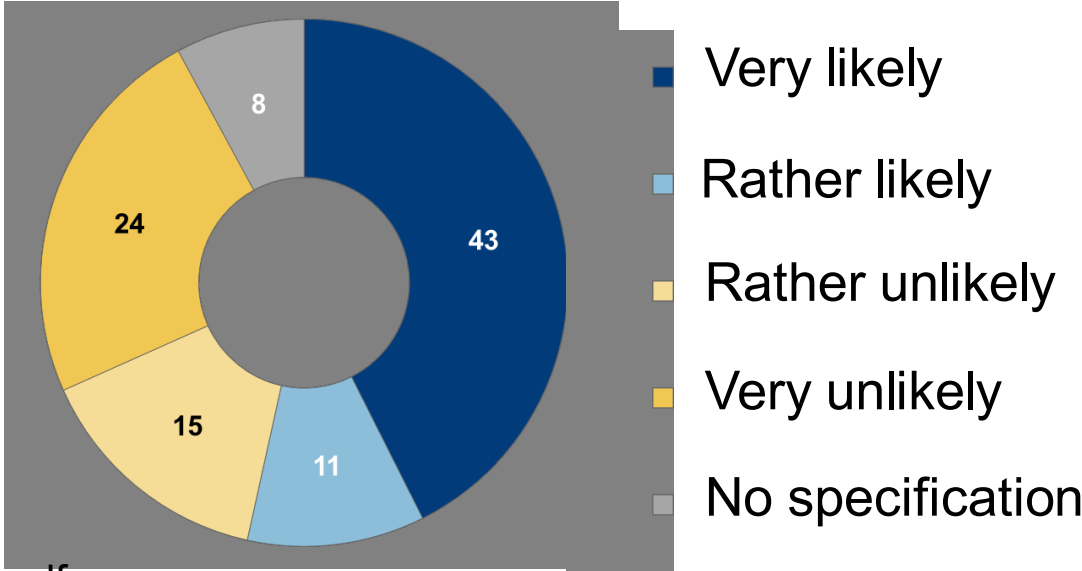


Do you carry a tattoo?

Above **45%** among youth



Likelihood of getting a tattoo in the future:



<https://mobil.bfr.bund.de/cm/350/bfr-verbrauchermonitor-2018-spezial-tattoos.pdf>
<https://www.presseportal.de/pm/52678/4382081>



Risk Assessment of Tattoo Inks: Challenges



- Missing test methods for intradermal toxicity
- Unknown degradation products
- Limited clinical evidence / epidemiological studies
- Distribution / Persistence in organs?
- Dose deposited in the skin?
- Fraction of the dose given to systemic distribution?

Reduction of Risks

- Full assessment of tattoo pigments not possible at present
- How can health risks be reduced without a comprehensive assessment of all health risks?

www.bfr.bund.de



Bundesinstitut für Risikobewertung

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Tattoo inks: minimum requirements and test methods

Opinion No 031/2021 of the BfR of 14 October 2021

Tattoo inks contain pigments and additives. According to the provisions of the German Food, Consumer Goods and Feed Code (Lebensmittel-, Bedarfsgegenstände- und Futtermittelgesetzbuch, LFGB), tattoo inks may not be used if there is any doubt as to their safety to health. Substances or mixtures for tattooing purposes are regulated in the REACH Regulation [entry 75 of Annex XVII of the REACH Regulation (Regulation (EC) No 1907/2006)]. However, there are as yet no binding criteria according to which a safety assessment of tattoo inks should be carried out. There is also a lack of suitable test methods and data for a health risk assessment. For example, little is known about adverse effects that may be associated with the injection of tattoo inks into the skin or about possible effects that may be induced in other organs. Therefore, the German Federal Institute for Risk Assessment (BfR) has developed minimum requirements for tattoo inks as well as test methods for manufacturers and distributors who are primarily responsible for the safety of their products.



Definition of minimum requirements



Goal:

- **Achieve constant chemical purity**
- **Identification of pigments not suitable for use in tattoo inks**

<https://www.bfr.bund.de/cm/349/tattoo-inks-minimum-requirements-and-test-methods.pdf>

REACH and BfR minimum requirements

REACH: Exclusion of substances classified according to CLP:

CMR 1A, 1B, 2

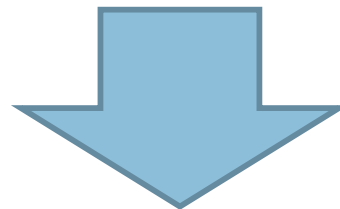
Skin Sens. 1, 1A, 1B

Skin Corr. 1, 1A, 1B, 1C, Skin Irrit. 2

Eye Dam. 1, Eye Irrit. 2

Non-classified substances are not restricted, but may also represent risks to tattooed humans, e.g.:

- High concentrations of impurities such as primary aromatic amines, organic solvents used in synthesis, metals
- Degradation into toxic metabolites *in vivo*
- Lack of data, e.g. for new compounds



Minimum requirements

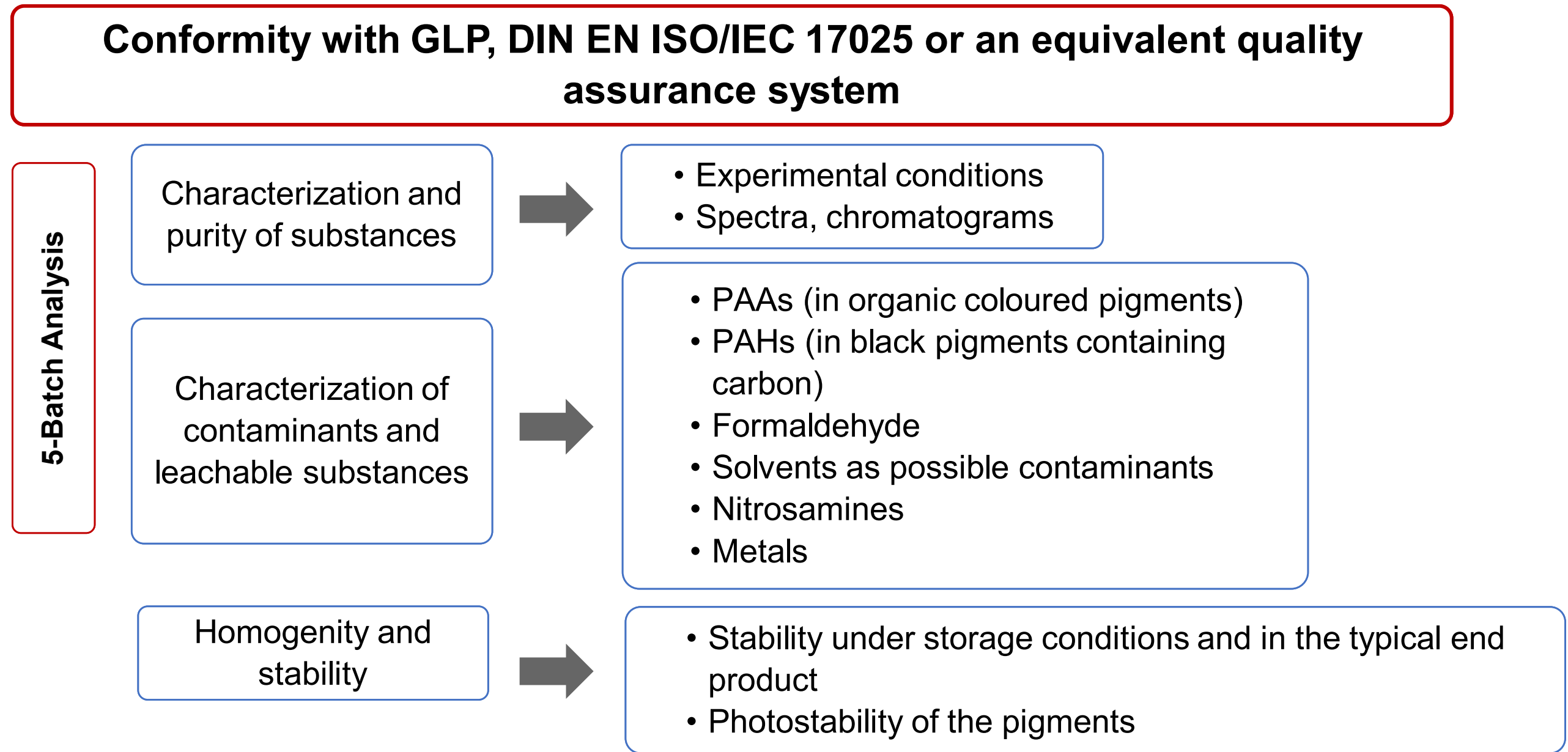
Minimum Requirements for Tattoo Pigments: An Overview

Minimum requirements for tattoo inks

- I Specifications for the ingredients of tattoo inks
- II Minimum toxicological requirements for tattoo pigments

Specifications for Ingredients of Tattoo Inks

Toxicological studies are only relevant when they rely on a known substance purity and a set of determined contaminants.



Minimum Requirements for Tattoo Pigments: An Overview

Minimum requirements for tattoo inks

I Specifications for the ingredients of tattoo inks

II Minimum toxicological requirements for tattoo pigments

Minimum Toxicological Requirements (I)

Step 1: Collection of all available data



- Literature
- Data generated for regulatory purposes (e.g. REACH)
- Assessment of applicability of *in silico* methods (e.g. QSARs) and read-across
- Human and epidemiological data (e.g. medical case reports)



Step 2: Review and evaluation of available data



- Existing data sufficient for evaluation?
- Exclusion criterion violated?
- Further testing necessary?



Consideration of existing oral / dermal *in vivo* studies when positive

Minimum Toxicological Requirements (II)



Step 3: Minimum requirements - *in vitro/in chemico* testing

- Consider compatibility of tests with the physico-chemical properties of pigments
- Test according to OECD Test Guidelines and GLP

**Skin
irritation &
corrosion**

**Eye irritation &
damage**

Skin sensitization

Phototoxicity

**Mutagenicity/genotoxicity
incl. photogenotoxicity**

Tattoo pigments that meet the minimum toxicological requirements reduce possible risks according to the current state of science and technology.

Data Gaps for Comprehensive Evaluation of Tattoo Pigments

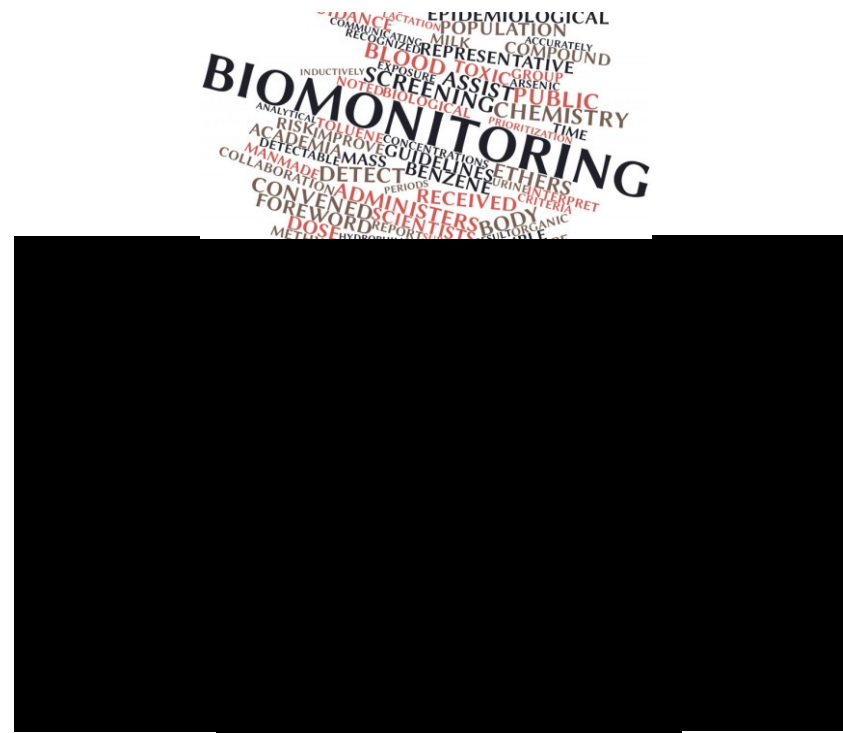
Short-term

1. Test materials, detection and quantification of pigments
2. Extraction and analysis procedure for PAHs



Medium-term

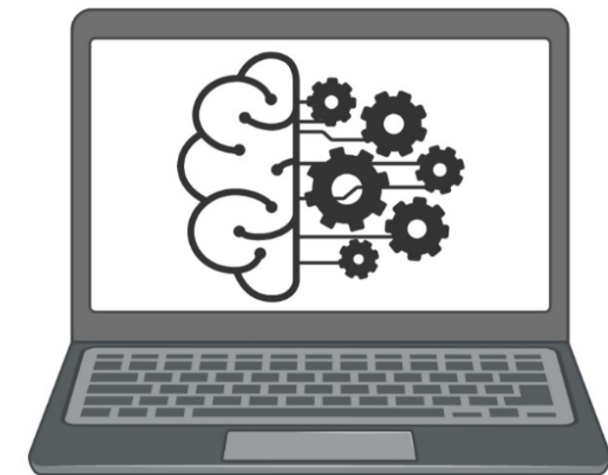
1. Human biomonitoring studies
2. Toxicokinetic studies
3. Grouping approaches



Long-term

1. *In vitro/ex vivo* methods and/or *in silico* models for intradermal application

In-silico
methods



Cohort and Biomonitoring Studies

LIFE-Follow-up Study



UNIVERSITÄT LEIPZIG

7000 Participants
Main target: association of tattoos and civilisation diseases
Chronic toxicity

Fragebogen über das Vorhandensein einer Tätowierung oder eines Permanent Make-ups

1. Bitte kreuzen Sie Zutreffendes an und füllen die für Sie in Frage kommenden Felder aus:

Haben Sie eine Tätowierung?	Ja	Nein	erste Tätowierung/Permanent Make-up erhalten?
Haben Sie Permanent Make-up?			Monat * Jahr

Wenn Ja, wann haben Sie die erste Tätowierung/Permanent Make-up erhalten? (Angabe in Monat und Jahr, z.B.: 04.2004 für April 2004)

Falls Sie keine Tätowierung(en) und/oder Permanent Make-up haben, endet der Fragebogen hier für Sie.
Beantworten Sie die folgenden Fragen bitte, wenn Sie Tätowierungen und/oder Permanent Make-up haben. Kreuzen Sie bitte die für Sie zutreffenden Antworten an.

2. Bitte machen Sie Angaben zur Farbe Ihrer Tätowierungen/Ihres Permanent Make-ups.

Welche Farbe hat Ihre Tätowierung / Tätowierungen?	Weiß	Gelb	Orange	Rot	Magenta	Violett	Blau	Grün	Braun	Schwarz
Welche Farbe hat Ihr Permanent Make-up?										

3. Bitte geben Sie anhand der Auswahlmöglichkeiten in der Tabelle Auskunft über Lokalisation und ungefähre Größe Ihrer Tattoos oder Ihres Permanent Make-ups.

Körperteil	Größe des Tattoos /des Permanent Make-up (ungefährer Durchmesser)			
	kleiner als 5 cm	5 bis 10 cm	10 bis 20 cm	größer als 20 cm
Gesicht	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
anderer Teil des Kopfes (außer Gesicht)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hals	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rumpf, Vorderseite - Bereich oberhalb der Taille	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rumpf, Vorderseite Bereich unterhalb der Taille	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

andere Körperregion, Welche?

Short-term biokinetics study



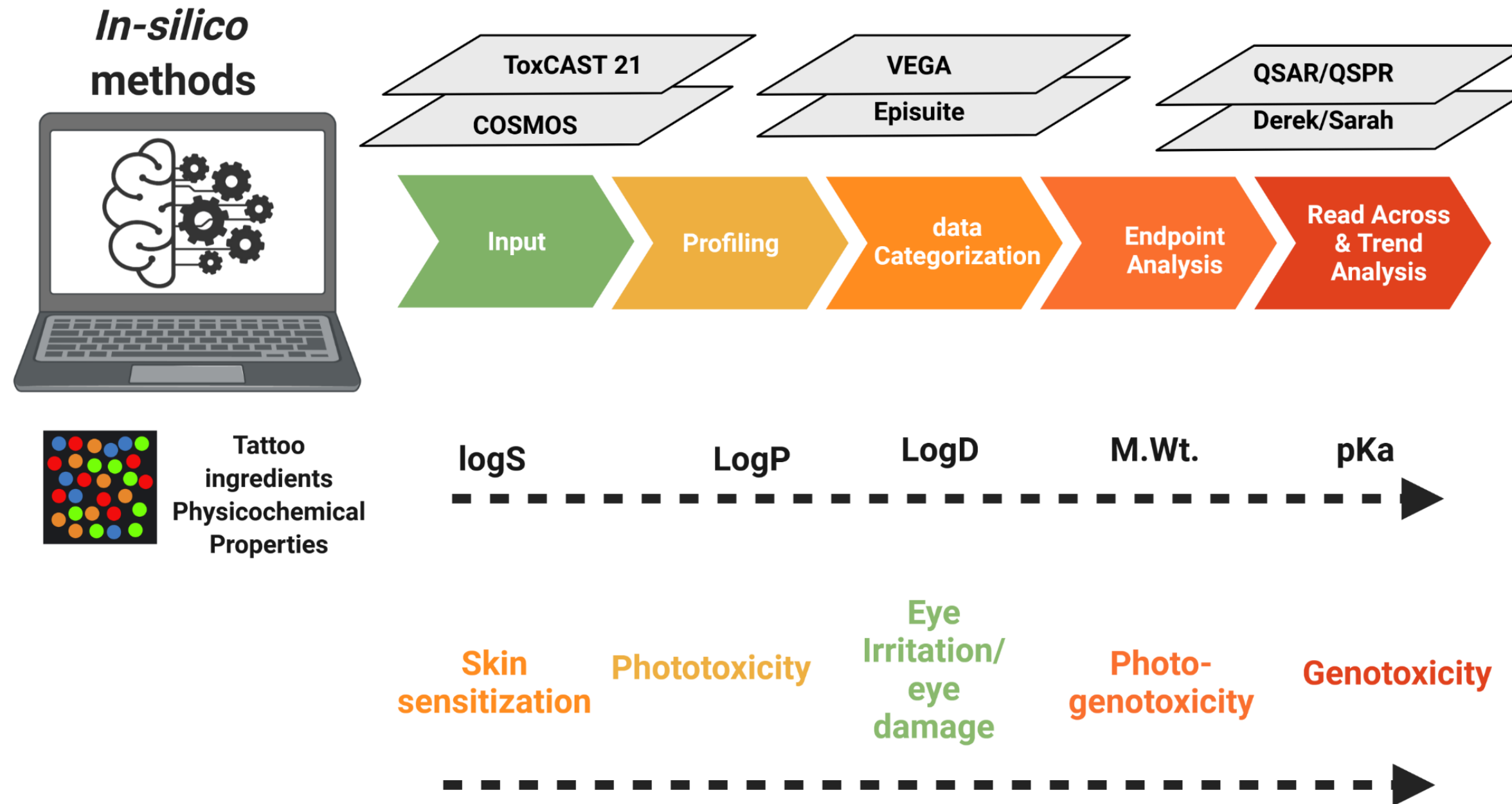
Main target: Exposure assessment and kinetics of soluble ingredients
<https://www.bfr.bund.de/cm/343/bioverfuegbarkeit-von-taetowiermittel-inhaltsstoffen-flyer.pdf>

Tattoos in cancer epidemiology



IVDK Extended medical anamnesis for tattooed persons

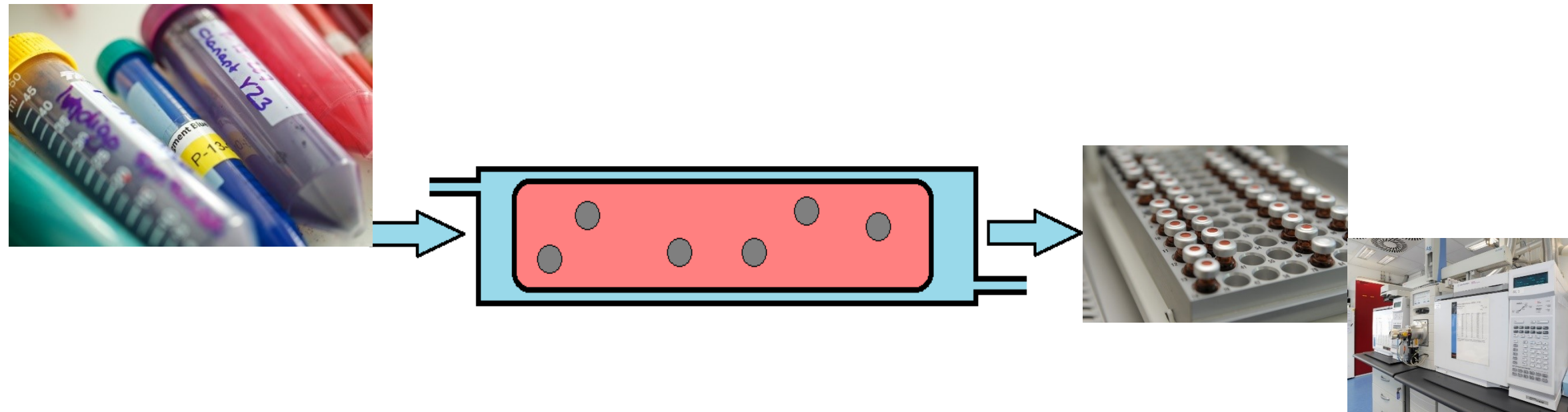




Abbreviations: Estimation Programs Interface Suite™ (EPI Suite), Toxicology Testing in the 21st Century (Tox21), Quantitative structure–activity relationship/quantitative structure–property relationships (QSAR/QSPR) models, LogS (Solubility), LogD (Distribution Coefficient D at PH=7.4), LogP (Octanol-water partition coefficient), M.Wt. (Molecular weight), pKa (The logarithmic acid dissociation constant)

To be developed: *In-vitro* approach for investigation of pigment dissolution

- Long-term dynamic dissolution testing of tattoo pigments in skin simulant
- External factors like UV or temperature
- Fractionated sampling and analysis of pigments and/or metabolites
- Identification of pigments that release harmful substances under physiological conditions



Steps towards implementation and tasks of the BfR

Manufacturers / distributors comply on a voluntary basis with data requirements for the:

- Specification of ingredients of tattoo inks
- Toxicological minimum requirements for pigments

- Review of the integrity and validity of the data
- No complete risk assessment possible today due to missing data & test methods
- No recommendation for pigments in tattoo inks
- Compliance with minimum requirements establishes a safety level according to the current state of art
- Chemical safety will be recognized by consumer and industry

Establishment of an international BfR-Committee on Tattoo Inks:

Independent experts who will advise BfR regarding tattoo ink safety

Thank you for your attention

Dr. Michael Giulbudagian, Dr. Peter Laux

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