COMMENTS AND RESPONSE TO COMMENTS ON OEL: PROPOSAL AND JUSTIFICATION

All comments and attachments including confidential information received during the consultation have been provided in full to the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Last data extracted on 13.11.2020

Substance name: Cadmium and its inorganic compounds
EC number: -
CAS number: -

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
12.11.2020	Italy	Italian Advisory Committee for the determination and updating of occupational exposure limit values and biological limit values relating to chemical agents (according to Article 232, paragraph 1, of Legislative Decree 9 April 2008, no. 81).	National Authority	1
Comment received				
ECHA Scientific report for evaluation of limit values for cadmium and its inorganic compounds at the workplace ECHA note – An attachment was submitted with the comment above. Refer to public attachment Cadmio comment.docx				
ECHA/RAC Response				
Your support for the recommendation to apply both air and biological limit values, and your support for the proposed values are noted.				

Date	Country	Organisation	Type of Organisation	Comment number
12.11.2020	Austria	Concerned OHS Activists	National NGO	2
Comment received				
– Use of "Practical threshold" concept is not justified for Cd (See ATTACHED file!) – Dose–response relationship for carcinogenicity is crucial and mandatory, but missing (See ATTACHED file!)				

– Incomplete citation of existing OELs in the Scientific Report provides biased information (See ATTACHED file!)

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on ECHA-scientific-report_Cadmium.pdf

ECHA/RAC Response

Thank you for your comments on the "practical threshold" and dose-response calculation for carcinogenicity. The sections related to these issues have been extensively revised and new information has been included. Information on the recent German acceptable cancer risk estimates has been added.

Regarding the existing OELs: Details on the current German OELs for have been included, as well a note stating that the current values are under revision.

Date	Country	Organisation	Type of Organisation	Comment number
12.11.2020	Germany	Department 4 - Hazardous Substances and Biological Agents - Federal Institute for Occupational Safety and Health	National Authority	3

Comment received

ECHA proposes an OEL of 1 µg Cd/m³ (inhalable fraction) together with a BLV of 2 µg Cd/g creatinine in urine to protect against both local effects on the lung and systemic effects (critical end-point: nephrotoxicity).
As stated by Department 4 Hazardous Substances and Biological Agents of the Federal Institute for Occupational Safety and Health in the CfE, we are of the opinion that cancer risk ratio(s) of non-threshold carcinogens such as Cd and Cd compounds should be communicated when an OEL is proposed.
ECHA assumes a practical threshold for carcinogenicity (lung cancer, relevant exposure is the respirable fraction) and states that because of this the derivation of a "dose-risk-relationship" (DRR) would not be necessary (p. 50). This is not in accordance with the guidance for OEL derivation, which says that the risk above the threshold for threshold carcinogens should also be indicated:
'In case of carcinogenicity, it is recommended to additionally present the dose-response for carcinogenicity (i.e. cancer risk estimates) above the threshold, if possible, as this may inform those involved in the decision making process (i.e. ACSH, European Commission, Council and European Parliament) of the health risks above the threshold level (e.g. for impact assessment). If it is not possible to derive the dose-response for carcinogenicity, the reasons should be stated.' (Appendix to Chapter R.8: Guidance for preparing a scientific report for health-based exposure limits at the workplace).
It is therefore necessary to derive a value for the respirable fraction of cadmium to describe the DRR above the threshold.
The current OEL of 1 µg/m³ (inhalable fraction) 'is considered conservative' by ECHA, which is stated as the reason why no reduction of the current value is necessary (p. 57). However, it should be justified why the proposed limit value is 'best estimate' and why it cannot be higher. This should be included in the part 'Proposal for OEL'.
We would also like to reflect on the relation between the airborne and biological limit value: With the newly proposed value, the arguments differ from the current entry in the CMD. Even at Cd workplaces where the air value of 1 µg/m³ is maintained, there is a long-term

risk of kidney damage and exceeding the BLV due to oral or dermal intake and exposure unrelated to the current workplace (former exposure, exposure due from non-occupational sources). The OEL must therefore be combined with the BLV. This means that biological monitoring is also necessary if the OEL of 1 µg/m³ is to be complied with, i.e. for all work with Cd. Similarly, Directive 98/24/EC regulates the same for lead. With that, the problem to establish a suitable lower limit for triggering biological and medical monitoring persists, however practical recommendations for the health surveillance of workers is made by the doctor and/or authority responsible and is not in the remit of the ECHA report.
In Germany, compulsory precautions must be taken in the event of repeated exposure during activities involving Cd. Cd biomonitoring is one of the necessary tests as part of precautionary measures. A possible cut-off criterion for precautionary measures is the German level of acceptance (0.16 µg/m³). The latter would have to be reconsidered, if activity-related oral intake is considered possible even in workplaces with very low air pollution.
In Germany, the Committee for Hazardous Substances agreed on tolerated and accepted risks related to uses of Cd and Cd compounds in 2014 (https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/910/910-cadmium.pdf?__blob=publicationFile&v=2). However, this derivation is currently under revision, taking into account new scientific evidence and is expected to be finalised very soon. Once the up-dated conclusions are available, they can be provided upon request.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 201112_Comm_FB4_BAuA_OEL_Report_Cd_Cd_compounds_.docx

ECHA/RAC Response

Your support to combine the OEL with the BLV is acknowledged.
The cancer risk sections and the justifications for the proposed values have been significantly revised. Thank you for the information on the updated German cancer risk documentation. ECHA has obtained the document, and the outcome of that is included in the updated report.

Regarding the German values for cadmium, it has been reflected that the values are currently under revision.

Date	Country	Organisation	Type of Organisation	Comment number
12.11.2020	Germany	German Federal Institut for Risk Assessment (BfR)	National Authority	4

Comment received

ECHA Scientific Report for evaluation of limit values for cadmium and its inorganic compounds at the workplace
EG-Nr.: 231-152-8

It is accepted that kidneys are the critical target organ for cadmium toxicity, with increased urinary excretion of low molecular weight proteins being the most relevant adverse effect. The report derives as point of departure (PoD) for renal effects the LOAEL from studies in the general population (2 µg Cd/g creatinine). This value is used as PoD for the derivation of a biological limit value (BLV) and an occupational exposure limit (OEL) taking into account a toxicokinetic model that correlates Cd-U levels to inhalation exposure.

The CONTAM panel of EFSA performed a meta-analysis for the derivation of a benchmark dose (BMD) value and its 95 %-confidence lower bound (BMDL), considering the kidney as

target organ and increased β2M excretion as clinical change. It concluded "that the urinary cadmium concentration of 1 µg per g creatinine or below, representing the internal dose, would indicate that 95 % of the European population would not exceed cut-off limits in the range of about 300 µg/g creatinine for β2M in urine" (EFSA 2009). EFSA used such value (1 µg Cd/g creatinine) to derive a tolerable weekly intake (TWI) value of 2.5 µg Cd/kg bw.

Using the same epidemiological dataset, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established in 2010 a provisional tolerable monthly intake (PTMI) of 25 □g/kg bw. In 2011, the CONTAM Panel evaluated the CONTAM and JECFA approaches and confirmed the TWI of 2.5 □g/kg bw for cadmium. A consideration of the different approaches is recommended.

For the correct interpretation of toxicological studies, the physicochemical properties of the substance have to be considered, such as for instance solubility, presence of particles, size and size distribution of the particles etc. In the evaluation of in vitro data for genotoxicity (paragraph 7.6.3) a study is examined, in which cadmium oxide is tested in four Salmonella typhimurium strains. In the study, no information is given as to the physicochemical properties of cadmium oxide and on the uptake of cadmium oxide in bacteria.

The validity of the test is therefore questionable.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comment_2020-11-11_OEL-Cd-compounds.docx

ECHA/RAC Response

The RAC opinion recommends now a BLV of 1 µg Cd/g creatinine which is in line with the EFSA approach.
A note on lacking information on update of cadmium in bacteria is added.

Date	Country	Organisation	Type of Organisation	Comment number
12.11.2020	Belgium	European Trade Union Confederation	Trade union organisation	5

Comment received

ETUC would like to thank ECHA for this new scientific report for evaluation of limit values for cadmium and its inorganic compounds at the workplace.
In ETUC views, ECHA's report should better substantiate why cadmium is considered a genotoxic carcinogen for which a practical threshold can be identified. Page 48, there are conflicting information between older data (Bolt and Huici-Montagud, 2008) and more recent data suggesting that direct interaction with DNA can not be ruled out (Bishak et al., 2015; Fischer et al., 2016). ECHA should therefore use a more cautious wording about the Mode of Action for carcinogenicity.

ETUC also suggests ECHA to provide a risk-exposure relationship as this will be useful for the future discussion in the Working Party on Chemicals within the EU Advisory Committee on Health & Safety. This is also consistent with the Guidance for preparing a scientific report for health-based exposure limits at the workplace and its appendix R.8-17 (chapter A.8-17.2.2.3).
Finally, ETUC suggest ECHA to clarify the status of the existing limit value for cadmium in Germany (0,16 µg/m³). There seems to be a confusion between the tolerable cancer risk (4:1000 worklife time) and the acceptable cancer risk (4:10 000). This should be corrected.

ECHA/RAC Response

The mode of action discussion for carcinogenicity has been updated to better reflect the

current understanding. No risk-exposure relationship has been derived, but reference is made to the recent BAuA estimates.

Regarding the existing OELs: Details on the current German OELs for have been included, as well a note stating that the current values are under revision.

Date	Country	Organisation	Type of Organisation	Comment number
12.11.2020	France	ANSES	National Authority	6

Comment received

all the differents comments on the OEL report are available in a word file transmitted in the section V (as an attached document)

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ECHA cadmium_V102020_V5.docx

ECHA/RAC Response

Title: The updated title is in line with all similar documents, reflecting that the document is now an appendix to the RAC opinion.

Section 3: Information on SVHC identification and uses regulated by the Fertilising Products Regulation has been added.

Section 4. Occupational exposure limits
It has been clarified that OELs cover Member States (MS) and some relevant organisation (and that the list is not exhaustive). For the French OELs it has been clarified that that the alveolar fraction corresponds to the respirable fraction.
Regarding the sections on biological limit values, the French values have been corrected as suggested by the comments. It has also been clarified that some of those are recommendations.

Section 6. Air monitoring of cadmium:

- The aim of the section is to show whether the OEL can be reliably measured and in this case the difficulty is to achieve very low concentrations. The adequate sampling strategy, including sampling volume etc for each specific case is out of the scope of the section. However, for those methods where the sampler for the inhalable fraction is not specified, the sampling time has also been calculated for a more common flow rate for inhalable samplers (2 l/min).
- The ISO 15202 and the DGF method have not been quoted together because even if based on same techniques, they have been studied and validated for different working ranges and there is a significant difference in the LOQ.
- The methods based ICP-MS have now been includes in the table.
- INRS Metropol methods have been updated as indicated
- The missing references have been included

Section 9: More details have been added to the text and to Table 15 on the French values, and other details have also been completed/corrected. However, the table presents examples and cannot interpreted as an exhaustive summary of all available approaches.
The justifications for the proposed OEL value (9.2.2.2) have been modified.
Your support for the urinary concentration as a biological indicator of internal dose/cumulative exposure is acknowledged.
Your support to apply a BLV together with an OEL is also acknowledged. It is also noted that you consider that the air limit value can only prevent/protect against local (respiratory) effects but not systemic effects.

The reference to the ANSES expert report has been included.
Your editorial suggestions have been considered and errors have been corrected.

Date	Country	Organisation	Type of Organisation	Comment number
11.11.2020	Germany	WirtschaftsVereinigung Metalle	Industry or Trade Association	7

Comment received

In general, WVMetalle plea for using all available high-quality information, including in this case the latest update of the cadmium and cadmium compounds evaluation performed by the German AGS subcommittee III, the scientific board for the assessment of hazardous risks within the AGS. The updated document will be brought forward to the AGS plenary meeting on 17th and 18th November 2020 for final validation. This reassessment will afterwards be published in the official gazette and will replace the existing (lower) exposure risk relationship (ERB) and the tolerance as well the acceptance values within the German technical rule TRGS 910 and TRGS 561. Unfortunately, the document is not available officially within the commenting period of this consultation. Nevertheless, Dr. Martin Wieske of WVMetalle - being a full member of AGS - will apply during the upcoming AGS meeting to hand over the validated document to ECHA immediately.
Please take this very recent AGS document into account when starting the discussion on the ECHA OEL recommendation on cadmium and its inorganic compounds. The updated AGS assessment results in an exposure value at the tolerance risk level of 4:1 000 at 2.6 µg Cd/m³ (respirable fraction), compared to the former value of 1.6 µg Cd/m³ (respirable fraction) at this risk level in the former linear approach of 2014. This makes a remarkable difference as the 1.6 µg Cd/m³ value was used in rounding down to the proposed OEL of 1 µg Cd/m³ (res-pirable, taken as inhalable) in the ECHA report.
In addition, we refer to the technical and scientific comments by the International Cadmium Association (ICdA). We fully support the robust set of comments on ECHA's scientific report for the evaluation of limit values for cadmium and its inorganic compounds at the workplace ICdA has submitted as this is in line with the German AGS subcommittee III evaluation. This is especially relevant when it comes to the preference the report gives to animal data over human epidemiological data, the existence of a threshold for cadmium kidney effects and the consideration of a sublinear dose-response relationship on the cancerogenic effect. The choice of the workplace air fraction to be considered to control adverse lung effects is also important. ICdA's comments also include a thorough analysis in support of the Scientific Committee on Occupational Exposure Limits (SCOEL) 2010 and 2017 Recommenda-tion/Opinion, which combine an OEL of 4 µg/m³ (respirable fraction) with a Biological Limit Value (BLV) set at 2 µg Cd/g creatinine, stressing that this is an effective alternative to the OEL currently set in the Carcinogens and Mutagens Directive.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-11-11_WVMetalle comment on ECHA OEL report on Cadmium.pdf

ECHA/RAC Response

Further details and justifications for the proposed OEL and BLV have been included in the report.

Information on the data presented in the recent AGS (BAuA) report has been added.

Date	Country	Organisation	Type of Organisation	Comment number
11.11.2020	Austria	AUVA (Austrian Workers	National Authority	8

		Compensation Board) -Prevention department		

Comment received

p. 7:
The proposed OEL of 0,001 mg Cd/m³ (1 µg Cd/m³) has an residual cancer risk. This risk should be shown in the report. As it is stipulated e.g. in the CMD 2019/983 (recital 9), information related to residual risk is valuable for any future work to limit risks from occupational exposure to carcinogens and mutagens, and should be made publicly available at Union level. Also it is demanded by ECHA in Appendix Guidance R.8- 17 (Guidance for preparing a scientific report for health-based exposure limits at the workplace) that in all cases the remaining uncertainties need to be clearly described, including the uncertainty surrounding the identification of a MoA threshold and the uncertainty in identifying the PoD. In some cases, especially for the second type of uncertainty, the remaining uncertainties may lead to the application of an assessment factor (R.8-17 chapter A.8-17.2.3.1 states (p. 20))

p. 16, 51, 57:
In Germany the current OEL (8 hour TWA)– derived by AGS (TRGS 910)- is 0,16 µg Cd/m³ (respirable fraction). This value is associated with an residual excess cancer risk of 4:10000 for work life- long exposure. But this cancer risk is to be adjusted in Germany to a risk of 4:100000. Therefore the target risk for an acceptable residual cancer risk should be 4:100000 (corresponding to an airborne concentration of 0,016 µg Cd/m³) to derive an OEL for cadmium and ist inorganic compounds.
(see also document: https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/910/910-cadmium.pdf?__blob=publicationFile&v=2)

ECHA/RAC Response

The mode of action discussion for carcinogenicity has been updated to better reflect the current understanding. No risk-exposure relationship has been derived, but reference is made to the recent BAuA estimates

Regarding the existing OELs: Details on the current German OELs for have been included, as well a note stating that the current values are under revision.

Date	Country	Organisation	Type of Organisation	Comment number
11.11.2020	Netherlands	Health Council of the Netherlands	National Authority	9

Comment received

See the commentary letter for specific comments

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Commentary letter RAC cadmium-DECOS.pdf

ECHA/RAC Response

The OEL established in the Netherlands has been included in table 5.
It is now specified in 9.2.1.3 that the OEL should be applied in combination with the BLV.
As the proposed OEL is not based on Thun et al. 1991, it was considered not necessary to discuss that study further.
The German cancer risk estimate (BAuA) (9.2.1.2) description has been revised due to a recent new evaluation. This is also reflected in 9.2.2.2.
Your suggestions for editorial corrections have been considered.

Date	Country	Organisation	Type of Organisation	Comment number
10.11.2020	Germany	<confidential>	Company Manufacturer	10

Comment received

We would like to thank ECHA for their report. Yet we support the scientific commentary made by ICdA on behalf of the Industry, concluding that an air limit value of 4ug/m3 Respirable fraction in combination with a biologic limit value of 2µg Cd/creatinine in urine is protective against adverse systemic health effects and cancer.

Furthermore, we support that while the occupational exposure limits should be based first on the risk to health, not necessarily on the analytical capability of the method, it is relevant to consider the sampling, analytical sensitivity and accuracy of the proposed OELV. Technical feasibility challenges could arise from compliance approaches and exposure measurement methodology (e.g., type of aerosol size selective sampler, pump etc) and we must therefore observe that values lower than this, such as the 1ug/m3 inhalable fraction, are rather unachievable in a large scale industrial setting.

ECHA/RAC Response

Further details and justifications for the proposed OEL and BLV have been included in the report.

Regarding the analytical capability, the report details in section 6 a number of available analytical methods. Some of them already show capability to measure airborne concentrations to show compliance with an OEL of 1 µg/m3 fulfilling the requirements of the EN 482.

Date	Country	Organisation	Type of Organisation	Comment number
10.11.2020	Belgium	<confidential>	Academic Institution	11

Comment received

Dear,
Attached you can find input from HBM4EU WP10 to the consultation of ECHA on the OEL report of cadmium.

Aggregated HBM data for cadmium from existing EU studies were obtained within HBM4EU through the national hubs and those data were harmonized within WP10.
In the pdf you can find a summary of the observations made, and the extracted summary statistics for cadmium in the individual data collections in the attached Excel file.

Kind regards,
Eva

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Submission ECHA consultation.zip

ECHA/RAC Response

Information on the HBM4EU data has been included in the report.

Date	Country	Organisation	Type of Organisation	Comment number
10.11.2020	Sweden	The Nordic Expert Group for Criteria Documentation of	International NGO	12

		Health Risks from Chemicals (NEG)		

Comment received

NEG strongly supports the approach of a combined use of an airborne OEL and a BLV. NEG also looks positively at the proposed values, however, further clarification of the derivation of the BLV is needed. See attachment for detailed page by page comments.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment NEG comments on ECHA Cadmium 2020.pdf

ECHA/RAC Response

Your support for the recommendation to apply both air and biological limit values, and your support for the proposed values are noted. Further justification for the proposed values has been added.

The list of OELs/BLVs has been updated including the amendments proposed.

Section 5: Information on the HBM4EU data has been included in the report. Your suggestions for editorial changes / improvement of section 5 have been considered and implemented.

Section 7: Thank you for the detailed proposals to improve the sections. Most of your editorial suggestions have been implemented. However, as the text (e.g. 7.2.2 and 7.3) is largely based on/copied from the SCOEL report it was decided not to make major changes or edit the way the data is presented. Specifically, for fertility effects, more studies have been included.

Sections 8-9: Thank you for the detailed proposals to improve the sections. Most of your editorial suggestions have been implemented. For the comment on Section 9.2.2.2, the risk estimates by BAuA were recently updated, which is described in earlier sections of the document, and also reflected in this section. On your comment on 9.2.4, the new proposed BLV is lower than in the circulated draft and takes also into consideration effects observed in studies on the general population. The justifications for the BLV have been updated.

Date	Country	Organisation	Type of Organisation	Comment number
10.11.2020	Czech Republic	Bochemie a.s.	Company Manufacturer	13

Comment received

Company BOCHEMIE a.s., Lidicka 326, Nový Bohumín, 73581 Bohumin, Czech Republic thanks ECHA for their report but commend the excellent scientific commentary made by ICdA on behalf of the Industry, concluding that an air limit value of 4ug/m3 Respirable fraction in combination with a biologic limit value of 2µg Cd/creatinine in urine is protective against adverse systemic health effects and cancer.

Furthermore, we support that while the occupational exposure limits should be based first on the risk to health, not necessarily on the analytical capability of the method, it is relevant to consider the sampling, analytical sensitivity and accuracy of the proposed OELV. Technical feasibility challenges could arise from compliance approaches and exposure measurement methodology (e.g., type of aerosol size selective sampler, pump etc) and we must therefore observe that values lower than this, such as the 1ug/m3 inhalable fraction, are rather unachievable in a large scale industrial setting.

ECHA/RAC Response

Further details and justifications for the proposed OEL and BLV have been included in the report.

Regarding the analytical capability, the report details in section 6. a number of available analytical methods. Some of them already show capability to measure airborne concentrations to show compliance with an OEL of 1 µg/m^3 fulfilling the requirements of the EN 482.

Date	Country	Organisation	Type of Organisation	Comment number
22.10.2020	Belgium	International Cadmium Association - ICdA	Industry or Trade Association	14

Comment received

Comments of the ICdA are given in Section V. Non-confidential attachment

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 20201022 International Cadmium Association comments.pdf

ECHA/RAC Response

Your support to set a BLV along with an OEL is noted.

Further details and justifications for the proposed OEL and BLV have been included in the report and in the RAC opinion.

Most of your editorial comments were considered and implemented.
In particular:

More details on the Park et al (2012) study were included.

Regarding cancer risk estimates, the recent estimates presented in the report by BAuA (2021) are now included and reflected in different sections of the report.

It has been made clear that in the studies on non-occupationally exposed pregnant women and developmental effects, there was no increase in exposure levels. The uncertainty related to low urinary cadmium levels and correlation with effects is discussed in the report, but still RAC considered biomonitoring of urinary cadmium levels as an important tool. In the toxicokinetics section it is mentioned that high gastrointestinal absorption rates have been observed in women with lowered iron stores.

The link between U-Cd and proteinuria and albuminuria is mentioned in the report and indicated as an uncertainty factor for the interpretation of bone and cardiovascular effects at low exposure conditions.

A sentence has been added to explain that in several of the human developmental toxicity studies, the urinary cadmium concentrations were not adjusted for diuresis (by correcting the measured concentrations with creatinine values), which causes a level of uncertainty regarding the interpretation of the findings.

It has been clarified that uncertainties are linked to the derivation of corresponding air concentrations from biological levels.

PUBLIC ATTACHMENTS
1. Cadmio comment.docx [Please refer to comment No. 1]
2. Comments on ECHA-scientific-report_Cadmium.pdf [Please refer to comment No. 2]
3. 201112_Comm_FB4_BAuA_OEL_Report_Cd_Cd_compounds_.docx [Please refer to comment No. 3]
4. Comment_2020-11-11_OEL-Cd-compounds.docx [Please refer to comment No. 4]
5. ECHA cadmium_V102020_V5.docx [Please refer to comment No. 6]
6. 2020-11-11_WVMetalle comment on ECHA OEL report on Cadmium.pdf [Please refer to comment No. 7]
7. Commentary letter RAC cadmium-DECOS.pdf [Please refer to comment No. 9]
8. Submission ECHA consultation.zip [Please refer to comment No. 11]
9. NEG comments on ECHA Cadmium 2020.pdf [Please refer to comment No. 12]
10. 20201022 International Cadmium Association comments.pdf [Please refer to comment No. 14]