WHITE PAPER

The Determination of Metals in Non-Medical Face Masks

Introduction

With the onset of the COVID-19 pandemic, the use of face masks by the general public has become a critical personal protective measure to minimize person-to-person transmission. While health care workers use medical or surgical masks, including the N-95 respirator face masks for the most complete protection, the general population uses non-medical, otherwise known as hygienic, face masks to greatly reduce the transmission of SARS-CoV-2 by capturing droplets and aerosols from those infected with the virus.

In response to the increased demand for both the number and variety of non-medical face masks, many companies are now producing them to meet the public's need. With this great variety, the quality and the safety of the face masks must be assessed. From a safety perspective, biocompatibility is an important criterion. A common standard for biocompatibility is based on ISO 10993; products are tested for characteristics and properties of the material, which include chemical, toxicological, physical, electrical, morphological and mechanical properties. Two important biocompatibility components that should be tested for are the levels of volatile organic compounds (VOCs) and metals. Work is available describing the analysis of VOCs in face masks; whereas, this work will discuss the considerations for the analysis of metals in face masks.

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Regulations for Metals in Face Masks

Globally, there are no consistent regulations or agreed-upon levels of metals in hygienic face masks, with different regions having different classifications, metals, and limits. However, ISO 18562-4:2017 Biocompatibility Evaluation of Breathing Gas Pathways in Healthcare Applications – Part 4: Leachables in Condensate[1] provides guidance. While not specific to hygienic face masks, ISO 18562-4:2017 discusses the sample preparation, analytes, and methodologies for evaluating the quality of the data.

ISO 18562-4:2017: Analytes and Concentrations

The analytes and limits are defined by USP <232>.[2] The limits are based on the route of administration: oral, inhalation, or parenteral. Since face masks cover the nose and mouth, the route of administration is inhalation. Table 1 shows the analytes and the maximum per daily exposure (PDE) for inhalation, as defined in USP <232>.

Table 1. Analytes and Maximum PDE for Inhalation, as Defined in USP <232>.

Elements	PDE (µg/day)
Au, Hg, Ir, Os, Pd, Pt, Rh, Ru, V	1
As	2
Cd, Co, Cr	3
Ni, Pb	5
Ag	7
Tl	8
Mo	10
Sb	20
Li	25
Cu	30
Sn	60
Se	130
Ba	300

USP <232> defines the relevant concentrations as the J value, according the following equation:

$$J = \frac{PDE}{\text{Maximum Daily Dose} * \text{Dilution Factor}}$$

PDE = maximum permissible daily exposure (µg/g)

Maximum Daily Dose = maximum amount of the medication consumed

Dilution Factor = dilution used in sample preparation = mass of sample/sample preparation volume

For breathing apparatus, ISO 18562-4:2017 defines the maximum daily exposure of condensate as 1 mL, which would be equivalent to the "Maximum Daily Dose" in the "J" equation. The mass of the sample can vary with the type of face mask analyzed, while the sample preparation volume is decided by the lab. The only requirement is that the water completely covers the face mask liner.

Given the variation in PDE among the elements, the J value can be complex to calculate. To facilitate this, PerkinElmer has a J-Value Calculator available,[3] where all parameters are entered, and the J values are determined.

ISO 18562-4:2017: Sample Preparation

The most important aspect to attaining meaningful results is establishing a sample preparation procedure. While total microwave digestion at elevated temperatures and pressures may seem like the obvious preparation technique since the total metal content in the face mask will be determined, this sample preparation is not clinically relevant since the wearer will not be exposed to all metals in the face mask – only those that are leached while wearing the face mask. Nevertheless, a risk assessment should be performed on random samples with total digestion to establish the presence and total concentrations of the analytes, as listed in Table 1.

ISO 18562 specifies that "leachable substances" should be analyzed. Three options are given for collecting the sample:

1. Collect condensate under clinically relevant conditions
2. Circulate water over the sample surface at a clinically relevant temperature
3. Provide aqueous extract on the internal gas contact surface at clinically relevant temperatures and time, following ISO 10993-12:2012[4]

The important points are that leaches/extractions should be used and should be conducted under clinically relevant temperatures and times. Since face masks cover the nose and mouth, body temperature (37 °C) is the appropriate temperature to perform the leach. However, since face masks can be worn from minutes to hours depending on the circumstance (i.e. grocery shopping or being in an office), leach timeframes can vary significantly.

ISO 10993-12:2012 states that devices which are in short-term contact with skin should be leached at 37 °C for less than 24 hours, but not less than 4 hours. However, ISO 18562-4:2017 states that "there is no clinical relevance to performing a 24-hour extraction on a medical device that is only intended to be used on a patient for 20 minutes." This statement emphasizes the importance of performing the extract for an appropriate time. Given the variability in the time face masks are worn, it makes sense to withdraw aliquots of the extraction medium at various times during the extraction.

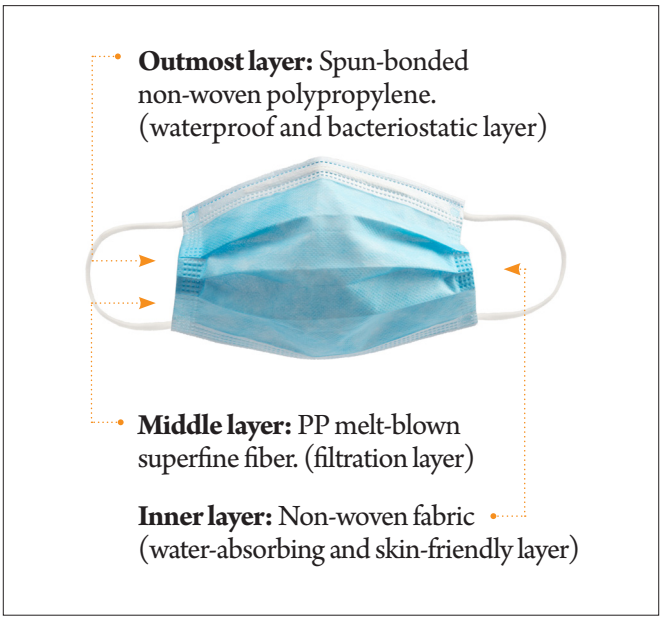

Figure 1. Components of a typical disposable hygienic face mask.

The third option for sample preparation states that the extract should be performed on "internal gas contact surfaces". Since most masks contain multiple layers, extraction should only be performed on the innermost layer which is in contact with the nose and mouth. Figure 1 shows the components of a typical disposable hygienic face mask, the most common type in use. Therefore, the inner layer of the mask should be removed for extraction, but it is very difficult to perform the extraction on only one side of the inner layer since it is so thin. However, to minimize non-contact surfaces undergoing extraction, the inner layer should not be cut into pieces. Instead, the extraction should be performed on the whole, intact inner layer.

Ideally, the extraction medium should be water, to simulate human breath, instead of acid. However, this presents an issue since the analytes listed in Table 1 are not stable in aqueous solutions without acid. A further complication is that the analytes are not all stable is a single acid: most of the analytes listed in Table 1 are stable in nitric acid, although several are not (i.e. the platinum group elements) – these are only stable in hydrochloric acid. Therefore, it is best to perform extraction with a mixture of hydrochloric and nitric acids to stabilize all analytes. However, because acid is more aggressive than water, this raises the concern that the concentration of analytes extracted with acid may not be representative of those which a user is exposed to given that human breath is non-acidic. To alleviate this discrepancy, a risk assessment should be performed on a representative sample from a package or batch via a total digestion of the inner layer of the face mask to see what analytes are present and, for those that are, if they are present at relevant concentrations, as established by the J value. Any analyte present in the leach at < 0.3 J is not considered important, as 0.3 J is a common actionable threshold within the pharmaceutical community when implementing USP <232>/<233>.

Considering the above discussion, sample preparation would involve:

1. Removing the inner layers from face masks
2. Performing a total digestion on one of the inner layers using a closed-vessel microwave digestion system
3. Performing a leach/extraction on the others by:
    a) Placing the liner in an extraction vessel
    b) Covering the liner with acid
    c) Capping the vessel
    d) Heating at 37 °C for a time representing the length of time a face mask would be worn

ISO 18562-4:2017: Evaluation of the Methodology

ISO 18562-2:2017 states that the methodology should be evaluated/validated following the criteria in USP <233>[5], as shown in Table 2: accuracy, repeatability, ruggedness, and system suitability. These criteria involve preparing 10 different samples of the same type and evaluating sample preparation, accuracy, and stability. These validations should be performed on the leachate, though they may also be performed on the total digestion as part of the risk assessment.

Table 2. Analytical Criteria Defined in USP <233> for Quantitative Procedures.

Criteria	Description
Accuracy	Spike recoveries of 0.5 J, J, and 1.5 J must be between 70-150%
Repeatability	The RSDs of measurements of six independent samples spiked at J must be less than 20%
Ruggedness	Six solutions must be analyzed on different days, with different instruments, or with different analysts. The RSDs over the 12 measurements must be less than 25%
System Suitability	The difference in the results of the high calibration standard (1.5 J) measured at the beginning and end of a batch must be < 20%

Summary

Although no specific methodology or regulations exist for the determination of metals in hygienic face masks, ISO 18562-4:2017 references USP methods <232> and <233> to define the analytes, concentrations, and validation of the analytical methodology. ISO 18562-4:2017 also lists three sample preparation options, including ISO 10993-12:2012. By combining criteria from both ISO and USP methods, the metal content in hygienic face masks can be determined.

References

1. ISO 18562-4:2017 Biocompatibility Evaluation of Breathing Gas Pathways in Healthcare Applications Part 4: Leachables in Condensate, ISO 2017.
2. General Chapter <232> Elemental Impurities – Limits, 2nd Supplement of USP 35-NF 30, United States Pharmacopeia.
3. PerkinElmer J-Value Calculator, PerkinElmer, 2019.
4. ISO 10993-12:2012 Biological Evaluation of Medical Devices – Part 12: Sample Preparation and Reference Materials, ISO 2012.
5. General Chapter <233> Elemental Impurities – Procedures, 2nd Supplement of USP 35-NF 30, United States Pharmacopeia.

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