

Minutes | April 18th, 2024

3rd Meeting of the BfR Commission on Tattoo Inks

The BfR Commission on Tattoo Inks advises the German Federal Institute for Risk Assessment (BfR) as an honorary and independent expert body on issues of tattoo ink safety and risk assessment by giving counsel to the BfR on the development and adjustment of analytical and toxicological methods (focus on human studies and NAMs) suitable for inks and pigments. The activities are performed in close cooperation with the existing bodies of standardisation such as the International Organisation for Standardisation (ISO) or the Organisation for Economic Co-operation and Development (OECD). Furthermore, the Commission ensures a continuous dialogue with the state surveillance agencies.

With its scientific expertise, the Commission advises the BfR and can assist the Institute as a network of experts in the event of a crisis. The Commission consists of 23 members appointed for a four-year term through an open tender and application procedure. They distinguish themselves through scientific expertise in their respective field. The members of the Commission are obliged to preserve confidentiality towards third parties and to fulfil their duties impartially. Any conflicts of interest regarding individual agenda items (TOPs) discussed in the meeting are subject to transparent queries and disclosure. The meeting minutes below reflect the scientific opinion of the BfR Commission. The Commission's recommendations are entirely advisory in nature. The Commission itself does not issue any decisions or expert opinions and is not authorised to issue instructions to the BfR (and vice versa), nor is it involved in the institute's risk assessments.

Item (TOP) 1 Welcome and adoption of the agenda

The chairperson opens the commission's 3rd meeting and welcomes the participants acknowledging the subcommission meetings held the previous day and the last meeting in November 2023. She highlights the presence of all subcommissions for the current meeting and invites attendees to raise

objections or propose additions to the agenda, if any. No objections are raised by the commission members.

Item (TOP) 2 Declaration on conflicts of interest

Participants are invited to declare any conflicts of interest, especially if changes occurred since the last meeting. The participants declare to have no conflict of interest. The consent of the participants to record the sessions is obtained.

Item (TOP) 3 Summary of previous subcommission meetings on 17.04.2024

The chairperson shortly summarises the presentations and discussions from the three subcommission meetings on the previous day.

In the analytics subcommission, the progress of the MALDI-ToF and FTIR development at BfR was presented. It was pointed out that there are still problems finding pigment traces and that the lack of pigment standards prevails. It was discussed if these standards should be pure or whether a known degree of purity would suffice and whether a prioritisation should be applied based on the (potential) hazards and risks of the individual pigments. The BfR proposed to investigate possible sources for the preparation or the supply of standard pigments. The urgent need for standards was confirmed by the commission members and the BfR's initiative was welcomed. Meanwhile, the BfR started the development of a tiered approach for the screening of tattoo pigments in inks and showed an early version. Again, such an approach was welcomed by the commission members and suggestions in regard to the inclusion of certain analytical techniques and decision nodes for specific pairs of pigments (e.g. PB 15:3 vs PB 60) were made. The suggested analytical methods and

preparation steps were discussed, including the regulatory applicability of these techniques.

In the toxicology subcommission session, the BfR presented on the application of an *in silico* toolbox integrated with experimental New Approach Methods (NAMs) for genotoxicity analysis for the safety assessment of tattoo pigments. In the following discussion, suggestions regarding the applied toxicological methodology were made to further advance the approach. Furthermore, the unique challenges of exposure estimation for tattoo inks and pigments are emphasised by commission members and it is discussed whether ISO 10993-17 guidelines should be adopted/adapted for risk assessment of tattoo inks.

In the technology and hygiene subcommission session, BfR reported on two studies on microbial contamination of products used during tattooing (i.e. tattoo inks and tattoo associated skin care products, respectively). In short, in both studies already opened products were analysed regarding their microbial contamination. Each study found small fractions (2 out of 39 and 5 out of 106, respectively) of contaminated samples.

Item (TOP) 4 BfR – Tiered approach for pigment screening

The BfR presented its draft of the tiered approach for tattoo pigments in inks, including some remarks received in the subcommission session, in order to discuss it within the whole commission. It was discussed that for the testing of regulatory limits (e.g. 0.1 %) HPLC methods are likely required. The problem of missing analytical standards and different options for acquiring tattoo pigments to be used as analytical standards were discussed. Commission members also reported that a synthesis is feasible and has led to 98 % purity. Nevertheless, it was agreed that such an approach is not feasible for widespread supply of standards for different laboratories or stakeholders. Regarding the purity of such standards, it was concluded that 100 % purity may not be required as long as the purity and

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impurities of these standards are known. Therefore, cleaning and characterising several pigments to create a library of the most relevant pigments was considered. The characterised pigments from such a library may then be used by different stakeholders, especially for equipment calibration and interlaboratory comparison. The use of NMR and the applicability and challenges for tattoo pigment and ink analysis were shortly discussed.

Item (TOP) 5 Guest speaker – Immunotoxic effects of tattoo ink in the immune compartment

A guest speaker presented on a mouse-based study of the immunotoxic effects of tattoo ink in the immune compartment. During the talk several key points were highlighted: the transportation of ink via the lymphatic system, the capture of the pigments by phagocytes and the initiation of an inflammatory response which leads to a chronic inflammatory environment. Furthermore, open questions regarding the consequences of ink accumulation under various conditions were raised. Following the presentation questions regarding the immunomodulatory effects of tattoo inks, the technical challenges when analysing ink-laden lymph nodes, the relevance of the presented findings in human models compared to mice, the importance of verification of the injected ink quantities, the estimation of tattooed ink fraction in blood, and the correlation between ink colour and observed chronic inflammatory responses were discussed.

Item (TOP) 6 BfR – Studies with relevance to microbial contamination of products used during tattooing

Since the sterility of tattoo inks is an important aspect, the two studies on microbial contamination of products used during tattooing introduced during the technology and hygiene subcommission were discussed within the commission with all members. In short, in both studies already opened

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products were analysed regarding their microbiological contamination. Each study found a small fraction (2 out of 39 and 5 out of 106, respectively) of contaminated samples. After the presentation, the advantages and disadvantages of analytical methods for microbiological contamination were briefly discussed. Similarly, different sterilisation methods and sterilisation standard operating procedures were discussed. The question was raised whether the sterilisation of tattoo inks should be required and whether this could also be included in a tiered approach. It was remarked that several tattoo ink manufactures include a sterilisation process. Nevertheless, it was mentioned that some sterilisation techniques may affect the stability of the pigments and can also initiate reactions of other constituents in the ink matrix creating hazardous substances in the process. It was discussed whether a sterilisation step should be an explicit requirement or whether a limit value for microbial contamination in the finished product would be the best approach.

Item (TOP) 7 Any other business

All members are satisfied with the discussion and no further points are raised.

Item (TOP) 8 Planning of the next meeting

A next round of online meetings is proposed for the following topics: analytics, toxicology, hygiene and technology. It is agreed to hold them between the end of June and beginning of July. The BfR has already distributed three polls to find the best date for each meeting.

Possible dates for the next general meeting of the BfR Commission on Tattoo Inks are discussed and it is decided that the 4th meeting of the BfR Tattoo Commission for Tattoo Inks should be scheduled for the end of

October or beginning of November and again take place as an online conference. BfR has sent out a poll to all members to determine the exact dates.

Contact

Administration of
BfR Commission on Tattoo Inks
tattooinkcommission@bfr.bund.de

Further Information on the BfR's Commissions
BFR-kommissionen@bfr.bund.de
bfr.bund.de/en/the_bfr_commissions-644.html