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Leachables in syringes containing ethanol, propofol or mRNA vaccine

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Background and Importance: Leachables are chemical compounds that migrate from packaging materials into the content during regular use. They can cause potential health risks alone or in interaction with other compounds of the pharmaceutical formulation. We expect a higher risk in lipophilic solvents such as complex emulsions. Especially in new formulations such as mRNA vaccines, leachables may cause unknown interactions and are possibly present in higher amounts. Identifying and quantifying this contamination is crucial to ensure product safety. Since the manufacturer (SPC) ensures that the stability of the vaccine in syringes is 12 hours after filling, knowledge about the leachables preparations is of interest.

Aim and Objectives: Our aim is to determine the concentration of leachables in syringes filled with lipophilic substances. In addition we seek to identify the major component of the leachables fraction.

Materials and Methods: Emulsions of Comirnaty®, propofol and ethanol were stored at room temperature in plastic syringes for 2 weeks. Leachables were quantified at 3, 5, 12 hours and 14 days after filling. The samples were analysed by HPLC (Ultimate 3000®, Thermo Scientific) coupled with mass spectrometry (4000 qTrap®, Sciex), GC-MS (8890GC System®, Agilent) and UV-spectrometry (DrugLog®, Pharmacolog).

Results: In all samples significant amounts of leachables could be detected irrespectively of the chosen method (Fig.1 and Fig. 2). Using GC-MS,the main leachable product, Vulkanox BKF, could be identified as main leachable, which was also confirmed by LC-MS. Quantification could be performed by HPLC-UV (Fig. 3). UV (Druglog®) provided more general confirmation of leachables, but lacked the specificity required for precise quantification. The concentration of Vulkanox BKF in Comirnaty® vaccine samples and propofol was similarly measured over time. In ethanol, all concentrations were more then ca. 10 times higher compared with the emulsions.

Identification of major leachable component

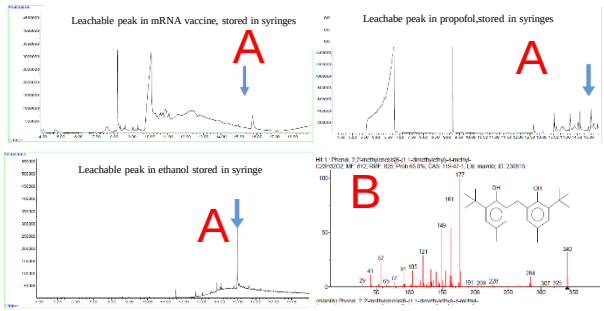

Fig.1: Identification of Vulkanox BKF by GC-MS with GC MS database
A = measured Mass Spektrum **B** = theoretical Mass Spectrum in the database

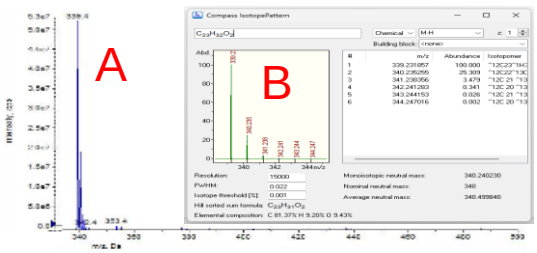

Fig.2: Identification of Vulkanox BKF by LC-MS
A = measured mass spectrum **B** = theoretical mass spectrum

Quantification of Vulkanox BKF at 210nm

Tab.1: Vulkanox BKF concentrations after storage in a syringe for 12h

Name	Conc. (µg/ml)	Name	Conc. (µg/ml)	Name	Conc. (µg/ml)
Comirnaty®	2,5	EtOH 12h	77,0	Propofol	6,1

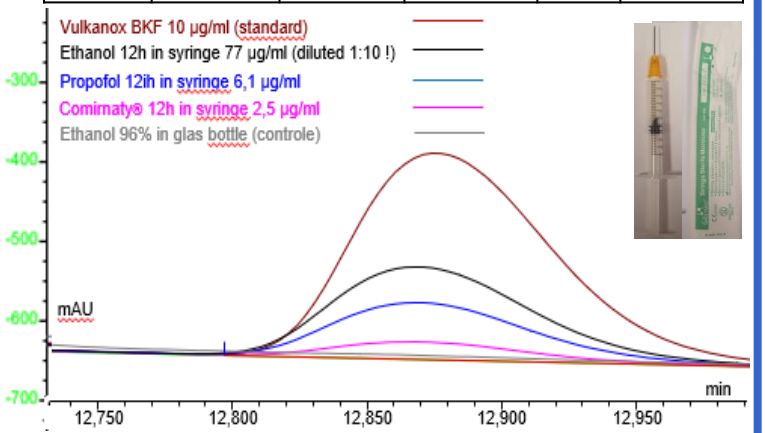

Fig.3: Quantification of Vulkanox BKF by HPLC-UV

Conclusions: Our data show that significant amount of leachable can be detected less then 12 hours. The measured concentrations itself are not hazardous, but it is important that a possible influence on the stability can not be ruled out. With mRNA-vaccines, sufficient knowledge on possible interactions is not yet published. Regulatory guidelines should ensure that the migration of leachables remains low. Since, prolonged exposure or higher concentrations of these compounds could increase risks.

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