EUROPEAN CHEMICALS AGENCY

Helsinki, 3 September 2020

Addressees
Registrants of JS_Nickel_metal listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of a decision
19/06/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Nickel
EC number: 231-111-4
CAS number: 7440-02-0

Decision number: [Please refer to the REACH-IT message which delivered this communication (in format TPE-D-XXXXXXXXXX-XX-XX/F)]

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***8 August 2023***.

A. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Extended one-generation reproductive toxicity study also requested, and specified, at B.1 below (triggered by Annex IX, section 8.7.3).

B. Requirements applicable to all the Registrants subject to Annex X of REACH

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route specified as follows with the Substance:

   - At least two weeks premating exposure duration for the parental (P0) generation;
   - Dose level setting shall aim to induce systemic toxicity at the highest dose level;
   - Cohort 1A (Reproductive toxicity);
   - Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation which must be followed to weaning.

You must report the study performed accordingly to the above specifications. Any expansions of the study design must be scientifically justified.

Conditions to comply with the requested information

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.
To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annexes VII, VIII and IX of REACH, if

you have registered a substance at 100-1000 tpa;

- you have to comply with the requirements of Annexes VII to X of REACH, if you have registered a substance at above 1000 tpa.

When a study is required under several Annexes of REACH, the reasons are provided in the corresponding appendices of this decision. The registrants concerned must perform only one study and make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants in accordance with Article 53 of REACH.

The Appendices state the reason for the request for information to fulfil the requirement set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Approved[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix A: Reasons for the request to comply with Annex IX of REACH

This decision is based on the examination of the testing proposal with the reference to Article 40(3)(b) of REACH.

1. **Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.)**

The basic test design of an extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is a standard information requirement under Annex IX to REACH, if the available repeated dose toxicity studies indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity. Furthermore column 2 defines the conditions under which the study design needs to be expanded.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 by the oral route in rats with 2-week premating exposure duration using nickel powder.

Adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity are observed in available studies. More specifically, the one-generation study (Kong et al. 2014) showed effects on sperm motility upon exposure to nickel micro-particles. In addition, there was appearance of cell apoptosis and death in testis, reduced birth survival rate and reduced feeding survival rate, and reduced body weight gain of pups. These findings are considered to be adverse effects.

Accordingly, an EOGRT study according to OECD TG 443 as specified in this decision is an information requirement for your registration, because Column 1 criteria at Annex IX, section 8.7.3 are met.

In your comments on the initial draft decision you expressed that the study design requested at Annex IX should be the same as the one requested at Annex X.

You must perform one study, only and the study design is the same for both Annex IX and Annex X.

For the specifications of the study design and considerations for alternative methods see Appendix B.

Appendix B: Reasons for the requirement applicable to all the Registrants subject to Annex X of REACH

This decision is based on the examination of the testing proposals with the reference to Article 40(3)(b) of REACH.

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement under Annex X to the REACH Regulation. Furthermore, column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 by the oral route in rats with 2-week premating exposure duration using nickel micron-size powder. You have provided the following justification and specification of the study design according to the criteria described in Column 2 of Section 8.7.3, Annex X: Basic study design. In particular, extension of Cohort 1B is not proposed because lack of classification for mutagenicity; there are no indications that an extended exposure will be necessary for the internal dose to reach steady state; and there are no indications that relevant modes of action of nickel metal are related to endocrine disruption. You propose not to include Cohort 3 because in existing data no severe statistically and/or biologically significant organ weight (spleen, thymus) or histopathological finding related to an immunology organ has been observed; the current inhalation DNEL is protective for immunotoxic effect such as a reduction in the number of antibody-producing spleen cells and the dermal DNEL is protective against sensitizing properties; and there is no evidence for a hormonal mode of action for immunotoxicity of nickel.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (extended one-generation reproductive toxicity study). ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA considers that the proposed study design needs further specification to fulfil the information requirement.

The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You proposed a 2 weeks premating exposure duration.

A minimum of 2-week premating exposure duration for P0 animals is required because the full spectrum of parameters on sexual function and fertility will be covered in the F1 animals.

Dose level selection

You have explained the basis for dose level selection as follows:

> *"The doses will be based on a weight of evidence from available toxicity and toxicokinetic studies conducted via the oral route, and if necessary, a dose range-finding study will be performed. The highest dose level will be set with either toxicokinetic information at a dose that induces some systemic toxicity, but not death*

or severe suffering of the animals. The study will include at least three dose levels and a concurrent control."

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level must aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a range-finding study (or range-findings studies) are reported with the main study.

You must provide a justification with your study report that demonstrate that the dose level selection meets the conditions described above.

In your comments on the initial draft decision you agree with the approach of dose-level selection in order to be compliant and not to be rejected due to too low dose levels.

Extension of Cohort 1B

If the Column 2 conditions of Section 8.7.3., Annex IX/X are met, Cohort 1B must be extended by mating the Cohort 1B animals to produce the F2 generation.

You have proposed not to extend Cohort 1B to produce the F2 generation, and have argued that

"The conditions for the production of the F2 Generation do not apply to the test substance. Data regarding carcinogenicity and genotoxic effects of nickel metal do not support a need to classify for the mutagenicity endpoint while mutation studies are ongoing; there are no indications that an extended exposure will be necessary for the internal dose of nickel metal to reach steady state since a one-generation study showed adverse effects with one dose of nickel metal micron-size powder (Kong et al., 2014). In addition, in previous rat studies with soluble nickel compounds (with higher bioavailability than the test substance) developmental effects (e.g., perinatal mortality) were identified in the first generation, and there have been no instances of the effects being amplified in the second generation (Ambrose et al., 1976; Smith et al., 1993; RTI, 1988a,b; SLI 2000b). Therefore, even though exposure to professionals and consumers exist, the proposed study design does not foresee the extension of cohort 1B to produce the F2 generation based on the criteria listed above."

In your comments on the initial draft decision you disagree with ECHA's rationale for extension of Cohort 1B to produce the F2 generation. You introduced several arguments.

(i) You agree that there is significant professional exposure, but ask for reconsideration of the consumer exposure "[...] *we recognize that professional use of nickel may involve exposure to powders via inhalation and some, albeit limited, absorption may occur. On this borderline case, we do not challenge ECHA's conclusion that there is significant professional exposure, but request that the finding of "significant" consumer exposure be reconsidered".*

(ii) You do not agree that there are triggers for the extension of Cohort 1B based on Kong *et al.* (2014) and you ask ECHA to reconsider the issue. You claim that:" *No matter the mechanisms that cause the reproductive effects (i.e. perinatal mortality) that can be induced by highly bioavailable soluble nickel compounds in rats, the effects are*

already seen in the first generation and are not magnified in the second generation in existing studies."

(iii) You continue addressing the reliability issues of Kong *et al.*, (2014), in particular the lack of reporting of oestrus cycle at the time of sacrifice in females, lack of information on sampling times of males, functional impact of the findings and question the relation of the treatment to the changes in serum hormonal levels and claim that: "*Whether the observed alterations are due to nickel treatment itself is questionable as there was no effect on mating, fertility or precoital intervals in this and other studies (Smith et al., 1993; Käkelä et al., 1999; SLI, 2000a,b). SLI (2000b) also reported no effect of nickel on estrous cyclicity, although lower doses were tested than in other studies in order to establish a reliable reproductive NOAEL.*" You further argue that: "[...] *the alterations in serum hormones observed in the nickel-treated male rats may be related to the order in which the rats were sampled. As with the female rats, there was no reported effect on fertility, raising the question of any functional impact of the reported hormone changes and their association with nickel treatment. Because the hormonal findings were reported in a single study with critical statistical and methodological shortcomings, it is our opinion that the Kong et al. (2014) data on female and male serum hormone alterations are not sufficiently reliable to indicate endocrine-disrupting mechanisms of action".*

(iv) Finally, you note that for animal welfare reasons, the generation F2 should not be included in the study since no new information is likely to be obtained. Instead, you propose a 10-week pre-mating period for the F0 generation.

However, ECHA considers that the criteria to extend the Cohort 1B are met, because:

- *Exposure*: The use of the Substance reported in the joint submission leads to significant exposure of consumers and professionals. There are exposure scenarios characterised by significant professional worker exposures, e.g. in manipulation of surface treated articles, sand blasting, thermal spraying, production of abrasive tools, production of batteries using nickel electrodes (PROCs 4, 5, 7, 9, 10, 13, 15, and 21). Examples of consumer exposures are the use of "nickel releasing surfaces" and "service life of surface treated articles (anodic coating) used by consumers".

  Your comments do not change this conclusion. You have provided no justification for reconsidering the finding of significant consumer exposure. ECHA points out, that your exposure scenarios contain the consumer use Cons CS 3: *Manipulation of surface treated articles (e.g. drilling, sawing) by consumers (AC 7).* For this contributing scenario you have estimated inhalation exposure of [redacted] and dermal exposure of [redacted] using MEASE version 1.02.01. When compared with the respective DNELs this yields an RCR of [redacted] for inhalation and [redacted] for dermal exposure. These exposure estimations indicate high consumer exposure. The RCRs and one very widespread use potentially affecting many consumers indicate significant consumer exposure.

- *Endocrine disruption indication*: Furthermore, there are indications of one or more modes of action related to endocrine disruption in the one-generation study performed with nickel metal micron-size powder (Kong et al. 2014). In that study, statistically significantly "*increased serum concentrations of follicle stimulating hormone (FSH) in females, increased luteinizing hormone (LH) in females, and decreased estradiol (E2) in females*" were observed, as well as "*decreased serum concentrations of FSH in males, decreased LH in males, and decreased testosterone (T) in males.*"

  Your comments do not change this conclusion.

Regarding your comment on the observed effects: the mechanisms/reasons of the observed effects (i.e. perinatal mortality caused by highly bioavailable soluble nickel compounds) are not known. However, the indications of effects related to hormonal (endocrine disrupting) modes of action, which trigger the extension of the Cohort 1B, are obtained using your Substance (micron-size nickel metal powder). The toxicity of the micron-size powder of nickel metal has not been investigated in F1 adults and F2 pups and there is a concern based on the findings from the one-generation toxicity study with the micron-size powder of nickel.

Regarding your comment on the reliability of the study: ECHA acknowledges that information on oestrous cycle stage at termination and sampling times of males are important. However, lack of reporting those does not invalidate the results from hormonal measurement, which are distinct. Similarly, you have provided no justification, even less demonstrated, that lack of effects on oestrous cycle, mating, fertility or precoital intervals mean that hormonal levels have not been affected. In females, increased serum concentrations of follicle stimulating hormone (FSH) (approximately 20% and 40% in mid and high dose groups, respectively), increased luteinizing hormone (LH) (statistically significant, dose-responsive effect) in all treatment groups, and decreased oestradiol (E2) were reported. Furthermore, changes in serum hormone levels were observed in males, too. In Kong *et al* (2014), after exposure to micron-size nickel metal powder, decreased serum concentrations of FSH (approximately 10% and 30% in mid and high dose groups, respectively) and testosterone (T) (approximately 15% and 35% in mid and high dose groups, respectively) were reported. Therefore, the available information shows dose-responsive changes in serum hormone levels of treated animals, which indicate one or more modes of action related to endocrine disruption and therefore supports triggering.

You do not specify the statistical and methodological shortcomings, however, ECHA considers the study reliable to be used for raising the concern for one or more modes of action related to endocrine disruption, and triggering further investigations and the unreported information identified above does not significantly affect the reliability of the study.

- The criteria for the study design of OECD TG 443 are described in column 2, Section 8.7.3 of REACH as already indicated above. For you Substance the criteria for inclusion of extension of Cohort 1B are met.

  Regarding 10 weeks premating exposure duration, it will in any case not produce information on reproductive toxicity of the offspring and cannot replace the extension of Cohort 1B. On the other hand, 10 weeks premating exposure duration is not requested for P0 generation because there is no concern for accumulation and 10 weeks premating exposure duration is covered before mating F1 animals.

In conclusion, the criteria to extend the Cohort 1B are met by Substance-specific information on exposure and Substance-specific indication of one or more modes of action related to endocrine disruption.

Therefore, the Cohort 1B must be extended.

The F2 generation must be followed to weaning allowing assessment of nursing and lactation of the F1 parents and postnatal development of F2 offspring. Investigations for F2 pups must

be similar to those requested for F1 pups in OECD TG 443 and described in OECD GD 151[2]. It is recommended to aim to 20 litter per dose group in order to have similar statistical power for investigations than in P0 generation.

Species and route selection

You proposed testing by oral route in rats. ECHA agrees with your proposal.

Outcome

According to Article 40(3)(b) of the REACH Regulation, you are requested to carry out the proposed test under modified conditions, as explained above.

Further expansion of the study design

No triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including Cohorts 2A and 2B and Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in column 2 of Section 8.7.3., Annex IX/X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[3].

ECHA acknowledges that in your comments, you agree to expand the study based on any findings or developments that arise prior to the conduct of the study, following ECHA guidance or requirements in other jurisdictions.

[2] http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2013)10&doclanguage=en
[3] ECHA Guidance R.7a, Section R.7.6.

Appendix C: Procedural history

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 8 January 2018

ECHA held a third party consultation for the testing proposals from 28 February 2019 until 15 April 2019. ECHA did not receive information from third parties.

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of the REACH.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and amended the request and the deadline.

Your comments represented a consolidated view of almost all recipients of the draft decision. ECHA did not receive any other comments.

Deadline to submit the requested information in this decision

The timeline indicated in the initial draft decision to provide the information requested is 24 months from the date of adoption of the decision.

In your comments on the draft decision, you requested an extension of the timeline to 32-38 months. You justified your request with the following arguments, which ECHA has evaluated:

- *"When the sponsor receives the final ECHA decision letter, they need to select a CRO, sign the quotation, and start to discuss the project with the selected CRO. In addition, the (usually large) amount of test item should be provided to the CRO. This period can easily take 3 months."*

  There is planning time included for that purpose in the EOGRTS deadline. ECHA considers, you have provided no justification to extend the deadline based on the specific circumstances of your case.

- *"The CRO needs to perform the analytical method development and validation. Taking into account some time to start, it will take 3 months to finish this"*.

  Analytical method development and validation is part of the planning time included in the standard EOGRTS deadline. You have provided no justification to extend the deadline based on the exceptional specificities of the Substance.

- *"In case the test item is intended to be administered via the diet but no repeated dose information is available, a diet stability/palatability needs to be performed. This will take 1 month"*.

  There is planning time included for that purpose in the EOGRTS deadline. You have provided no justification to extend the deadline based on the specificities of the Substance.

- *"In most cases, a dose range finding study (DRF) is needed to select dose levels for the EOGRTS. Usually as DRF an OECD 421 study will be performed. This study will take 10 weeks of in-life and 10 weeks of reporting. Altogether (including start-up time), this will take 6 months"*.

This time is not included in the EOGRTS deadline, as registrants may under their own responsibility, but are not required to, perform the DRF before initiating the EOGRTS.

• *"Based on chemical characteristics, it can be decided to determine postnatal exposure in the pups during the OECD 421 study. To be able to measure this, a bioanalytical method should be developed and validated. Especially, these capacities are currently very limited. So it will easily add 3 additional months before the 421 study can start"*.

For this particular type of substance, ECHA considers that you have not demonstrated the need.

• *"Moreover, in case these analyses show that the pups are not exposed through the milk, an additional DRF study in which dosing of juvenile animals should be performed. This will take an additional 3 months"*.

For this particular type of substance, ECHA considers that you have not demonstrated the need.

• *"After this period of 13 to 19 months, the EOGRTS can start.*
• *The EOGRTS in-life period is 7-9 months (based on 2- or 10-weeks premating and second generation).*
• *The CRO needs 4-5 months for reporting of the draft (depending on the cohorts), and it will take 3 months for finalization.*
• *Altogether, it will take 27-36 months from final ECHA decision to final report of the EOGRTS."*

- • *"In addition, the testing results will need to be incorporated into the CSR for submission to ECHA. In light of this information, we request at least 32 months from the FD to the submission of the results of a base study, and 38 months if additional cohorts (cohort 1B extension, cohort 3) need to be included in the final study design". "We would like to also point out that from our exchanges with test labs, we are aware that they are heavily booked. The 32 months that we request above may only be sufficient if we get an early and informal (not legally binding) indication from ECHA as to by when at the latest we can expect the FD. Should we get such an indication, we would already contact a laboratory with a view to reserving a time slot. This would not reduce the overall amount of time justified above, but simply ensure that we could start with the steps outlined above as soon as the FD is issued".*

Currently ECHA does not indicate to registrants as to by when at the latest they can expect the adopted decision.

ECHA has considered your arguments and has only partially granted the request based on the indication that the testing facilities are heavily booked, dropping of cohort 3 and set the deadline to 32 months.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix D: Observations and technical guidance

1. This testing proposal examination decision does not prevent ECHA from initiating compliance checks at a later stage on the registrations present.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State(s).

3. Test guidelines, GLP requirements and reporting

   Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

   Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

   Under Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries'[4].

4. Test material

   Selection of the test material(s)

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account the impact of each constituent/impurity is known to have or could have on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/impurity.

   Technical reporting of the test material

   The exact elemental composition (including impurities) of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents and impurities of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

   Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[5].

[4] https://echa.europa.eu/practical-guides
[5] https://echa.europa.eu/manuals

5. List of references of the ECHA Guidance and other guidance/ reference documents[6]

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 in this decision.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[7]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

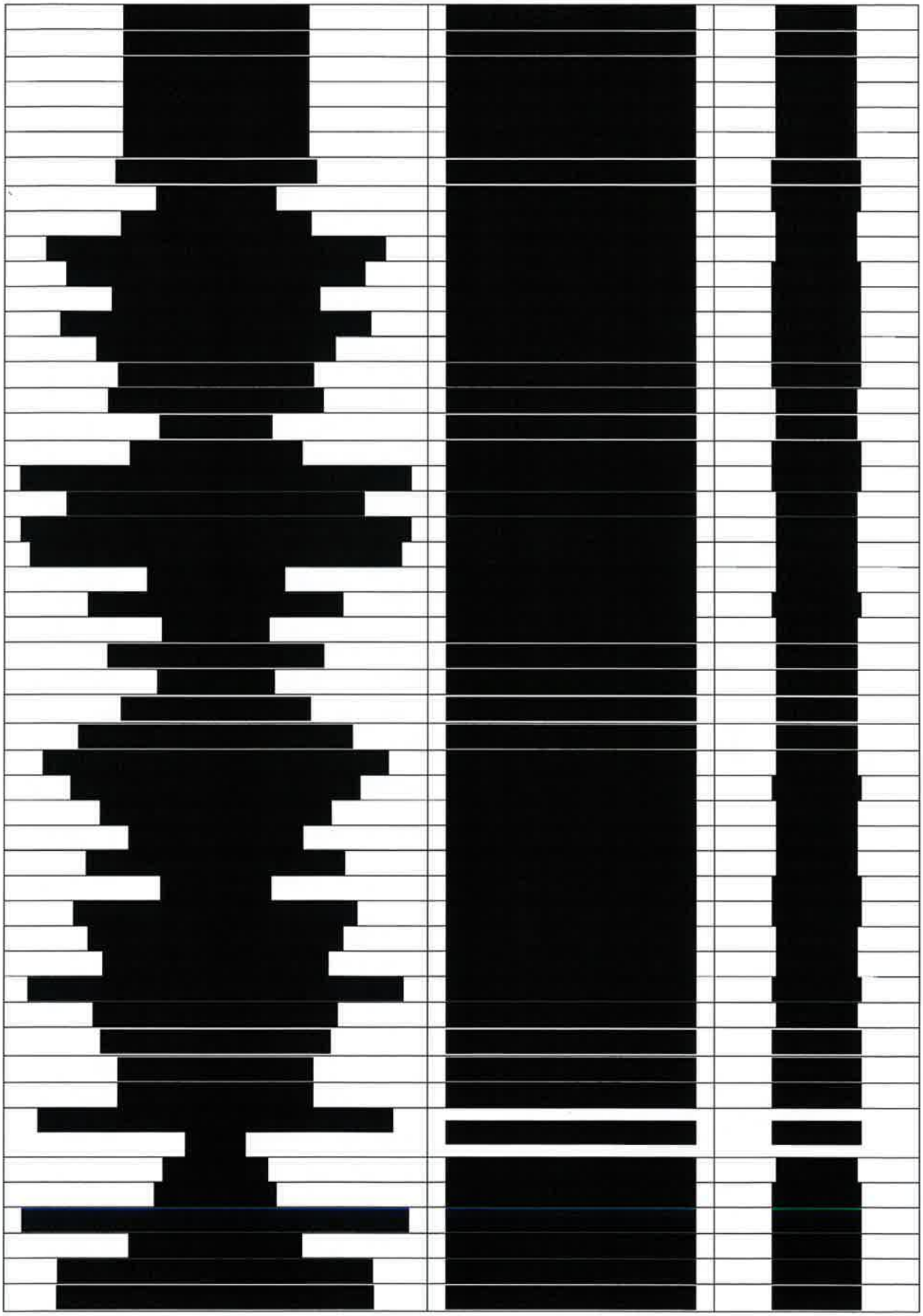
Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

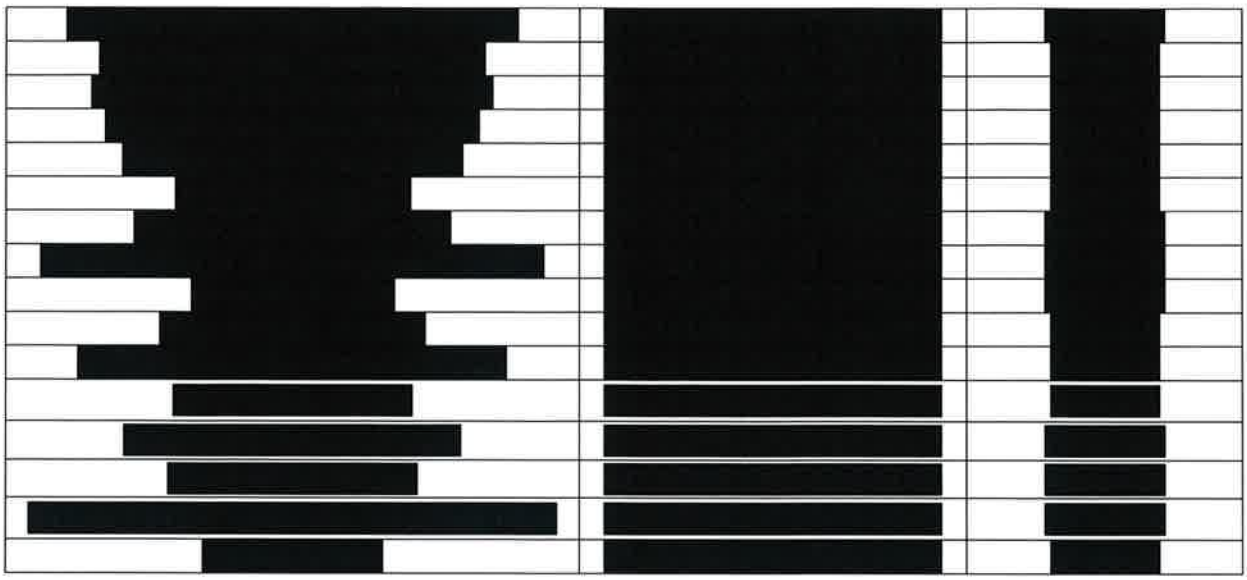
OECD Guidance documents[8]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document supporting the OECD TG 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD151.

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix E: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fulfilled
[redacted]	[redacted]	[redacted]





Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.