ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114300156-65-01/F Helsinki, 12 June 2015

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For Citral, CAS No 5392-40-5 (EC No 226-394-6), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for Citral, CAS No 5392-40-5 (EC No 226-394-6), submitted by [redacted] (Registrant). ECHA notes that in the joint submission covering the current registration, the Chemical Safety Report (CSR) is not provided by the lead registrant on behalf of the member registrants. The scope of this compliance check is limited to the standard information requirements of Annex I and Section 2 of Annex VI, while the compliance check concerning the information requirements laid down in Annexes VII to X was done on the lead registrant dossier of this joint submission.

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates submitted after 15 January 2015, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2015.

This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

The compliance check was initiated on 2 June 2014.

On 15 September 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 21 October 2014 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments. The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 15 January 2015 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

Subsequently, proposals for amendment to the draft decision were submitted.

On 20 February 2015 ECHA notified the Registrant of the proposals for amendment of the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposals for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposals for amendment received and amended the draft decision.

On 2 March 2015 ECHA referred the draft decision to the Member State Committee.

By 23 March 2015, in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. In addition, the Registrant provided comments on the draft decision. The Member State Committee took the comments on the proposals for amendment of the Registrant into account. The Member State Committee did not take into account the Registrant's comments on the draft decision as they were not related to the proposals for amendment made and are therefore considered outside the scope of Article 51(5).

A unanimous agreement of the Member State Committee on the draft decision was reached on 7 April 2015 in a written procedure launched on 26 March 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

A. Information related to chemical safety assessment and chemical safety report

Pursuant to Articles 41(1), 41(3), 10(b), 14 and Annex I of the REACH Regulation the Registrant shall submit in the chemical safety report:

1. A reassessment of the skin sensitisation hazard information on a basis of the study giving rise to highest concern
or
A full justification for why the study giving rise to the highest concern was not chosen to draw conclusions for skin sensitisation and a robust study summary for the study chosen (Annex I, 3.1.5. of the REACH Regulation);

2. Revised DNELs for workers and for the general population using the assessment factors recommended by ECHA
or
A full justification for not using the recommended assessment factors in the DNEL derivation (Annex I, 1.4.1 of the REACH Regulation);

3. Exposure assessment and risk characterisation to demonstrate that the risk to the environment can be considered to be adequately controlled (Annex I, Sections 5 and 6 of the REACH Regulation);

4. The description of the use "use of cleaning agents – industrial" shall be revised.

5. A qualitative assessment of likelyhood that skin irritation is avoided when implementing exposure scenarios (Annex I, 6.5 of the REACH Regulation);

B. Deadline for submitting the required information

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation the Registrant shall submit to ECHA by **21 December 2015** an update of the registration dossier containing the information required by this decision.

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

A. Information related to the chemical safety assessment and chemical safety report

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

1. A reassessment of the skin sensitisation hazard information on the basis of the study giving rise to highest concern or a full justification why the study giving the highest concern was not chosen to draw conclusions for skin sensitisation and a robust study summary for the study chosen (Annex I, Section 3.1.5. of the REACH Regulation)

Annex I, Section 3.1.5. of the REACH Regulation requires that the study giving rise to the highest concern shall be used and a robust study summary shall be prepared for that study or studies and included in the technical dossier. In addition, Annex I, Section 3.1.5. stipulates that if a study giving rise to the highest concern is not used, then this shall be fully justified.

In the technical dossier, the Registrant has chosen the Local Lymph Node Assay (LLNA) and two Guinea Pig Maximisation Studies (GPMT) as key studies. Another LLNA, another GPMT study, and a review article on skin sensitisation are included as supporting studies. However, no robust study summary is available for the Human Repeated Insult Patch Test (HRIPT) which was used in the CSR for the derivation of the DNEL for local effects. There is no published standard testing guideline for HRIPT and, in addition, the HRIPT method was not described sufficiently. Therefore, it is not possible to assess with which method and under which conditions the test was carried out.

Human data will normally take preference over animal data in DNEL derivation (see: Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health, version 2.1, November 2012, paragraph 8.1.2.8.). However, the reporting of the studies must be sufficient to allow for the assessment of such human data. In this case, the reliability of the HRIPT could not be assessed, since the HRIPT test was not sufficiently described and since there is no validation study that would have assessed the reliability of the test.

According to the CSR, both the LLNA and the HRIPT studies lead to similar dose descriptor (NOAEL of about 1400 µg/cm^2). However, the DNEL based on the LLNA would be significantly lower than the DNEL based on the HRIPT, since according to the LLNA model,

interspecies variation is taken into account as an assessment factor. Therefore, the LLNA study gives rise to the highest concern.

The Registrant, in his comments submitted according to Article 51(1) of the REACH Regulation, notes that since both HRIPT and LLNA lead to similar dose descriptors, an interspecies assessment factor is not needed. Furthermore, the Registrant points out that intraspecies variation is taken into account. He also claims that "A robust study summary of the mentioned HRIPT and the reasoning given above will be included and the respective endpoint summary will be rephrased in the updated dossier." ECHA notes that even the updated dossier does not include a robust study summary for the HRIPT test, only a "critical reevaluation of existing studies". In fact, the endpoint study record has not been modified at all after the draft decision was sent (latest modification in 2010). ECHA also notes that the justification for using hazard data from HRIPT instead of LLNA is not provided. Therefore, the draft decision was not amended.

Based on the above, and in accordance with Annex I, Section 3.1.5 of the REACH Regulation, the Registrant is requested to re-assess the skin sensitisation using the LLNA study, or in the alternative, to justify the fact that the study giving rise to the highest concern was not chosen and to prepare a robust study summary for the study.

2. Revised DNELs for workers and for the general population using the recommended assessment factors by ECHA or a full justification for not using the recommended assessment factors in DNEL derivation (Annex I, Section 1.4.1. of the REACH Regulation)

Annex I, Section 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:

- the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
- the nature and severity of the effect;
- the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies.

The ECHA "Guidance on information requirements and chemical safety assessment" (Volume 8, R8, version 2.1, updated in November 2012) provides further details and default factors which should be applied to derive DNELs in the absence of substance specific information.

The assessment factors (AF) applied by the Registrant and the default assessment factors recommended in the ECHA Guidance are given in detail in Annex I attached to this decision.

ECHA observes that the Registrant has not followed the recommendations of ECHA's Guidance R.8 and has not provided a full justification for the derivation of DNELs in line with Annex I, 1.4.1. In particular, ECHA notes that for the systemic DNELs for inhalation route interspecies variation is not addressed at all and for systemic DNELs for dermal route, only allometric scaling is taken into account, whereas the remaining difference has not been addressed.

Furthermore, ECHA notes that for long-term local DNELs derived for dermal route based on skin sensitisation (LLNA), the exposure duration (subacute to chronic) was not taken into account at all as an assessment factor.

Thus the Registrant shall revise his DNELs by applying the recommended assessment factors appropriate in this case. In the alternative, the Registrant shall, in accordance with Annex I, 1.4.1, provide a full justification for the current DNEL derivation for workers and

for the general population provided in the chemical safety report.

The Registrant, in his comments submitted according to Article 50(1) of the REACH Regulation, notes that in the updated dossier substance specific assessment factors have been used. He also notes that since dose descriptor is based on the impaired body weight gain and local respiratory irritation, allometric scaling sufficiently takes into account interspecies variation. The Registrant also refers to ECETOC guidance and to other publications to support the use of the assessment factors used.

ECHA points out that, according to ECHA Guidance R.8, deviations from default assessment factors should be justified with substance-specific arguments. More specifically the introductory part of paragraph R.8.4.3, page 22 reports: "*However, when the available data do not allow the derivation of substance-specific or analogue-specific assessment factors, default assessment factors should be applied.*" Moreover, ECHA underlines that the guidance document R.8 was developed and approved in cooperation with the Member States, industry and non-governmental organisations in order to define further the derivation of DNELs according to the provisions of Annex I section 1.4.1 of the REACH Regulation. ECHA notes that in the updated dossier there are no substance specific assessment factors which would be justified by any substance specific information. As no adequate substance-specific justifications were provided to deviate from default assessment factors, ECHA is of the opinion that default ECHA assessment factors should be used.

Concerning allometric scaling, ECHA points out that the draft decision and its Annex I do not challenge the Registrant's choices concerning allometric scaling. Instead ECHA underlines the need of substance-specific arguments to justify the Registrant's choice not to apply an AF of 2.5 for remaining interspecies AF when deriving each of the DNELs. ECHA notes that according to Table R.8-6 of ECHA guidance such a default AF would not be needed for local effects on skin, eye and gastrointestinal (GI) tract via simple destruction of membranes, which is not the case for the registered substance. Indeed, the Registrant did not provide any substance specific arguments for deviating from this default assessment factor.

Finally, ECHA notes that the Registrant justifies the use of intraspecies assessment factor of 3 (workers) and 5 (general population) by general references to ECETOC guidance and with two scientific articles referred in that guidance. ECHA notes that the Registrant has not substantiated how the effect levels in the studies available would allow to conclude that a lower intraspecies AF than the default would apply. ECHA concludes that the Registrant did not adequately justify why interspecies and intraspecies AFs deviating from defaults would fulfil the condition of Annex I, 1.4.1. concerning uncertainty arising from intra- and interspecies variation.

Concerning DNEL for skin sensitisation, ECHA notes that the Registrant doesn't provide any information to support the idea that "the relevant parameters, i.e. induction of skin irritation and skin sensitization, are considered to depend on threshold concentrations rather than exposure duration" and that, therefore, for skin sensitisation assessment factor for exposure duration is not needed. In conclusion, the draft decision was not amended.

Based on the above, the Registrant shall revise his DNELs and reassess related risks. The results of the studies requested under section II.X shall be taken into account when revising the DNELs. If DNELs are not revised, this shall be fully justified. The chemical safety report shall be amended accordingly.

3. Exposure assessment and risk characterisation to demonstrate that the risk to the environment can be considered to be adequately controlled (Annex I, 5. and 6. of the REACH Regulation)

According to Annex I, Section 0.6, the Registrant is required to perform a Chemical Safety Assessment (CSA) for the registered substance. The CSA shall cover 1) human health hazard assessment, 2) human health hazard assessment of physicochemical properties, 3) environmental hazard assessment and 4) PBT and vPvB assessment. The CSA shall also consider exposure assessment and risk characterisation if as a result from these steps, the substance is assessed to be a PBT or vPvB or meets the criteria for any of the hazard classes or categories set out in Annex I to Regulation (EC) No 1272/2008 (CLP Regulation).

Furthermore, according to Annex I, Section 5.0 of the REACH Regulation, the objective of the exposure assessment is to make a quantitative or qualitative estimate of the dose/concentration of the substance to which humans and the environment are or may be exposed. Pursuant to the same paragraph the assessment shall cover any exposures that may relate to the hazards identified in Sections 1 to 4 of Annex I of the REACH Regulation.

The Registrant has waived the exposure assessment and risk characterisation for the environment based on the following statement: "*In the chemical safety assessment performed according to Article 14(3) in connection with Annex I section 3 (Environmental Hazard Assessment) and section 4 (PBT/vPvB Assessment) no hazard was identified. Therefore according to REACH Annex I (5.0) an exposure estimation is not necessary. Consequently all identified uses of the substance are assessed as safe for the environment.*"

It is apparent from the CSA that the Registrant has self-classified the substance as R38 (irritating to skin) and R43 (may cause sensitisation by skin contact) according to Annex I of Directive 67/548/EEC, and as Skin Irrit. 2 (H315: Causes skin irritation), Eye Irrit. 2 (H319: Causes serious eye irritation) and Skin Sens. 1 (H317: May cause an allergic skin reaction) according to Regulation (EC) 1272/2008. Therefore the substance is hazardous regarding skin corrosion/irritation (hazard class 3.2), serious eye damage/eye irritation (hazard class 3.3) and respiratory or skin sensitisation (hazard class 3.4) according to the definition given in Annex I to Regulation (EC) No 1272/2008. Consequently, the chemical safety assessment of the registered substance shall also include exposure assessment, exposure estimation, and risk characterisation.

Moreover, the CSA explicitly states that substance related effects were detected in short-term toxicity to fish (96h-LC50: 6.78 mg/L, 96h-NOEC: 4.6 mg/L, based on mortality), short-term toxicity to aquatic invertebrates (48h-EC50: 6.8 mg/L, 48h-NOEC: 3.13 mg/L, based on mobility) and toxicity to algae (72h-EC10: 3 mg/L, based on growth rate). Therefore, hazard is identified in aquatic toxicity and, thus an exposure assessment should be carried out for the environment.

In view of ECHA, Annex I, section 0.6 of the REACH Regulation, requires that a substance that meets the criteria for hazard class 3.1 to 3.6 set out in Annex I to Regulation (EC) No 1272/2008 shall be subjected to exposure assessment and risk characterisation. In addition, the Registrant has in the present case identified environmental hazards as short term toxicity to fish, short-term toxicity to aquatic invertebrates and toxicity to algae, which according to Annex I, section 5.0 of the REACH Regulation, shall be taken into account in the exposure assessment.

The Registrant, in his comments submitted according to Article 50(1) of the REACH Regulation, argues that the starting point to consider the scope of the exposure assessment is Annex I, Section 5.0 of the REACH Regulation which provides that an exposure assessment for environment has to be performed only if environmental hazards have been identified.

With regard to these comments ECHA points out the following:

Generally, two of the main purposes of both the REACH and CLP Regulation are to ensure a high level of protection of human health and the environment (Article 1(1) of the REACH and CLP Regulation respectively). The additional steps in a chemical safety assessment of exposure assessment and risk characterisation serve this objective as they allow estimating and characterising any risk to mankind or the environment. The formal arguments of the Registrant that this shall be done only for CLP-classified hazards ignore this overall context.

Both the REACH and CLP Regulation distinguish between the terms 'hazard', 'hazardous' and 'hazard classes'. The legislator would have used the term 'hazard classes' only if that was his intention for Annex I, Section 5 to the REACH Regulation. This becomes clear from the distinct references used in Article 3 of the CLP Regulation, Article 14(4) and Annex I, Sections 0.6.3. and 5. to the REACH Regulation. Under REACH, a hazard is identified by the results generated from the tests used to fulfil the information requirements set out in Annexes VII to XI. Pursuant to Article 13(3) of the REACH Regulation tests define endpoints/effects to be observed and reported for identification of (no)effect levels/concentrations and therefore, if a hazard is identified it is when an adverse effect is observed.

The REACH and CLP Regulations can be interpreted in a coherent and consistent way without reducing unnecessarily their respective scopes. The chemical safety assessment/report is regulated by law in order to assess and document that any risks arising from a substance are adequately controlled during manufacture and use. The burden of safe use lies with operators. ECHA therefore considers the additional steps of exposure assessment and risk characterisation for any identified hazard irrespective of classification as a measure in line with the precautionary principle that is underpinning the REACH Regulation (Article 1(3)) and which the Registrant seems to ignore.

Pursuant to Annex I, Section 3.0.2. of the REACH Regulation five environmental spheres shall be assessed for hazards. Annex I, Sections 5 and 6 require an exposure assessment and risk characterisation for the "*environmental spheres for which exposure to the substance is known or reasonably foreseeable*". Following the Registrant's line of reasoning, the environmental exposure assessment and risk characterisation would only be possible for the aquatic environmental sphere since the results for a number of standard data requirements for the other environmental spheres (e.g. information on soil/sediment toxicity,) do not lead to the classification of substances as hazardous, as no hazard classes or classification criteria exist for those other environmental spheres. It cannot be correct that a large part of standard data requirements set out in the REACH Annexes would become irrelevant. Instead, the legislator has a clear intention to use the standard information required in Annexes VII to X of the REACH Regulation for the hazard assessment without prejudice of classification needs.

For reasons of proportionality, the requirement of an exposure assessment and risk characterisation is limited to those substances meeting the criteria for classification of any hazard class/category set out in Article 14(4) of the REACH Regulation/Annex I CLP Regulation. In that regard the request by ECHA to understand exposure and risk of the substance subject to the present decision is not exceeding of what is appropriate and necessary to attain the objectives of the legislation.

ECHA has issued guidance on when exposure assessment and risk characterisation are expected (Guidance on information requirements and chemical safety assessment Part B: Hazard assessment; Version: 2.1; December 2011).

In conclusion, ECHA took the view that the request for an environmental exposure assessment for the substance is warranted. The draft decision was not amended.

Therefore, the Registrant is requested to perform a complete exposure assessment for the environment covering all life-cycle stages of the registered substance originating from manufacture and identified uses, and subsequently perform a risk characterisation for each exposure scenario to demonstrate the safe use of the substance. The Registrant is requested to update the dossier accordingly.

4. The description of the use "use of cleaning agents – industrial" shall be revised.

The technical dossier in section 3.5 (and also the CSR in the corresponding section) contains a scenario for the "use of cleaning agents – industrial". For use description of this scenario the Registrant assigned an Environmental release category "ERC 8a: Wide dispersive indoor use of processing aids in open systems". Following the rationale of this specific ERC as defined in Guidance R.12 and R.16, it is intended for uses by the public at large (consumers) or professional users. For industrial uses the corresponding descriptor is ERC 4 – the use of the related release factors might result in wrong calculations.

Therefore the Registrant shall review the description of this use. In case of missing information for distribution figures within the supply chain the Registrant has to calculate the environmental exposure for industrial and wide dispersive uses based on worst case assumptions regarding tonnages used as indicated in guidance R.16. This would mean that for industrial uses the complete EU tonnage has to be assumed for local exposure estimation. Deviations from this assumption need to be supported by a sound justification.

5. A qualitative assessment of likelihood that skin irritation is avoided when implementing exposure scenarios (Annex I, 6.5 of the REACH Regulation)

Annex I, Section 6.5.of REACH requires that for those human effects for which it is not possible to determine a DNEL, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out. In this case, DNELs have been derived for threshold effects. However, no qualitative assessment has been carried out for local effects on skin due to irritancy, even though the substance is classified for skin irritation. More specifically, there are no risk management measures for skin protection other than gloves. Therefore, it is possible that skin irritation is not avoided by the risk management measures in other parts of the body than hands. The ECHA practical Guide "How to undertake a qualitative human health assessment and document it in a chemical safety report" (Practical Guide 15) provides further details on how to carry out a qualitative assessment.

The Registrant, in his comments submitted according to Article 51(1) of the REACH Regulation, notes that the risk characterisation is based on both a conservative enough DNEL and a conservative exposure assessment. Therefore, gloves as a risk management measure are considered sufficient. He also notes that additional phrase "Avoid skin contact" will be included into relevant exposure scenarios of the updated dossier.

ECHA agrees with the Registrant that the absence of skin irritation is ensured in hands for which gloves are used as a risk management measure. However, no qualitative risk assessment has been done for other parts of the skin than hands. Furthermore, addition of phrase "Avoid skin contact" is not a sufficient risk management measure to protect other areas of the skin than hands. Therefore, the draft decision was not amended.

Therefore, the Registrant is requested to perform a qualitative assessment of likelihood that

skin irritation is avoided when implementing exposure scenarios.

IV. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]
Claudio Carlon
Head of Unit, Evaluation

Annex I.

Assessment factors (AF) applied by the Registrant:

For workers - systemic long term – inhalation route:
- intraspecies: 3
- exposure duration: 2
- quality of the database: 2

(overall AF: 12)

For workers - systemic long term – dermal route:
- interspecies: 7
- intraspecies: 3
- exposure duration: 1
- dose response: 3

(overall AF: 63)

For workers – local long term –dermal route:
- intraspecies: 10
- exposure duration: 1

(overall AF: 10)

For the general population - systemic long term – inhalation route:
- intraspecies: 5
- exposure duration: 2
- quality of the database: 2

(overall AF: 20)

For the general population - systemic long term – dermal route:
- interspecies: 7
- intraspecies: 5
- dose response: 3
- exposure duration: 1

(overall AF: 105)

For the general population – local long term –dermal route:
- intraspecies: 10
- exposure duration: 1

(overall AF: 10)

For the general population - systemic long term – oral route:
- interspecies: 7
- intraspecies: 5
- exposure duration: 1
- dose response: 3

(overall AF: 105)

The default assessment factors recommended in the ECHA Guidance[1]:

For workers - systemic long term – inhalation route:
- interspecies: 2.5 (remaining differences between species non related to allometry)
- intraspecies: 5 (workers)
- exposure duration: 2 (sub-chronic to chronic)

[1] Link to ECHA guidance document R.8 is: http://echa.europa.eu/documents/10162/17224/information_requirements_r8_en.pdf

(overall AF: 25)

For workers - systemic long term – dermal route:
- interspecies - allometric correction: 7 (mouse to human)
- interspecies - remaining differences: 2.5 (non-related to allometry)
- intraspecies: 5 (workers)
- exposure duration: 1 (chronic)
- dose response relationship - (LOAEL starting point): 3 (majority of cases)
  (overall AF: 262.5)

For workers – local long term –dermal route:
- intraspecies: 5
- exposure duration: depends on the length of the study

For the general population - systemic long term – inhalation route:
- interspecies: 2.5 (remaining differences between species non related to allometry)
- intraspecies: 10 (general population)
- exposure duration: 2 (sub-chronic to chronic)
  (overall AF: 50)

For the general population - systemic long term – dermal route:
- interspecies - allometric correction: 7 (mouse to human)
- interspecies - remaining differences: 2.5 (non-related to allometry)
- intraspecies: 10 (general population)
- exposure duration: 1 (chronic)
- dose response relationship - (LOAEL starting point): 3 (majority of cases)
  (overall AF: 525)

For the general population – local long term –dermal route:
- intraspecies: 10
- exposure duration: depends on the length of the study

For the general population - systemic long term – oral route:
- interspecies - allometric correction: 7 (mouse to human)
- interspecies - remaining differences: 2.5 (non-related to allometry)
- intraspecies: 10 (general population)
- exposure duration: 1 (chronic)
  (overall AF: 175)