The Director General

Maisons-Alfort, 23 October 2020

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on the estimation of potential risks associated with wearing masks treated with silver zeolite and silver-copper zeolite

On 15 October 2020, ANSES received a formal request from the Directorate General for Risk Prevention, the Directorate General for Health, the Directorate General for Labour and the Directorate General for Competition Policy, Consumer Affairs and Fraud Control to conduct the following expert appraisal: Estimation of potential risks associated with wearing masks treated with silver zeolite and silver-copper zeolite.

1. BACKGROUND AND PURPOSE OF THE REQUEST

As part of efforts to control the COVID-19 pandemic, recommended barrier gestures include wearing a mask, particularly when social distancing is impossible. Masks are compulsory in all public areas, whether open or closed, as well as in most workplaces.

Excluding a number of specific work situations where masks are required as personal protective equipment, the protective face coverings worn to control the spread of the COVID-19 pandemic can be made of washable and reusable cloth. Using washable cloth masks prevents a significant amount of waste.

In this context, the company Hanes France has brought to market cloth masks comprising three superimposed layers of white cotton jersey. To produce these masks, Hanes conducted tests to demonstrate their compliance with technical requirements relating to air permeability and to the effectiveness of particle filtration for non-medical use. The labelling on the masks states that the cloth has been treated with silver zeolite and silver-copper zeolite.

Silver zeolite and silver-copper zeolite are biocidal active substances whose use is regulated by European Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products (known as the Biocides Regulation). Both substances are included in the European review programme of existing active substances[1] for the following biocidal product types (PTs): 2 (disinfectants not intended for direct application to humans or animals), 4 (disinfectants for surfaces in contact with foodstuffs), 7 (film preservatives - particularly paints) and 9 (fibre, leather, rubber and polymerised materials preservatives). These silver compounds are used primarily in manufactured articles to protect them from microbial damage (PTs 7 and 9), or to endow them with antimicrobial properties (PTs 2 and 4).

According to the Biocides Regulation therefore, the use of these two substances in fabric may concern either PT 2 or PT 9.

Following an assessment by the Swedish authorities, appointed as the evaluating competent authority, the European Commission adopted decisions in November 2019 not approving silver copper zeolite and silver zeolite as existing active substances for use in biocidal products of product-types 2 and 7. They can therefore no longer be used for applications relating to PT 2 and PT 7.

For PT 4 and PT 9, the assessments of these two active substances are not yet complete. As a result, they can be used to protect the fibres of treated fabric (PT 9).

More generally, the active substances silver zeolite, silver-copper zeolite and other silver compounds are used in the manufacture and treatment of many articles, including consumer products (paint, sealant, textiles, furnishings, hygiene or healthcare items, etc.) in order to provide them with antimicrobial properties.

Following questions in the press on the safety of these two substances and the risk incurred by people wearing these protective masks, ANSES was asked to estimate the potential risks associated with wearing masks treated with silver zeolite and silver-copper zeolite. As the masks are already in use today, an urgent assessment was requested.

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French standard NF X 50-110 “Quality in Expert Appraisals – General requirements of Competence for Expert Appraisals (May 2003)”.

The appraisal was carried out by the ANSES Regulated Products Assessment Department (DEPR) with the support of the Risk Assessment Department (DER). It was discussed and approved by the “Biocidal substances and products” Specialized Expert Committee (CES) on 22 October 2020.

ANSES analyses interests declared by experts before they are appointed and throughout their work in order to prevent any risks of conflicts of interest in relation to the points addressed in expert appraisals.

[1] Commission Delegated Regulation (EU) No 1062/2014 of 4 August 2014 on the work programme for the systematic examination of all existing active substances contained in biocidal products referred to in European Regulation (EU) No 528/2012 of the European Parliament and of the Council.

The experts' declarations of interests are made public via the ANSES website (www.anses.fr).

In response to the request and taking account of the urgency of the question raised, ANSES did not carry out a review of the scientific literature but relied on assessments carried out by the public authorities and already peer-reviewed at European level. The assessment carried out is therefore based on:

- the two draft Competent Authority Reports (draft CARs) produced as part of the European assessment of these two biocidal active substances for product types 2, 4, 7 and 9. These assessment reports, prepared by the Swedish competent authority and yet to be finalised (not publicly available to date), have been reviewed by the European member states and were presented at the meeting of the Biocidal Products Committee (BPC) of the European Chemicals Agency (ECHA) in December 2018.

- The opinion of the ECHA Committee for Risk Assessment (RAC) of 4 December 2015 proposing harmonised classification of silver-zinc zeolite[2].

- The assessment report on copper sulphate pentahydrate as a biocidal active substance for PT 2, published in September 2013[3].

ANSES also relied on the technical information provided by Hanes France on Monday 19 October 2020 at its request. Not all of this information was supported by experimental test reports, so it could not be checked by ANSES.

Moreover, ANSES contacted the Belgian authorities, the US Food and Drug Administration (FDA) and the US National Institute for Occupational Safety and Health (NIOSH) to discuss any studies carried out by their organisations in relation to protective masks treated with silver compounds.

[2] https://echa.europa.eu/documents/10162/ce343f0e-623b-7678-586e-613dffbcfe06

[3] https://echa.europa.eu/fr/information-on-chemicals/biocidal-active-substances/-/disas/factsheet/1276/PT02

3. Analysis and conclusions of the CES

3.1. Physico-chemical characteristics of the active substances and treated fabric

According to the information provided by Hanes France and its supplier, the manufacturer of the biocidal product used to treat the fabric of the masks is part of a consortium that submitted applications for the approval of the two active substances at European level. Moreover, it is on the list of authorised suppliers as set out in Article 95 of the Biocides Regulation. It is therefore expected that the physico-chemical characteristics of the active substances contained in the biocidal product will be as described in the assessment reports of the competent authority.

3.1.1. Physico-chemical properties of the active substances

From a physico-chemical viewpoint, it is important to make a distinction between two entities:

- The zeolite
- The Ag^+ and Cu^{2+} cations incorporated within the zeolite.

Zeolites are crystalline aluminosilicates of natural or synthetic origin. Characterised by high thermal stability, they are considered as insoluble in solvents (including water). They have an organised microporous structure and are non-volatile (vapour pressure considered as zero). The zeolite used to prepare the active substances contained in the masks is synthetic. It is a Linde Type-A zeolite (also called zeolite A) characterised by the formula $Na_n.Al_nSi_{1-n}O_2.xH_2O$, containing micropores of controlled size.

The active substances are obtained through an ion exchange process in which silver Ag^+ ions (or silver Ag^+ ions and copper Cu^{2+} ions) replace some of the sodium ions, thereby forming silver zeolite (or silver-copper zeolite). The silver and copper ion content is known in the case of the zeolites used in the treatment of Hanes brand masks.

Based on the particle-size distributions specified in the dossiers submitted for the approval of these active substances, neither the silver zeolite nor the silver-copper zeolite used to make the Hanes masks are considered as nanoparticles, as defined by the EU regulation. Laser diffraction analyses show that the zeolite crystals have a diameter of between 0.39 µm and 23 µm, with an average of between 2.5 and 2.8 µm. As a result, they cannot be described as nanoparticles, which have a diameter of less than 0.1 µm.

Nor are they considered to include silver nanoparticles (metal), as the process does not include a redox reaction following the ion transfer stage. The silver ions are not therefore reduced to elemental silver. Looking beyond the improbable event of the formation of silver nanoparticles, the very structure of zeolite A would prevent their release in the form of nanoparticles: the diameter of the channels connecting the micropores of the zeolites in which the Ag^+ ions are found is around 0.4 nm for zeolite A. Given the diameter of a silver atom (0.29 nm), the formation of nanoparticle aggregates of elementary silver in the pores (1.1 nm in diameter in zeolite A) could result only in a monoatomic release.

3.1.2. Active substance content in the treated fabric

Several processes exist for fabric treatment. For cotton masks, the mixture used contains silver zeolite and silver-copper zeolite. It is called Agion AM-B10G Slurry. This mixture also contains an acrylic polymer binder to permanently bind the zeolites to the cotton fibres.

The three layers of fabric making up the masks were treated with the zeolite/binder mixture. The content guaranteed by the manufacturer in the treated fabric before washing is as follows (see Table 1).

Table 1: active substance content of the masks

Substance	Identification (CAS No.)	mg for a 15g mask	ppm (µg/g of mask)
Silver-copper zeolite	130328-19-7	21	1363
Silver zeolite	130328-18-6	14	909
Silver equivalent	*7440-22-4*	*1*	*69*
Copper equivalent	*7440-50-8*	*1.2*	*80.5*

The copper content specified is consistent with the copper content of the silver-copper zeolite described in the application for approval submitted at European level. However, the silver content is likely to be 93 ppm rather than 69 ppm based on the average silver content of the two zeolites, as specified in the European assessment. Taking a conservative approach, the experts therefore applied a value of 93 µg Ag/g of mask for the risk assessment.

In a liquid medium, the rate of release of Ag^{+} and Cu^{2+} ions depends on the medium with which the zeolites are in contact. The rate of release depends primarily on the presence in the medium of cations, able to replace the silver and copper ions in the zeolite, and of molecules with an affinity for copper or silver ions, thus promoting their release. This phenomenon is expected to be the cause of the decrease in metal ion content observed after the masks have been washed or after they come into contact with sweat and saliva.

3.1.3.Technical characteristics of the mask

The masks sold by Hanes are protective masks comprising three layers of treated cotton jersey of 135 g/m². The fasteners are made of reinforced cotton with covered elastic.

The mask is 12.7 cm high in the middle and 17.8 cm wide. The surface area of the treated fabric in contact with the skin is therefore assumed to be 226 cm².

Hanes provided the results of a study assessing the amount of silver and copper released every time the mask is machine washed (washing conditions are not described in detail). The results show silver and copper content to fall by 19% and 27% respectively after the first wash. After 20 washes, less than 20% of the initial silver and copper content remains in the mask.

There are two – possibly concomitant – explanations for this decrease: either the washing process mechanically separates some of the zeolites present on the fibres of the fabric, or an ion exchange takes place owing to the many cationic species present in the detergent.

3.2. Identification of the hazards of silver zeolite and silver-copper zeolite

The hazard properties of the two active substances – silver-copper zeolite and silver zeolite – were described in the two draft assessment reports of the Swedish competent authority, as part of the European assessment submitted to the BPC in December 2018.

The zeolite, and also the incorporated silver and copper ions, can represent a potential hazard for human health.

3.2.1.Toxicological profile of the zeolite

The risks to human health associated with the use of zeolite A were assessed as part of the HERA (Human and Environmental Risk Assessment) initiative set up by industrial groups representing formulators, manufacturers and suppliers of cleaning products. HERA published a comprehensive review of the toxicological data available on zeolite A in January 2004[4]. This assessment was reviewed by the Swedish authorities as part of the approval applications for both active substances.

Zeolite A (sodium aluminium silicate) is not acutely toxic by the oral and dermal route. Zeolite A is non-irritating to the skin and only slightly irritating to the eyes through mechanical friction if it is in the form of an undiluted powder.
Based on available studies, zeolite A is not a skin or respiratory sensitiser. It is neither genotoxic nor carcinogenic.

Studies on chronic toxicity by the oral route have shown that zeolite A can cause adverse effects in the urinary tract, but only at high doses.

A study of chronic toxicity by the inhalation route in primates showed local dust effects such as focal non-suppurative inflammatory reactions (bronchiolitis and alveolitis) in monkeys exposed to 1.6 and 50 mg/m^3 for six hours, five days a week for up to 55 weeks.

The non-suppurative inflammation decreased in severity, without disappearing completely, in the groups receiving high and medium doses after a 90-day recovery period. The upper respiratory tracts of the primates were not affected. There was no evidence of progressive fibrotic lung disease or systemic toxicity in this study or in other less reliable studies on rats, guinea pigs or hamsters.

In the absence of the original study report, it is only possible to conclude that local inflammation of the lungs can be expected after inhalation. However, since the maximum dose (50 µg/L) is well below the threshold dose required by the OECD guideline 413[5] (5 mg/L), other possible effects at higher doses cannot be ruled out.

Data on developmental toxicity show that zeolite A is not teratogenic. Long-term toxicity studies show that the reproductive organs are not affected by the ingestion or inhalation of zeolite A.

[4] Human & Environmental Risk Assessment on ingredients of European household cleaning products, Zeolite A represented by CAS Number 1344-00-9 (Sodium Aluminium Silicate) and by CAS Number 1318-02-1 (Zeolites), Version 3.0, January 2004.
[5] OECD Guideline 413 (Sub-chronic) Inhalation Toxicity: 90-day study

In view of the toxicological profile of the zeolite, the Swedish authorities considered the toxic effects of the two active substances – silver zeolite and silver-copper zeolite – to be caused by the release of Ag^+ and Cu^{2+} ions. Given that the uses studied as part of the European assessment do not include the wearing of masks, exposure through inhalation was considered as negligible. This approach was validated by the BPC during the EU review.

Wearing a mask is nevertheless likely to lead to exposure through inhalation. If zeolite particles are transferred through the inhaled air, given the effects observed in the experimental study on primates and in comparable conditions of exposure, a reversible lung inflammation cannot be ruled out.

3.2.1. Toxicological profile and toxicity reference values of silver ions

In the absence of a complete toxicology data set for each of the active substances containing silver, the different toxic effects were assessed on the basis of a data set generated from several active substances containing silver[6].

Based on data specific to each substance (silver content of the active substance, silver ions released from the active substance in conditions reproducing physiological conditions), the actual exposure to silver in the different studies was calculated in order to establish the NOAEL[7] as a silver ion equivalent. This approach was considered as acceptable at European level.

Toxicokinetic data

Oral absorption: Based on the most robust data obtained with silver nitrate, it was established that 5% of the silver ions released by the active substances are absorbed orally.

Dermal absorption: The dermal absorption of silver considered in the European assessment reports is based on studies taken from the scientific literature, conducted using water-soluble silver salts. These studies show that dermal absorption is generally lower than 1%. These data were used to refine the default absorption value from 100% to 5% as a conservative estimate. This conclusion is supported by the fact that oral absorption (5%) rarely exceeds dermal absorption.

Acute toxicity

Acute toxicity studies in animals show low acute toxicity by the oral and dermal routes and by inhalation. In consequence, silver ions are not classified for acute toxicity.

Irritation/sensitisation

Silver-copper zeolite may cause transient skin and eye irritation, but does not trigger classification. Similarly, silver zeolite may cause eye irritation but does not require labelling as hazardous.

Silver-copper zeolite does not cause skin sensitisation reactions in guinea pigs. Based on a weight-of-evidence approach, silver zeolite is also not considered as a sensitiser.

Genotoxicity

[6] Silver chloride, silver glass, silver sodium hydrogen zirconium phosphate, silver zeolite, silver-copper zeolite, silver-zinc zeolite, silver nitrate, silver(I) oxide.

[7] No observed adverse effect level

The results obtained from silver-zinc zeolite and silver-copper zeolite show a low clastogenic potential *in vitro*. An *in vivo* COMET assay carried out on rats with silver-zinc zeolite was negative. On a weight-of-evidence approach, this allowed us to rule out a genotoxic effect of silver-copper zeolite and silver zeolite.

Carcinogenicity

No specific information exists on the carcinogenic potential of the two active substances, silver-copper zeolite and silver zeolite.

The data available for silver-zinc zeolite and copper sulphate show no carcinogenic potential.

Other toxicities

No neurotoxic or immunotoxic effects were observed in available toxicity studies involving biocidal active substances containing silver ions. Furthermore, the assessment of endocrine-disrupting properties has not been finalised.

Repeated toxicity / reference values

Sub-chronic exposure to a substance containing silver results in elevated alkaline phosphatase levels along with pigmentation of the tissues and organs. These effects are commonly observed in studies on silver.

The most robust data available are based on combined chronic/carcinogenicity studies of mice and rats based on silver-zinc zeolite. The results of these studies show an increased incidence of ovarian cysts, pigmentation of the liver and pancreas and decreased organ weight in mice, along with pigmentation of the liver, kidneys, pancreas, stomach, lymph nodes and choroid plexus in rats.

Organ and tissue pigmentation appears to be an intrinsic property of silver ions, constituting an early marker of silver toxicity. This effect is therefore taken into consideration for the derivation of toxicicological reference values.

The NOAELs established in relevant studies for the derivation of a short-, medium- and long-term acceptable exposure level (AEL) for the active substance are shown in
Table 2 below.

Table 2: Key studies for the derivation of AEL

Study period	Study	Route of administration	Relevant effects	NOAEL
Medium term	Silver sodium hydrogen and zirconium phosphate, 90 days Rats	Oral	Pigmentation of the pancreas and Harderian gland in females Elevated alkaline phosphatase (ALP) in males	21 mg/kg bw/d* Silver ion equivalent: 0.3 mg/kg bw/d
Long term	Silver-zinc zeolite Combined chronic/ carcinogenicity study 105 weeks Rats (non GLP)	Oral	Pigmentation of the liver, kidneys, pancreas, stomach, lymph nodes and choroid plexus	6 mg/kg bw/d** Silver ion equivalent: 0.09 mg / kg bw/d

*Conversion estimate based on data obtained with silver sodium hydrogen and zirconium phosphate
**Conversion estimate based on data obtained with silver-zinc zeolite

The lowest NOAELs for the medium- and long-term toxicity of silver ions were based respectively on the 90-day study of rats conducted with silver sodium hydrogen and zirconium phosphate and on the 105-week combined chronic study on rats conducted with silver-zinc zeolite. These NOAELs were recalculated to take account of the silver content of the substance tested and the rate of release of the silver ions.

In order to derive the toxicological reference values, an oral absorption of 5% and a safety factor of 100 (10 for intra-species variability and 10 for inter-species variability) were used.

In the absence of any observed acute toxicity effect, it is not possible to define a toxicity reference value for short-term exposure. The conservative approach set out in the European assessment is to use the medium-term AEL as the short-term AEL. This value is based on the no observed effect level in rats exposed for 90 days[8].

• Short/medium-term AEL = 0.3 mg/kg bw/d x 5% / 100 = 0.15 µg/kg bw/d (silver ion equivalent)

• Long-term AEL = 0.09 mg/kg bw/d x 5% / 100 = 0.045 µg/kg bw/d (silver ion equivalent)

Reprotoxicity

For silver zeolite, no specific data are available regarding reproductive and fertility toxicity.

A developmental toxicity study is available concerning silver-copper zeolite in rats: no developmental toxicity was observed in pups from dams treated with up to 2,000 mg/kg bw/d. No substance-specific information is available relating to fertility.

Silver-zinc zeolite is classified as a category 2 reproductive substance (Repr. 2; H361d) Suspected of damaging the unborn child (classification harmonised since ATP10 came into force in 2017 (Reg. 2017/776)). It is not classified for effects on fertility, or for effects through or on breastfeeding.

In the 2015 opinion on the classification of silver-zinc zeolite, the ECHA Committee for Risk Assessment (RAC) concluded that there was a potential embryotoxic effect in rats at doses where the dams were not severely affected by the treatment. This was manifested primarily by a decrease in the viability of the foetuses/pups, observed to varying degrees in developmental toxicity studies conducted with silver chloride (post-implantation losses, mortality of all offspring, increased incidence of hydronephrosis and cryptorchidism) and silver acetate (slight increase in the percentage of litters with late foetal death) and in a two-generation study with silver-zinc zeolite (lower number of births (F1[9]), higher stillbirth rate, lower live birth rate, reduced pup weight, lower thymus weight, increased incidence of hydronephrosis). A two-generation study of rats conducted with a different active substance containing silver also observed a lower number of births (F1), along with a smaller live litter size on day 1 (F2[10]), and a lower thymus weight.

[8] The dossier assessed by the Swedish authorities contains a short-term repeated toxicity study that was not taken into account as it was considered to be of lower quality. This study shows a NOAEL 27 times higher than the NOAEL used to derive the medium-term AEL.

[9] F1 = generation of animals with treated parents

[10] F2 = generation of animals born from generation F1

Owing to the structural similarities between silver zeolite, silver-copper zeolite and silver-zinc zeolite, and the similarity of the effects observed with other silver salts that do not contain zinc, the European assessment concluded that silver zeolite and silver-copper zeolite also met the criteria for classification as Repr. 2; H361d.

Based on these data concerning the developmental toxicity of silver-zinc zeolite, a developmental NOAEL was extrapolated for silver zeolite and silver-copper zeolite, expressed as a silver ion equivalent of 1.5 mg/kg bw/d.

To assess the risk associated with the wearing of treated masks, the medium-term AEL was used. The developmental NOAEL expressed as a silver ion equivalent of 1.5 mg/kg bw/d is five times higher than the value used to derive the medium-term AEL. This value is also 16 times higher than the NOAEL used to derive the long-term AEL.

3.2.2. Reference values for copper

No specific data are available on the release of copper ions under physiological conditions. However, given that the active substance is an ion exchanger, it is realistic to assume that copper ions are also released. The potential risks arising from the copper ions released by the treated articles can be assessed by assuming a release of 100% (or a refined value if relevant migration data are available) and by comparing levels of exposure with the reference values established by the EU for copper sulfate pentahydrate.

The toxicological profile of copper is described in the assessment report on copper sulfate pentahydrate, which was approved as an active substance under the Biocides Regulation for type 2 products[11].

In the case of copper sulfate, the short-, medium- and long-term AELs were calculated on the basis of the NOAEL of 1,000 ppm, corresponding to 16.3 mg Cu/kg bw/day obtained in the 90-day oral study of rats conducted with copper sulphate (adverse effects on the kidney and stomach). As a result, the systemic NOAEL, based on the NOAEL of 16.3 mg Cu/kg bw/d and oral absorption of 25%, is 4.1 mg Cu/kg bw/d.

The safety factor considered for short- and medium-term exposure is equivalent to 50, with 5 for inter-species variation and 10 for intra-species variation. The safety factor considered for long-term exposure is thus equivalent to 100, with 5 for inter-species variation and 10 for intra-species variation, plus a factor of 2 for extrapolation of the duration. The AELs considered are therefore as follows:

- short-term AEL = 4.1 / 50 = 0.082 mg Cu/kg bw/d
- medium-term AEL = 4.1 / 50 = 0.082 mg Cu/kg bw/d
- long-term AEL = 4.1 / 100 = 0.041 mg Cu/kg bw/d

A dermal absorption of 5% for copper was considered in order to assess the risk.

[11] Copper sulfate pentahydrate Product-Type 2 (Disinfectants and algaecides not intended for direct application to humans or animals) - September 2013, FR

3.3. Estimating user exposure

Two scenarios were built to assess the exposure of an adult to silver and copper when wearing the mask on healthy skin.

- The first scenario considers the exposure of an adult wearing two new unwashed masks (contrary to the manufacturer's indications) for four hours each over an eight-hour period. This exposure is considered as acute. It takes account primarily of the increased quantity of silver and copper ions released during the first few hours of contact between the new fabric and the skin.

- The second scenario considers the exposure of an adult wearing masks that have been washed once, for eight hours per day. This exposure is considered to be repeated over the medium term. This second scenario does not take account of the observed decrease in zeolite content following subsequent washes.

The routes of exposure considered were dermal and inhalation. The oral route was not considered to be relevant, since wearers are not expected to put the mask in their mouths.

The mask is made from three layers of cotton, each with a density of 135g/m². To calculate the surface area of the mask in contact with the skin, the entire area of 226 cm² was considered to be in contact with the skin of the wearer's face.
The mask was considered to contain 45 ppm of silver from the silver zeolite, 48 ppm of silver from the silver-copper zeolite and 80.5 ppm of copper from the silver-copper zeolite.

A systemic risk assessment was carried out for the dermal and inhalation routes for the silver from both zeolites and for the copper from the silver-copper zeolite.

According to the hypotheses validated by the Swedish competent authority and the physico-chemical characteristics of the substances, the release of silver and copper ions is facilitated by sweat and by the molecules present on the skin as well as by friction with the skin. The moisture exhaled by the wearer is also likely to lead to the release of ions. The inner layer of the mask, which is in direct contact with the skin, therefore contributes directly to the level of exposure, while the middle and outer layers contribute in a more limited way since they are not in contact with the skin. Nevertheless, when the mask is worn, these two layers can become damp and therefore likely to release silver and copper ions.

In the absence of specific information on the actual transfer of ions between damp layers of fabric, two hypotheses were tested for each scenario:

- In the first hypothesis (hypothesis A), the entire surface of a single layer of the mask was considered to be in direct contact with the skin in order to assess dermal and inhalation exposure.
- In the second hypothesis (hypothesis B), which is very conservative, the three layers of fabric were considered to contribute in the same way to the release of silver and copper ions.

Dermal route

Exposure scenarios for the dermal route are considered as "worst-case" scenarios, based on the fabric coming into contact with the skin when damp. The data on the migration rates of silver from textiles to the skin were taken from the assessment carried out by the Swedish competent authority on silver zeolite and silver-copper zeolite. These data show a decrease in the migration of silver over time, enabling a distinction to be made between an initial migration rate, applicable for the first two hours, an intermediate migration rate for the next six hours in the case of new fabric, and a constant migration rate applicable for routine use. These rates are expressed as a % per hour.

- For silver-copper zeolite, the migration rates were taken from an experimental study available in the EU file, assessing the release of silver in sweat.

- For silver zeolite, the migration rates were extrapolated from the data above, applying a factor of 10 for a worst-case approach.

For copper, as no information is available on migration rates from textile to skin, a migration rate of 100% was used by default.

Inhalation

No information is available concerning the transfer of silver and copper from the mask to the respiratory tract. By default, it was decided to consider the transfer rate from the textile to the skin as identical to the transfer rate from the textile to the respiratory tract, for both silver and copper. Similarly, by default, the entire surface of the mask was considered to contribute to exposure through inhalation.

Table 3: scenario 1: exposure of an adult wearing two new unwashed masks over a period of eight hours

Scenario [1]: Two new unwashed masks worn for four hours each on healthy skin over an eight-hour day		
For the dermal and inhalation routes, the exposure to copper and silver was calculated using the following formula: Internal dose = concentration in the textile x textile density x migration rate x area in contact with the mask x absorption / body weight The rate of silver migration in a new mask worn over four hours was calculated by totalling the migration rate for each four-hour period. The initial migration rate was applied for the first two hours and the intermediate migration rate for the next two hours.		
Parameters	Value	Source
Adult weight	60 kg	Recommendation 14 issued by the BPC Ad hoc Working Group on Human Exposure
Surface of the mask in contact with the skin	226 cm^2	Manufacturer data
Fabric density (1 layer)	135 g/m^2	Manufacturer data
Silver from the silver zeolite		
Silver content of the silver zeolite in one layer of the mask in contact with the skin (hypothesis A)	137 µg	Manufacturer data
Silver content of the silver zeolite in all three layers of the fabric (hypothesis B)	412 µg	Manufacturer data
Dermal absorption of silver	5%	Silver zeolite assessment report

Migration rate of the silver in the silver zeolite – fabric to skin – one mask for four hours	27%	Calculation based on data in the silver zeolite assessment report
Inhalation absorption of silver	100%	Default value
Silver from the silver-copper zeolite		
Silver content of the silver-copper zeolite in one layer of the mask in contact with the skin (hypothesis A)	146 µg	Manufacturer data
Silver content of the silver zeolite in all three layers of the fabric (hypothesis B)	439 µg	Manufacturer data
Dermal absorption of silver	5%	Silver-copper zeolite assessment report
Migration rate of the silver in the silver-copper zeolite – fabric to skin – one mask for four hours	2.7%	Calculation based on data in the silver-copper zeolite assessment report
Inhalation absorption of silver	100%	Default value
Copper		
Copper content of the silver-copper zeolite in one layer of the mask in contact with the skin (hypothesis A)	0.25 mg	Manufacturer data
Copper content of the silver-copper zeolite in all three layers of the fabric (hypothesis B)	0.74 mg	Manufacturer data
Migration rate of the copper in the silver-copper zeolite – fabric to skin	100%	Default value
Dermal absorption of copper	5%	Assessment report on copper sulphate pentahydrate PT 2
Inhalation absorption of copper	100%	Assessment report on copper sulphate pentahydrate PT 2

Table 4: estimated internal doses of silver for scenario 1

Scenario	Estimated internal dose through the dermal route [µg/kg bw/d]	Estimated internal dose through inhalation [µg/kg bw/d]	Estimated internal dose through the oral route [µg/kg bw/d]	Total estimated internal dose [µg/kg bw/d]
Scenario [1] Hypothesis A	**Silver from the silver zeolite**			
	0.062	1.2	n.a.	1.3
	Silver from the silver-copper zeolite			
	0.0066	0.13	n.a.	0.14
	Total silver			
				1.4
Scenario [1] Hypothesis B	**Silver from the silver zeolite**			
	0.19	3.7	n.a.	3.9
	Silver from the silver-copper zeolite			
	0.020	0.40	n.a.	0.41
	Total silver			
				4.3

Table 5: estimated internal doses of copper for scenario 1

Scenario	Estimated internal dose through the dermal route [mg/kg bw/d]	Estimated internal dose through inhalation [mg/kg bw/d]	Estimated internal dose through the oral route [mg/kg bw/d]	Total estimated internal dose [mg/kg bw/d]
Scenario [1] Hypothesis A	0.00020	0.0041	n.a.	0.0043
Scenario [1] Hypothesis B	0.00061	0.012	n.a.	0.013

Table 6: exposure of an adult wearing masks washed once over an eight-hour day

Scenario [2]: Mask worn on healthy skin for eight hours a day every day over two months, after one wash		
Scenario 2 uses the same formula as scenario 1 to calculate internal doses by the dermal and inhalation routes. Concerning silver and copper content after the first wash, a decrease of 19% for silver and 27% for copper was considered, based on the information provided by the manufacturer. The rate of silver migration for masks routinely worn eight hours a day was calculated by summing the migration rate for each hour of the eight-hour period. The constant migration rate was applied to the eight hours.		
Parameters	**Value**	**Source**
Adult weight	60 kg	Recommendation 14 issued by the BPC Ad hoc Working Group on Human Exposure
Surface of the mask in contact with the skin	226 cm^2	Manufacturer data
Fabric density (1 layer)	135 g/m^2	Manufacturer data
Silver from the silver zeolite		
Silver content of the silver zeolite in one layer of the mask in contact with the skin after one wash (hypothesis A)	111 µg	Manufacturer data
Silver content of the silver zeolite in all three layers of the fabric after one wash (hypothesis B)	333 µg	Manufacturer data
Dermal absorption of silver	5%	Silver zeolite biocide dossier
Daily migration rate of the silver from the silver zeolite (medium term) – fabric to skin	4.1%	Calculation based on data in the silver zeolite assessment report
Inhalation absorption of silver	100%	Default value
Silver from the silver-copper zeolite		
Silver content of the silver-copper zeolite in one layer of the mask in contact with the skin after one wash	118 µg	Manufacturer data
Silver content of the silver-copper zeolite in all three layers of the fabric after one wash (hypothesis B)	355 µg	Manufacturer data
Dermal absorption of silver	5%	Silver-copper zeolite biocide dossier

Daily migration rate of the silver from the silver-copper zeolite (medium term) – fabric to skin	0.41%	Calculation based on data in the silver-copper zeolite assessment report
Inhalation absorption of silver	100%	Default value
Copper		
Copper content of the silver-copper zeolite in one layer of the mask in contact with the skin after one wash	0.18 mg	Manufacturer data
Copper content of the silver-copper zeolite in all three layers of the fabric after one wash (hypothesis B)	0.54 mg	Manufacturer data
Migration rate of the copper in the silver-copper zeolite – fabric to skin	100%	Default value
Dermal absorption of copper	5%	Assessment report on copper sulphate pentahydrate PT 2
Inhalation absorption of copper	100%	Assessment report on copper sulphate pentahydrate PT 2

Table 7: estimated internal doses of silver for scenario 2

Scenario	**Estimated internal dose through the dermal route [µg/kg bw/d]**	**Estimated internal dose through inhalation [µg/kg bw/d]**	**Estimated internal dose through the oral route [µg/kg bw/d]**	**Total estimated internal dose [µg/kg bw/d]**
Scenario [2] Hypothesis A	**Silver from the silver zeolite**			
	0.0038	0.075	n.a.	0.079
	Silver from the silver-copper zeolite			
	0.00040	0.0080	n.a.	0.0084
	Total silver			
				0.088
Scenario [2] Hypothesis B	**Silver from the silver zeolite**			
	0.011	0.23	n.a.	0.24
	Silver from the silver-copper zeolite			
	0.0012	0.024	n.a.	0.025
	Total silver			
				0.26

Table 8 estimated internal doses of copper for scenario 2

Scenario	**Estimated internal dose through the dermal route [mg/kg bw/d]**	**Estimated internal dose through inhalation [mg/kg bw/d]**	**Estimated internal dose through the oral route [mg/kg bw/d]**	**Total estimated internal dose [mg/kg bw/d]**
Scenario [2] Hypothesis A	0.00015	0.0030	n.a.	0.0031

Scenario [2] Hypothesis B	0.00045	0.0090	n.a.	0.0094

3.4. Characterisation of the risk to users

3.4.1.Methodology for including both substances in the risk assessment

As the masks contain more than one active substance (silver and copper), the risk assessment for exposure to several active substances was based on the ECHA guidance for assessing biocidal products[12] (ECHA BPR guidance, Vol III, Part B).

The first step (Tier 1) involves checking the acceptability of the risk associated with each substance in the mask by comparing exposure values to the AEL of each substance and calculating a hazard quotient. In the second step (Tier 2), if the hazard quotients are less than 1, the additive effects are considered by adding up the hazard quotients of each active substance and calculating a hazard index.

3.4.2.Choice of toxicological reference values

There is no appropriate TRV for acute exposure. By default, exposure was compared to the medium-term AEL, even though this value is highly conservative (based on the NOAEL in rats exposed for 90 days).

For repeated exposure, given that wearing the mask is considered to correspond to medium-term exposure, exposure values were compared to the medium-term AEL[13].

3.4.3.Quantitative risk assessment

Scenario [1]

Table 9: Assessment of the systemic risks associated with silver - scenario 1

Scenario	AEL [µg/kg bw/d]	Total estimated internal dose [µg/kg bw/d]	Total estimated internal dose / AEL (%)	Tier 1 = Hazard quotient
Scenario [1] Hypothesis A	0.15	1.4	956%	9.6
Scenario [1] Hypothesis B	0.15	4.3	2869%	29

[12] https://echa.europa.eu/documents/10162/23036412/biocides_guidance_human_health_ra_iii_part_bc_en.pdf/30d53d7d-9723-7db4-357a-ca68739f5094

[13] In European dossiers, owing to the potentially wide range of consumer articles treated with silver, user exposure to all treated articles is considered to be chronic (possible multiple exposures to a variety of treated articles) even though each distinct scenario (exposure to one type of treated article) corresponds to short- or medium-term exposure, leading to short-term user exposure being compared with a long term AEL. Although this approach is conservative, it allows the consideration of multiple exposures to a variety of treated articles. Nevertheless, in the context of this request, where the sole objective is to estimate the potential risks associated with wearing the mask, this approach does not appear to be relevant.

Table 10: Assessment of the systemic risks associated with copper - scenario 1

Scenario	AEL [mg/kg bw/d]	Total estimated internal dose [mg/kg bw/d]	Total estimated internal dose / AEL (%)	Tier 1 = Hazard quotient
Scenario [1] Hypothesis A	0.082	0.0043	5%	0.05
Scenario [1] Hypothesis B	0.082	0.013	16%	0.16

Based on the estimated scenarios and on a comparison with the highly conservative medium-term AEL indicating the absence of observed effects in rats exposed for 90 days, the hazard quotient calculated is greater than 1 for both hypotheses (based on one or three layers).

Scenario [2]

Table 11: Assessment of the systemic risks associated with silver - scenario 2

Scenario	AEL [µg/kg bw/d]	Total estimated internal dose [µg/kg bw/d]	Total estimated internal dose / AEL (%)	Tier 1 = Hazard quotient
Scenario [2] Hypothesis A	0.15	0.088	58%	0.58
Scenario [2] Hypothesis B	0.15	0.26	175%	1.75

Table 12: Assessment of the systemic risks associated with copper - scenario 2

Scenario	AEL [mg/kg bw/d]	Total estimated internal dose [mg/kg bw/d]	Total estimated internal dose / AEL (%)	Tier 1 = Hazard quotient
Scenario [2] Hypothesis A	0.082	0.0031	3.8%	0.038
Scenario [2] Hypothesis B	0.082	0.0094	12%	0.12

Table 13: Assessment of the combined risks associated with silver and copper - scenario 2 / hypothesis A

Total hazard quotient for silver	0.58
Copper hazard quotient	0.038
Final hazard index (Tier 2)	**0.62**

The assessment carried out shows that the hazard indexes linked to wearing the mask over the medium term are less than 1 in the case of hypothesis A (based on one layer) but greater than 1 in the case of hypothesis B (based on three layers).

3.5. Discussions of the CES on "Biocidal substances and products"

The assessment of exposure was limited to the use of the mask, without taking account of other possible sources of exposure to silver and copper compounds.

Based on the data available on zeolites, only dermal and inhalation exposures to silver and copper were assessed. Local effects cannot be ruled out if zeolites are released from the mask and inhaled.

The key parameters taken into consideration for the assessment were based on the information provided by Hanes and the assessment carried out by the Swedish competent authority.

The risk assessment was carried out on the basis of two scenarios:

- an estimate of the short-term risk, based on the wearing of two new masks successively on the same day without prior washing (contrary to the manufacturer's recommendations). For this scenario, the calculated hazard quotient exceeds the threshold value, indicating a possible risk. However, this conclusion must be qualified, owing to the many uncertainties relating to exposure and the toxicological reference value used.

    - Inhalation exposure, which is the main contributor to the calculated level of exposure, was overestimated in the absence of a relevant exposure scenario for this use and the possibility of fine-tuning the quantitative assessment:
        - the entire surface of the treated fabric contributed to exposure, including the parts that are not in contact with the respiratory tract,
        - 100% of the ions released by the three layers of fabric were inhaled and absorbed.

    - The migration rate of silver ions from the silver zeolite was overestimated in the absence of appropriate experimental data.

    - The migration rate applied to dermal exposure was used to estimate inhalable quantities.

    - In the absence of observed acute effects or the possibility of determining a relevant reference value for short-term exposure, this exposure was compared with a value ensuring no effect for medium-term exposure. The effects underlying this medium-term reference value are themselves early effects (organ pigmentation).

Therefore, taking account of all the above factors, no serious adverse effects on human health are expected from wearing new unwashed masks.

- An estimation of the medium-term risk, based on the wearing of masks that have been washed at least once, for eight hours a day. For this scenario, the assessment found no adverse effects if only one layer of fabric was considered to contribute to exposure (hypothesis A). However, in the very conservative hypothesis whereby the entire surface area of the treated fabric is considered to contribute to exposure, a risk cannot be ruled out. This assessment (scenario 2, hypothesis B) includes several uncertainties:

- Inhalation exposure, which is the main contributor to the calculated level of exposure, was overestimated in the absence of a relevant exposure scenario for this use and the possibility of fine-tuning the quantitative assessment:
  - the entire surface of the treated fabric contributed to exposure, including the parts that are not in contact with the respiratory tract,
  - 100% of the ions released by the three layers of fabric were inhaled and absorbed.

- The migration rate of the silver ions from the silver zeolite was overestimated in the absence of appropriate experimental data.

- The migration rate applied to dermal exposure was used to estimate inhalable quantities.

- The outer layer and middle layer are not expected to contribute as much to exposure as the internal layer: while the release of silver and copper ions cannot be ruled out owing to the mask gradually becoming damp during use, the mobility of these ions in dermal or inhalation absorption will be lower than the result of modelling in direct contact with the skin. In addition, the mask does not become damp in the same way across the entire surface area. The sides rarely if ever become damp and therefore contribute far less to exposure.

- Finally, the assessment considered the active substance content of a mask after one wash only, whereas silver and copper content actually decrease with each wash. According to the information provided by Hanes, after around a dozen machine washes in compliance with the manufacturer's recommendations, the silver and copper content of the mask is reduced by a factor of three.

Based on all the information available, the CES concludes that it is impossible to rule out any risks associated with wearing Hanes brand masks, given all the uncertainties, but that these risks can be limited by correct usage (washing before the first use and after each use, wearing for a maximum of four hours, changing masks as soon as they become damp).

Furthermore, the benefits of treating the fabric have yet to be assessed. It should also be noted that other fabric masks treated with silver-based active substances, including those intended for children, are concerned by this issue.

4. Agency conclusions and recommendations

Wearing a protective mask is one of the barrier gestures put in place as part of efforts to control the COVID-19 pandemic. Using washable cloth masks prevents significant amounts of waste. Cloth masks meeting filtration requirements should therefore be preferred.

Hanes sells washable masks made from a fabric treated with two active substances, silver zeolite and silver-copper zeolite, authorised as PT9-type biocides: fibre, leather rubber and polymerised materials preservatives.
The active substances – silver zeolite and silver-copper zeolite – and other silver compounds are used in the manufacture and treatment of many articles, including consumer products (paint, sealant, textiles, furnishings, hygiene or healthcare items, etc.) in order to provide them with antimicrobial properties. The assessment of these active substances used for fibre protection is still under way at EU level, with Sweden as the competent authority for the assessment.

In a request received on 15 October 2020, ANSES was asked to estimate the potential risks associated with wearing masks treated with silver zeolite and silver-copper zeolite.

ANSES endorses the conclusions of the CES on "Biocidal substances and products"
The assessment of exposure was limited to use of the mask, without taking account of other possible sources of exposure to silver compounds.

The zeolite in the masks is a crystalline aluminosilicate of synthetic origin, containing micropores of controlled size in which some of the sodium ions have been replaced by silver Ag^+ ions (or silver Ag^+ and copper Cu^{2+} ions). Based on the data available on zeolites, only dermal and inhalation exposures to silver and copper were quantified. Local effects, such as inflammation, cannot be ruled out if zeolites are released from the mask and inhaled.

The risk assessment for dermal and inhalation exposure to silver and copper was based on two scenarios:

- An estimation of the risk associated with wearing two new masks successively on the same day, without prior washing.
- An estimation of the risk associated with wearing masks that have been previously washed (at least once) for eight hours a day.

The key parameters taken into consideration for the assessment are based on the information provided by Hanes on 19 October 2020 and the assessment carried out by the Swedish authorities. It is important to note that these exposure scenarios are associated with a number of uncertainties, primarily in relation to the inhalation and migration of silver and copper from the mask fabric. As a result, highly conservative hypotheses were adopted.

Acute risks

In the absence of any observed acute effects and in view of the impossibility of establishing a relevant reference value for short-term exposure (see 3.2.2), no serious adverse effects on human health are expected. This analysis is supported by the absence of any adverse effects reported to the Poison Control and Toxicovigilance Centres (CAP-TV) associated with the wearing of masks, as of 19 October 2020.

Risk of effects on reproduction

Based on the ratio between the reference values of the critical effect applied for the assessment and those of the reprotoxic effects (taking into account the data available on the toxicity of silver,

silver-copper and silver-zinc zeolites), the Agency notes that the hazard quotient is lower than 1 for the use of prewashed masks. **In consequence, previously washed masks are not considered to carry a reprotoxic risk.**

Medium-term risks

- For the **wearing of new masks without prior washing,** the calculated hazard quotient exceeds the threshold value, indicating a possible risk. However, this conclusion must be qualified in view of the many uncertainties regarding exposure (see 3.5) and the fact that users are not expected to wear only new masks without prior washing. **ANSES reiterates the importance of systematically washing fabric masks before wearing them for the first time.**

- Assuming that **masks are worn in full compliance with the manufacturer's instructions for use** (washed before the first use and after each use, worn for four hours maximum, changed when damp): **the assessment found no harmful effects on human health**.

- **However, if the mask is worn in conditions that reflect reality more closely, i.e. wearing a mask when damp and on the basis of the conservative hypotheses detailed in this opinion, the risks cannot be ruled out, in view of the uncertainties (see 3.5).**

It should be noted that ANSES did not assess the effectiveness of the antimicrobial treatment of the fabric. Furthermore, it would be useful to have an explanation of the expected user benefits gained by wearing a mask treated with silver compounds: chemical treatment with biocidal active substances is not a prerequisite for complying with the technical requirements established for protective cloth masks. It should be noted that unless the manufacturer makes a claim relating to the biocidal properties of a treated article, it is not usually required to indicate the presence of biocidal active substances on the label.

In conclusion, ANSES underlines the need for better regulation of the use of antimicrobial treatments in articles, particularly everyday consumer goods. The implementation of the Biocides Regulation contributes to this regulation. ANSES recommends that every effort be made at European level to ensure that the assessment of biocidal active substances included in the review programme is completed as soon as possible, so that biocidal products receive marketing authorisation and that treated articles contain only active substances approved for the proper type of product.

In cases where it is established that using these substances in treated articles could lead to unacceptable risks for human health or the environment, ANSES recommends including restrictions on use in articles in the conditions of approval of biocidal active substances.

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KEYWORDS

Biocides, treated fabric, silver zeolite, silver-copper zeolite, protective mask