SAFETY ASSESSMENT OF CADMIUM IN VINE AND WINE

OIV

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OIV - International Organisation of Vine and Wine
12, Parvis de l'UNESCO
F-21000 Dijon - France www.oiv.int
E-mail: sanco@oiv.int

COORDINATORS

Jean-Claude Ruf, OIV Scientific Director
Marcos Araujo, OIV Safety and Health Head of Unit

AUTHORS

Arina Antoce (RO)
Angelika Paschke-Kratzin (DE)
Aurélie Camponovo (FR)
Elisabetta Romeo (IT)
Patrizia Restani (IT)
Pierre Genest (FR)
Pierre-Louis Teissedre (FR)
Raquel Romano (AR)
Regina Vanderlinde (BR)
Rena Kosti (GR)
Tony Battaglene (AU)
Victoria Moreno Arribas (ES)

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Daniela Costa, OIV Communication Officer - layout

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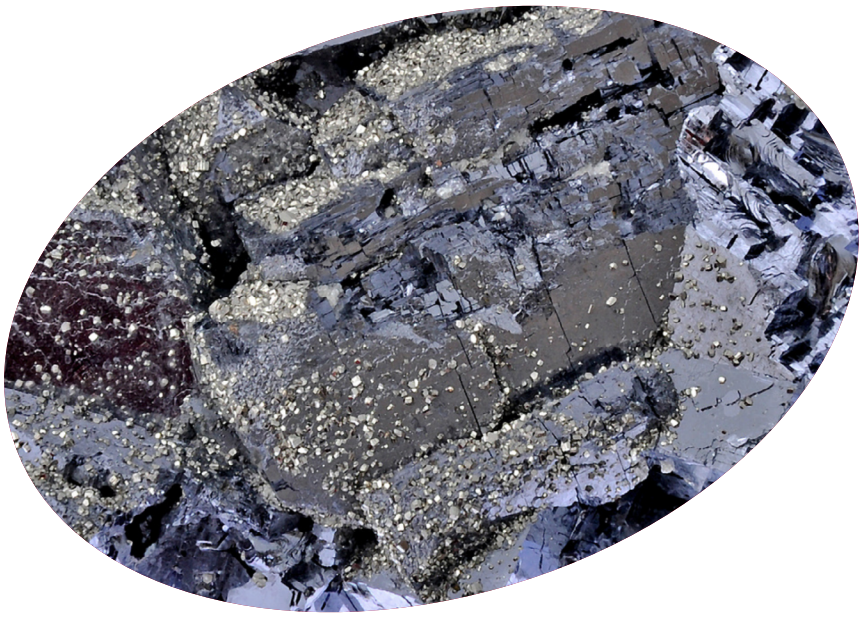
INTRODUCTION

Cadmium (Cd) is a heavy metal representing an environmental contaminant from natural, industrial, and agricultural sources. Cadmium is an indirect genotoxic carcinogen, and its presence consequently poses a high risk to public health.
Food chains are the main source of cadmium exposure for the non-smoking general population. According to the last JECFA assessment (2021) , the main sources of dietary cadmium exposure are cereals and cereal-based products (rice and wheat), vegetables (root, tuber, and leaf vegetables), fish and seafood (mainly molluscs). The minor contribution was identified for cocoa and cocoa-based products (JECFA 2011, JECFA 2021). Alcohol beverages, such as wine and beer, should represent a minor dietetic source of cadmium.
During the last meeting of the OIV Food Safety group, in the framework of the safety assessment of different compounds found in vitivinicultural products, an eWG was established for preparing a working document on “cadmium” coordinated by the OIV secretariat and including Australia, France, Germany, Italy, Argentina, Spain, Romania and the OIV.
This document analyses the presence of cadmium in wine, the source of contamination and those conditions modulating the relative residues. From the study's conclusion, OIV will publish a guideline about the identification and quantification of cadmium in wine and recommendations to avoid residues above the established limits.



DIETARY EXPOSURE

JECFA (Joint FAO/WHO Expert Committee on Food Additives)

In this assessment dated 2011, JECFA stated that the highest mean concentration of cadmium was reported for: vegetables (including dried); meat and poultry offal; shellfish/molluscs; nuts and oilseeds; coffee, tea, and cocoa; and spices. In the evaluation of 2021 (JECFA 2021), the contribution of cocoa products to dietary cadmium exposure was considered minor, even where the consumption of cocoa products is relatively high.
Estimates of dietary exposure in different geographical areas are reported in Table 1.

Table 1 - National and regional estimates of dietary exposure to cadmium for adults (JECFA 2011)

Country or region	Treatment of ND occurrence data in exposure estimates	Mean exposure (µ/kg bw per month)	High exposure (µg/kg bw per month)
Australia	ND = 0 and LOD	2.2-6.9	-
Chile	Not specified	9	-
China	ND = LOD/2	9.9	-
Europe	ND = LOD/2	9.10[a]	12.1[b]
Japan	Not specified	12	-
Lebanon	ND = LOQ/2	5.2	6.9[c]
Republic of Korea	ND = LOD	7.7	-
USA	ND = O	4.6	8.1[d]

[a] Median of mean exposure estimates for 16 European countries.
[b] Sum of 95th percentile exposure (consumers only) for the two food categories with highest exposure plus mean exposure (whole population) for the other food categories.
[c] Calculated from mean food consumption and highest cadmium concentrations in each food category.
[d] Calculated from distributions of both food consumption and cadmium occurrence data; high exposure equals 90th percentile of exposure.

ND: Not determined;
LOD: Limit of Detection;
LOQ: Limit of Quantification.

Source: JECFA,2011

EFSA (European Food Safety Authority)

Data reported by EFSA (2012) about the dietetic sources of cadmium are illustrated in Table 2.

Table 2 – Minimum and maximum relative contributions in per cent of twenty broad food categories to overall lower bound mean cadmium exposure across the survey included for each age group

Food categories	Toddlers		Other children		Adolescents		Adults		Elderly		Very elderly	
	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
Grains and grain-based products	15.7	34.5	19.2	35.1	21	35.5	17.1	33	20.9	29	21.3	30.5
Vegetables and vegetable products	9.02	20.5	3.7	21.4	3.45	19.9	4.66	25.9	16.1	28.4	14.5	27.4
Starchy roots and tubers	6.49	26	6.54	20.7	6.07	19.7	5.54	30.5	6.6	22.5	7.46	26.3
Legumes, nuts and oilseeds	0.16	3.53	0.23	8.86	0.44	14.8	0.64	5.17	0.44	4.29	0.59	2.32
Fruit and fruit products	2.41	6.74	1.82	5.04	1.54	3.57	1.49	3.94	3.06	5.48	3.07	5.86
Meat and edible offal	2.36	10.9	2.72	9.95	3.86	10	5.51	24.5	7.26	19.2	5.58	14.2
Fish and other seafood	1.08	15.9	1.31	22.8	0.85	28.3	1.2	31.2	0.8	19.6	0.8	13
Milk and dairy products	3.95	11.3	1.43	11.8	1.38	7.38	1.25	4.37	1.46	4.45	1.69	4.08
Eggs and egg products	0	0.22	0	0.2	0	0.19	0.05	0.2	0.07	0.2	0.07	0.19
Sugar and confectionary	0.83	15.7	2.2	17.7	2.22	11.9	1.02	7.86	0.57	4.13	0.53	3.73
Animal and vegetable fats and oils	0.15	1	0.16	2.36	0.16	0.91	0.23	1.94	0.46	1.8	0.52	1.01
Fruit and vegetable juices	1	4.63	0.78	4.37	0.7	5.85	0.33	3.61	0.29	2.44	0.17	2.21
Non-alcoholic beverages	0	1.24	0.16	4.02	0.45	4.5	0.42	6.79	0.58	5.27	0.66	5.3
Alcoholic beverages	0	0.01	0	0.04	0	0.43	0.26	2.04	0.25	1.51	0.19	1.61
Drinking water	0.24	1.91	0	1.08	0	1.31	0.1	1.43	0.16	1.15	0.11	1.03
Herbs, spices and condiments	0.47	6.44	0.05	3.02	0.09	3.04	0.73	2.93	0.57	2.22	0.67	3.14
Food for infants and small children	1.12	15.6	0.09	1.11	0	0.04	0	0.02	0	0	0.01	0.01
Products for special nutritional use	0	0.28	0.01	0.63	0.01	3.13	0.05	1.64	0.04	1.08	0.04	1.21
Composite food	0	6.78	0.03	28.5	0.05	18.9	0.05	22.2	0.04	7.48	0.03	8.96
Snacks, desserts, and other foods	0	5.18	0.67	4.43	0.68	2.91	0.21	2.85	0.15	0.58	0.17	0.65

As reported in Table 2, the food groups that contribute significantly to dietary cadmium exposure are: cereals and cereals products, vegetables; starchy roots or tubers; meat or fish and relative products. Alcoholic beverages are among the minor dietetic sources for cadmium, with a maximum contribution ranging from 0.43 in adolescents to 2.04% in adults. The concentration of cadmium in 3410 alcoholic beverages (beer and substitutes, wine and substitutes and other alcoholic beverages and substitutes) has been collected by EFSA (2009); 2371 samples of wine were included of which 59% were below the limit of detection (LOD). The mean value in wines was 0.011±0.0016 mg/kg (m±SD), and the highest content was 0.0125 mg/kg.

USA

According to ATSDR (DengServices, 2012), the primary dietary sources of cadmium exposure in USA are: lettuce and spinach; potatoes and grains; peanuts; soybeans, and sunflower seeds.

SOURCES OF CADMIUM IN WINE MAKING PROCESS

Unlike contamination with other metals, which can come from the contact of wine with materials and equipment used in winemaking, cadmium is mostly transferred from the grapes (or other parts of the vine), which acquire it from the soil. It can be naturally found in the earth's crust and ocean water. It can also be present in other inorganic materials, such as non-ferrous metals, fossil fuels, cement, and phosphate fertilisers (IARC, 2018). In wine, cadmium contamination depends on natural or exogenous factors, mainly linked to vineyard management. Where the soil has a low concentration of cadmium, grapes or wines grown in that area are normally low in cadmium level. The principal factors modulating grape contamination are (Mena et al., 1996):

- Soil type and composition.
- Climate.
- Use of pesticides or fertilisers containing cadmium.
- Chemical composition of the specific batch used.
- Respect of the pre-harvest interval of the pesticide.
- Localisation of absorption: leaves or roots.
- Grape variety.
- Wine treatment (fining, filtration, etc.) (Redan et al., 2019).

SAFETY ASSESSMENT

General aspects

Safety assessment of human cadmium exposure plays a key role, given that it is an element known by its toxic effects on the human species. Various toxicological committees and organisations have established the maximum doses to which humans can be exposed.

Tobacco is the most important source of cadmium for humans, but a significant intake has also been observed in infants when mothers are exposed to cadmium during pregnancy or lactating period. The vegetarian population is normally more exposed than the corresponding omnivorous one due to the greater consumption of vegetables. Spirits, and especially wines, are not expected to pose a significant risk, as no elevated cadmium concentrations have been reported to date in these beverages.

IARC (International Agency for Research on Cancer)

According to the document published in 1993 (IARC, 1993), IARC evaluated cadmium as follows:
1. There is ***sufficient evidence*** in humans for the carcinogenicity of cadmium and its compounds;
2. There is ***sufficient evidence*** in experimental animals for the carcinogenicity of cadmium compounds;
3. There is ***limited evidence*** in experimental animals for the carcinogenicity of cadmium as a metal;
4. Cadmium and cadmium compounds are **carcinogenic to humans (Group 1)**.

JECFA/WHO

In 2021, JECFA Secretariat considered it appropriate to revise the dietary exposure of cadmium by all food sources, including chocolate and cocoa products (JECFA 2021). JECFA did not modify the Provisional Tolerable Monthly Intake (PTMI) of 25 µg/kg b.w., established in the 73rd meeting (JECFA 2011). This value reflected the long half-life of cadmium in humans. In particular, the PTMI was based on long-term bioaccumulation in the kidneys, with the steady state not achieved until after 45-60 years of exposure. Dietary exposure above the PTMI for limited periods may be of lesser concern in younger age groups.

EFSA

In 2009, EFSA published an opinion on cadmium in food (EFSA 2009) when a tolerable weekly intake (TWI) of 2.5 µg/kg body weight was established. The value was established on the basis of scientific data showing that, in humans, cadmium absorption after ingestion is relatively low (being 3-5%), but its persistence in kidneys and liver is very long since the biological half-life ranges from 10 to 30 years.

CDC/USA (Center for food Disease Control and Prevention)

In its document dated September 2012, the Agency for Toxic Substances and Disease Registry (DengServices 2012) of the USA Department of Health and Human Services reported some proposals about the limit of exposure recommended for humans. ATSDR considered all the possible ways of exposure: inhalation, oral by food or water, and dermal route. They reported that the sensitive targets of cadmium toxicity are kidneys and bones when the oral route is considered and kidneys and lungs for inhalation. Other reported adverse effects were observed in humans and in animals: reproductive toxicity, hepatic, haematological and immunological effects. ATSDR used the parameter "Minimal Risk Level" (MRL), which is defined as an estimation of the daily exposure to cadmium that is likely to be without appreciable risk of adverse effects (non-carcinogenic) in humans for a specified period of time.
According to this concept, an MRL for chronic oral intake of cadmium (> 1 year) has been estimated as 0.1 mg Cd/kg/day.

Based on similar scientific data underlining the risk of renal effects, EPA established a Reference Dose (RfD) of 0.5 mg/kg/day when cadmium is present in water or 1 mg/kg/day in food. In general, the RfD is an estimate of the daily exposure of humans (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Similarly to Acceptable Daily Intake ADI (no-observed-adverse-effect-level NOAEL /Safety Factor), the RfD (NOAEL/ UF x MF) adds the modifying factor to the uncertainty factor (UF) (EPA-IRIS 2012).

LIMITS IN WINE FOR CADMIUM

OIV

The Member-states of the OIV have been very concerned about cadmium in wines for many years and have adopted different recommendations on cadmium in wines. The current OIV cadmium limit is 0.01 mg/L (10 µg/L).

CADMIUM LEVEL IN WINE

WHO/GEMS (Global Environment Monitoring System) Food database on cadmium levels in wine

Data from the WHO/GEMS Food Database have been elaborated in Table 3.

Region name	Number of samples	Average level	Min	Max	SD	Unit	LOD	LOQ	Year
EURO	479	0.132	0	22	1.128	µg/kg	7.894	26.255	2011-2015
PAHO	14	0	0	0	0	mg/kg	0.150	1.501	2011-2015
EURO	456	0.117	0	25	1.241	µg/kg	4.519	15.036	2016-2019
PAHO	64	0	0	0	0	µg/kg	0.065	0.364	2016-2018
WPRO	7	Nd	-	-	-	mg/kg	0.005	0.025	2014
WPRO	1	0.028	-	-	-	mg/kg	0.005	0.025	2014

Legend:
EURO – Europe region;
PAHO – Pan American Health Organisation;
WPRO - Western Pacific

Source: https://extranet.who.int/gemsfood/Search.aspx

Official data from OIV Member States

Argentina

The Maximum level allowed in Argentina is 0.01 mg/L. In all samples controlled, cadmium residues were lower than 0.01 mg/L, the limit of quantification (LOQ).

Austria

Seventy-one wine samples from Austria were analysed, 23 red and 48 white.
The limit of quantification (LOQ) was 0.001 mg/L.

Wine	Number	LOQ	Min.	Max.	Average	Unit
Red wine	23	0.001	0.001	0.003	0.00109	mg/L
White	48	0.001	0.001	0.003	0.00154	mg/L

Brazil

Information from 158 wines samples were sent from Brazil. The total average 0.614 µg/L.

Wine	Cultivar	Region	Min.	Max.	Average (µg/L)	Nº samples
Commercial *Vitis vinifera* red wine	Various	Various	< LOD	5.80	0.67	33
Commercial *Vitis vinifera* white wine	Various	Various	0.17	1.40	0.46	15
Commercial *Vitis vinifera* rosé wine	Various	Various	0.20	1.00	0.60	2
Commercial red table wine	Various	Various	0.04	0.74	0.33	11
Commercial rosé table wine	Various	Rio Grande do Sul	0.27	0.27	0.27	1
Commercial white table wine	Various	Various	< LOD	0.35	0.24	6
Vitis vinifera red fortified wine	Various	Various	< 0.02	1.56	0.80	7
Vitis vinifera white fortified wine	Goethe / Moscato giallo	Various	< 0.02	0.80	0.40	4
Sparkling wine	Various	Various	0.08	1.01	0.52	9
Experimental *Vitis vinifera* white wine	Verdejo / Viognier	São Francisco Valley	< LOD	2.0	0.94	15
Experimental *Vitis vinifera* red wine	Cabernet Sauvignon / Merlot	Various	0.11	8.70	1.38	54
Experimental *Vitis vinifera* white wine	Saint Emilion	Campanha	_	_	0.76	1
Total of samples	158					

France

Four hundred and forty-six wines were analysed from France, of which 215 red, 82 white, 55 rosés, 69 sparkling and 25 naturally sweet wine. In 96% of analysed wines, cadmium residues were not detectable.

Wine	Number of samples	Minimum value µg/L	Average value µg/L	Maximum value µg/L
White	9	1	1.5	4.4
Rosés	1	1.4	1.4	1.4
Red	4	1	1.2	1.8
Sparkling	3	1	1.2	1.5
Sweet	1	1.4	1.4	1.4
All wines	18	1	1.4	4.4

They were quantified in 4% of wines at an average content of 0.0014 mg/L and a median of 0.0012 mg/L. The levels ranged from 0.001 to 0.0044 mg/L. 96% of wines are below 0.001 mg/L and 99.8% < 0.002 mg/L. 100% of the wines analysed complied with the OIV limit of 0.010 mg/L.

Italy

Italy sent data coming from two certified laboratories specialised in oenology. In both cases samples were analysed before commercialisation, therefore any wines that do not comply with the law would not be marketed. The data provided by the first laboratory, carried out in the period 2017-2021 (up to 8/21), included a total of 5226 wines. The LOD of the method was 2 µg/L and the LOQ was 5 µg/L. Cadmium was not detectable in all the samples, apart from one case in which the content was 7.6 µg/L, therefore still below the OIV limit of 10 µg/L. Eighteen thousand seven hundred and twenty-four wines were analysed by the second laboratory of control: 111104 red, 6579 white, and 1059 rosé. Three wines (two red and one white) were above the limit of 10 µg/L.

Wine	n° of samples	Unit	Media	median	Min	Max	SD
Red wine	11103	µg/L	0.20	0.16	0.00	6.52	0.22
White wine	6579	µg/L	0.25	0.19	0.00	35.43	0.59
Rosé wine	1059	µg/L	0.20	0.18	0.00	2.64	0.15
All	18724	µg/L	0.22	0.17	0.00	35.43	0.39

Considering the total samples, 3 wines were above the present limit of 10 µg/L and 14 (from two laboratories) above the proposed limit of 5 µg/L. The latter corresponds to 0.06% of total wine samples.

Republic of Moldova

In Moldova the allowed limit of cadmium in wine is 0.01 mg/L. This country sent data on 1184 samples of wines, without specification of type. In all samples the cadmium content was lower than the limit of quantification.

Nº sample	LOQ	Unit	Concentration
1184	<0.003	mg/L	ND

New Zealand

Data on six wine samples were sent by New Zealand.

Wine	N° sample	Min	Max	Average	Unit
Red	1	-	-	0.0002	mg/L
White	5	0.0002	0.0004	0.0003	mg/L

Romania

The maximum limit allowed in Romania is 0.01 mg/L. Concentration of cadmium in the wine of 4 grape varieties (white - Sauvignon blanc and Fetească regală; red - Fetească neagră and Merlot) analysed in 5 wine regions of Romania (Dealu Bujorului, Murfatlar, Târnave, Iași, Ștefănești-Argeș determined in two consecutive years (2016-2017).

Wine	Number of samples	Minimum value µg/L	Average value µg/L	Maximum value µg/L
White	20	2	5.65	9
Red	4	2	6.50	9
All wines	24	2	5.89	9

Considering the maximum values, all 24 wines were under the present limit of 10 µg/L, but some maximum values and the average are above the proposed limit of 5 µg/L.

In the vine canes the accumulation of cadmium ranged from 0.19 to 0.63 mg/kg, with red varieties tending to accumulate more than the white ones. The accumulation in grapes is influenced also by the region and on the absorption of the cadmium from soil.

Below are reported the concentration of cadmium in the canes of grape varieties analysed in 5 wine regions of Romania, in two consecutive years (2016 and 2017).

Grape	Number of samples	Minimum value in cane mg/kg	Average value in cane mg/kg	Maximum value in cane mg/kg
White	20	0.19	0.25	0.35
Red	4	0.47	0.55	0.63
All	24	0.19	0.33	0.63

In the vine leaves cadmium accumulation varied in the range of 0.18-0.35 mg/kg, with no correlation with the wine region, variety or the accumulation observed in the vine canes.

Spain

Spain does not have a limit of cadmium in wines. Data on 141 wine samples, with a limit of quantification of 0.001 mg/L, showed that all samples were below the limit recommended by OIV.

Year	Samples number	Results in µg/L	Min	Max	SD
2012	19	0.55	0.55	0.00	0.977
2013	43	0.25	-0.04	0.78	1.161
2014	5	0.20	0.15	0.25	0.047
2015	25	0.14	0.00	0.41	0.097
2016	21	0.10	0.00	0.64	0.144
2017	19	0.17	-0.08	1.19	0.271
2018	5	0.25	0.05	0.5	0.186
2019	2	0.25	0.22	0.29	0.049
2020	2	0.24	0.21	0.26	0.035

OIV members data

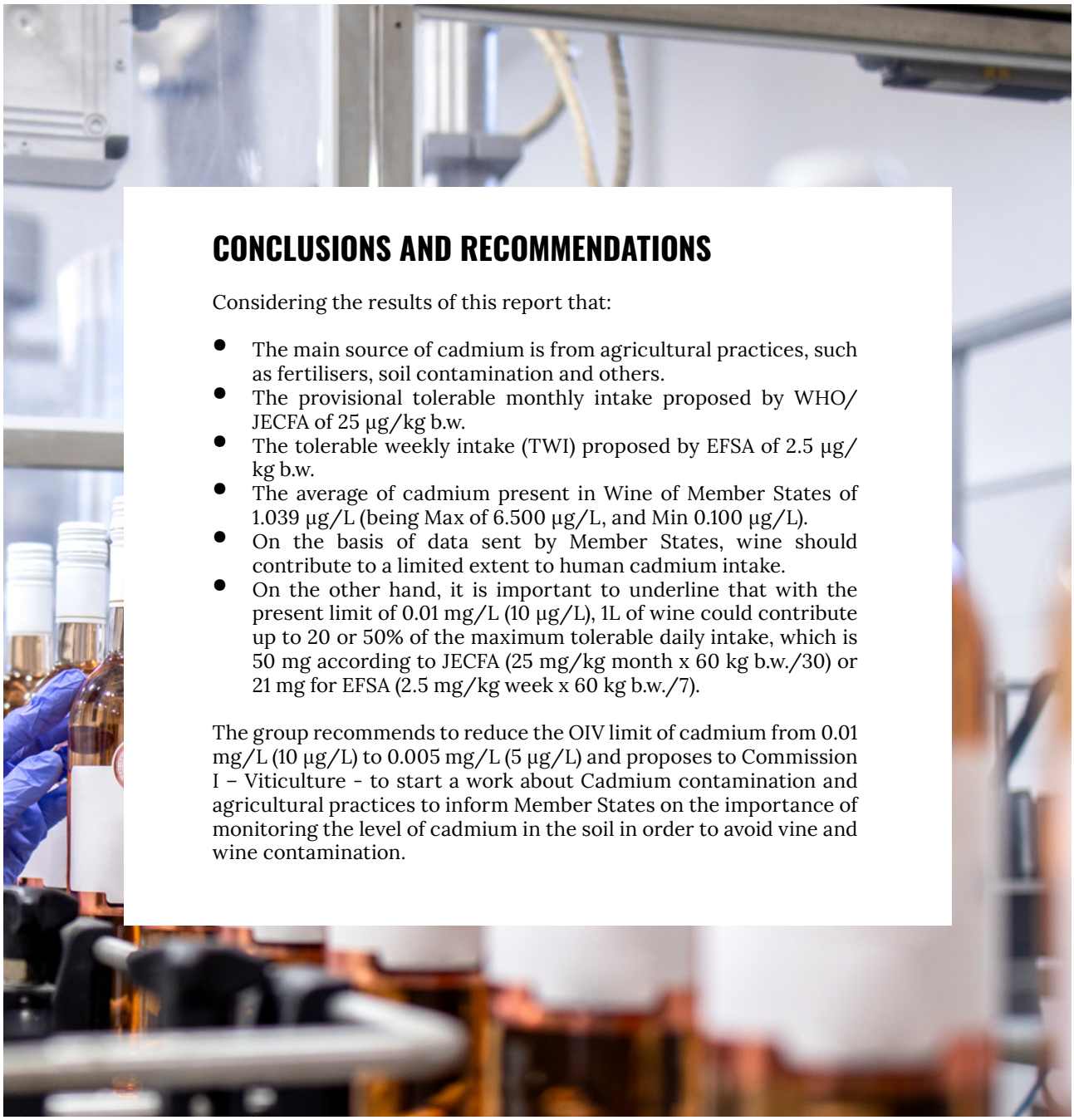
Considering the data sent by Member States, few pre-marketing samples had cadmium residues above the actual OIV limit (10 µg/L).

Average	Min	Max	Unit
1.039	0.100	35.450	µg/L

OIV METHODS OF ANALYSIS

OIV recommends the method OIV-MA-AS322-10 be used to measure cadmium concentrations in biological samples. It uses the methods of atomic absorption spectroscopy (AAS) and inductively coupled plasma atomic emission spectroscopy (ICP/AES).

The OIV method is determined directly in the wine by graphite furnace atomic absorption spectrophotometry.



CONCLUSIONS AND RECOMMENDATIONS

Considering the results of this report that:

- The main source of cadmium is from agricultural practices, such as fertilisers, soil contamination and others.
- The provisional tolerable monthly intake proposed by WHO/ JECFA of 25 µg/kg b.w.
- The tolerable weekly intake (TWI) proposed by EFSA of 2.5 µg/ kg b.w.
- The average of cadmium present in Wine of Member States of 1.039 µg/L (being Max of 6.500 µg/L, and Min 0.100 µg/L).
- On the basis of data sent by Member States, wine should contribute to a limited extent to human cadmium intake.
- On the other hand, it is important to underline that with the present limit of 0.01 mg/L (10 µg/L), 1L of wine could contribute up to 20 or 50% of the maximum tolerable daily intake, which is 50 mg according to JECFA (25 mg/kg month x 60 kg b.w./30) or 21 mg for EFSA (2.5 mg/kg week x 60 kg b.w./7).

The group recommends to reduce the OIV limit of cadmium from 0.01 mg/L (10 µg/L) to 0.005 mg/L (5 µg/L) and proposes to Commission I – Viticulture - to start a work about Cadmium contamination and agricultural practices to inform Member States on the importance of monitoring the level of cadmium in the soil in order to avoid vine and wine contamination.

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