Information session on

How to submit a CLH dossier

26 May 2021

…… starting at 10.00 *Helsinki time

Welcome and introduction

Stella Jones
Head of Unit, Hazard I

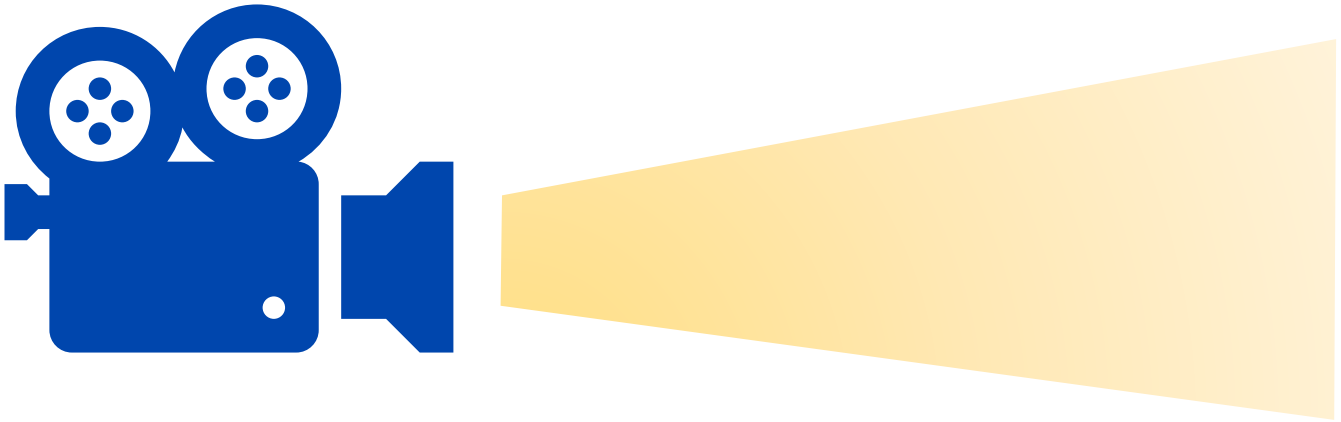
Christel Schilliger-Musset
Director
Directorate Hazard Assessment

First .....

Housekeeping

Recording

This information session is streamed and recorded



Practicalities and good practices

- All microphones will be muted
- Please turn your video off – presenters will have videos on
- There will be no hand raising function
- Comments/questions to be submitted using Slido
- Please do not use the chat function for questions as these cannot be monitored
- Please refrain from using the chat to socialise
- In case you need to reach us during the webinar: send an e-mail to: **classification@echa.europa.eu**

To comment/ask questions -> use Slido

- All questions and comments by Slido
- All questions will be addressed but some might be replied after the webinar due to their complexity
- The complete Q&A and presentations will be published on the webinar page in the coming weeks

Send your questions using Slido

- Go to Sli.do and type in the event code **#CLHdossier** or scan the QR code below with your phone
- Question not answered?
  Contact us: echa.europa.eu/contact

Join at
Sli.do
#CLHdossier

Opening remarks

Christel Schilliger-Musset
Director
Directorate Hazard Assessment

Dossier Submitter Support

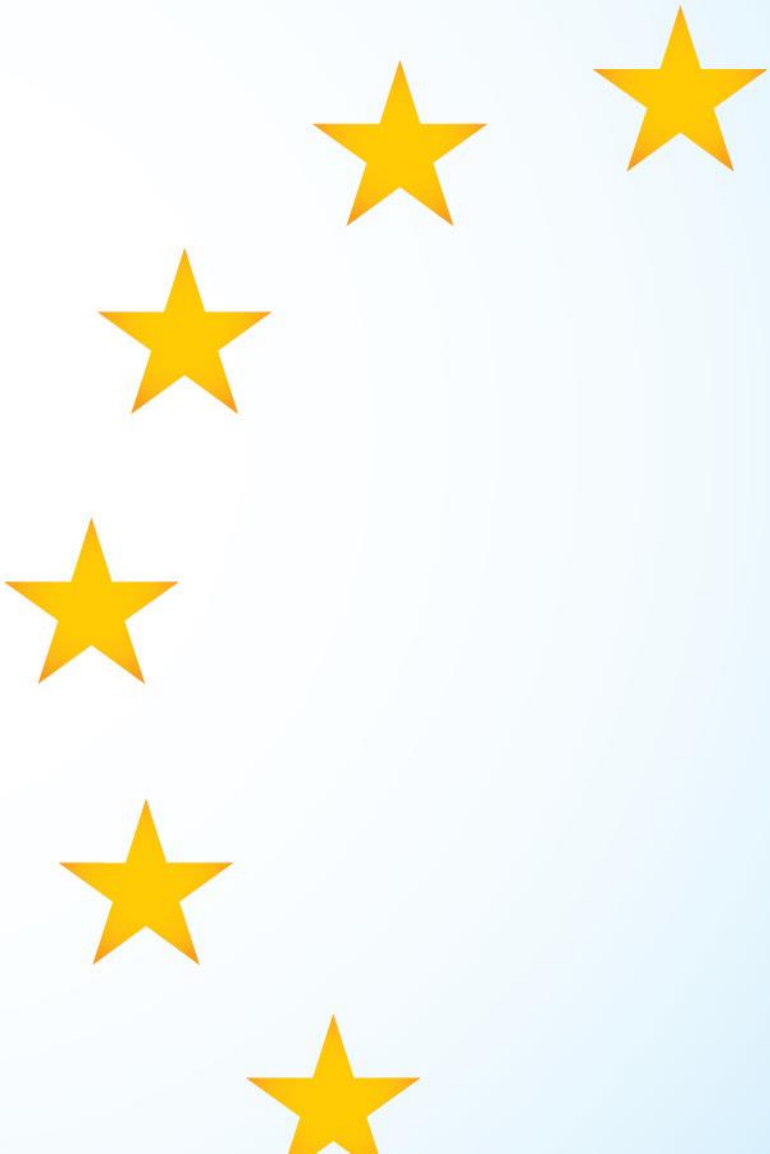
- CLH: important tool for risk management
  - Outcome of ECHA Grouping work
  - Chemicals Strategy for Sustainability
- MS visits pre pandemic
  - to collect information and feedback on CLH process
- ECHA Work Programme Document
  - to develop DS support for CLH dossiers

Chemicals Strategy for Sustainability

- Commission communication - October 2020
- Objectives:
  - better protect citizens and the environment
  - boost innovation for safe and sustainable chemicals
- Commission Inception Impact Assessments open for public consultaion (until 1 June)
  - CLP: Revision of EU legislation on hazard classification, labelling and packaging of chemicals (europa.eu)
- CLP revisions for new hazard classes
  - Development of new hazard classes and categorisation for:
    - PMT and vPvM
    - Endocrine Disruptors
    - PBT/vPvB

Introduction

Stella Jones
Head of Unit, Hazard I Classification



Introduction

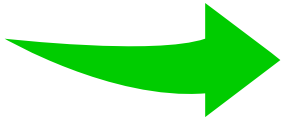
- Harmonised classification dossiers
- Workshop to webinar
- Programme today

CLH- Harmonised classification dossiers

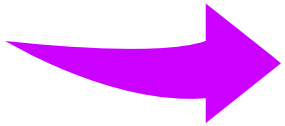
- The CLH process has an important role in protecting human health and the environment
- CLH is an important tool for risk mangement
- CLH – 3 key phases
  - Phase 1 – Dossier submission
  - Phase 2 – RAC opinion development
  - Phase 3 – Entry into Annex VI of CLP Regulation
- Today is focusing on:
  - Phase 1 and the submission of dossiers
  - plus an insight into RAC

Today is about .....

Dossier Submitter involvement



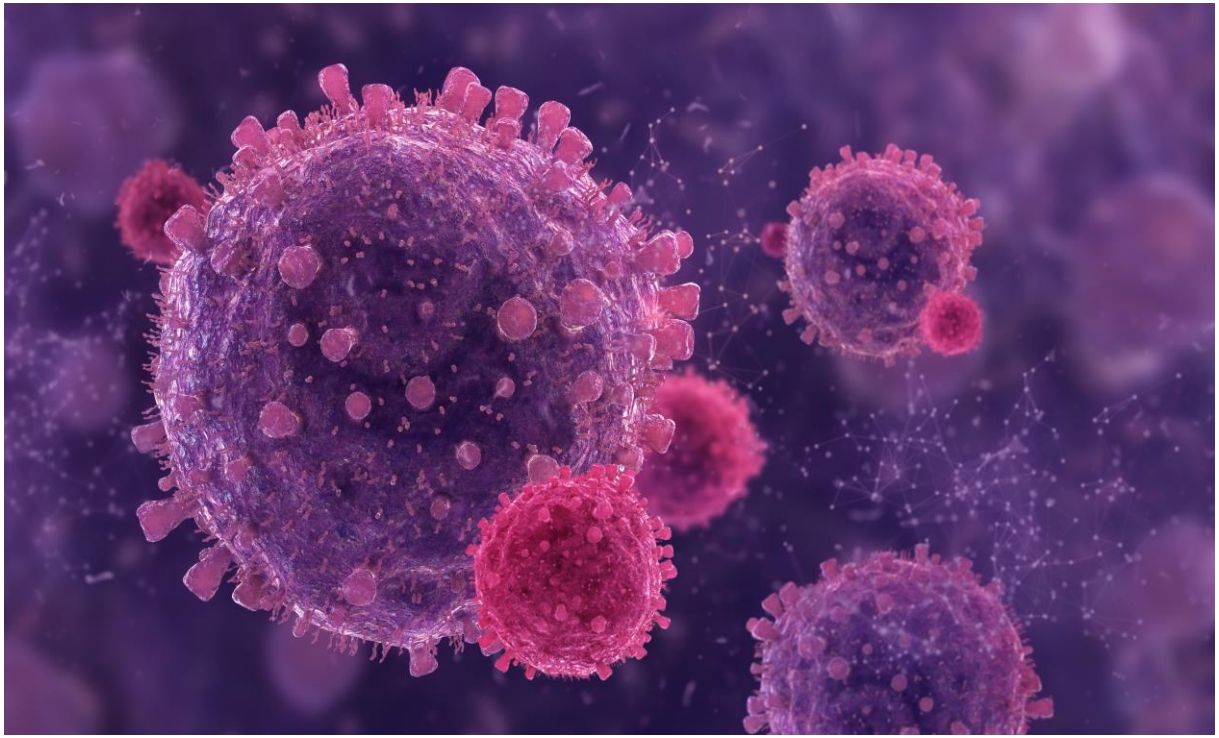
Smooth processs



Good opinions

What happened to the Workshop?

- a very very small ”being” that stopped the World!



… so

- At first we delayed … then we had a re-think!
  - change to a remote meeting
  - change in format
  - how to capture the information and interactions we hoped for from a workshop?
- And we came up with ….
  - To draft a Practical Guide to address the challenges and obstacles that dossier submitters encounter
  - To publish ”How to submit a CLH dossier” and
  - To have a three part event to support the publication:
    1. To organise a webinar/information session to launch the Practical Guide and the survey
    2. To do a survey to collect information
    3. To organise a follow up webinar to inform on the survey

Programme today…

Moderator: Stella Jones, Head of Unit, Hazard I-Classification, ECHA

Timing*	Title	Speaker
10:00—10:15	Welcome and introduction	Stella Jones Christel Schilliger-Musset
10:15—11:15	Practical guide Q&A	Chiara Perazzolo Ari Karjalainen Konstantinos Prevedouros
11:15—11:45	Data protection and confidentiality	Bo Balduyck Valeria D'Agostini
11:45—12:15	Break	
12:15—12:45	RAC & CLH dossiers	Tim Bowmer
12:45—13:15	Historical control data	Chiara Perazzolo
13:15—13:45	Presentation of the survey and the follow-up information session	Pia Korjus
13:45—14:00	Conclusions and closing	Stella Jones

*Helsinki time

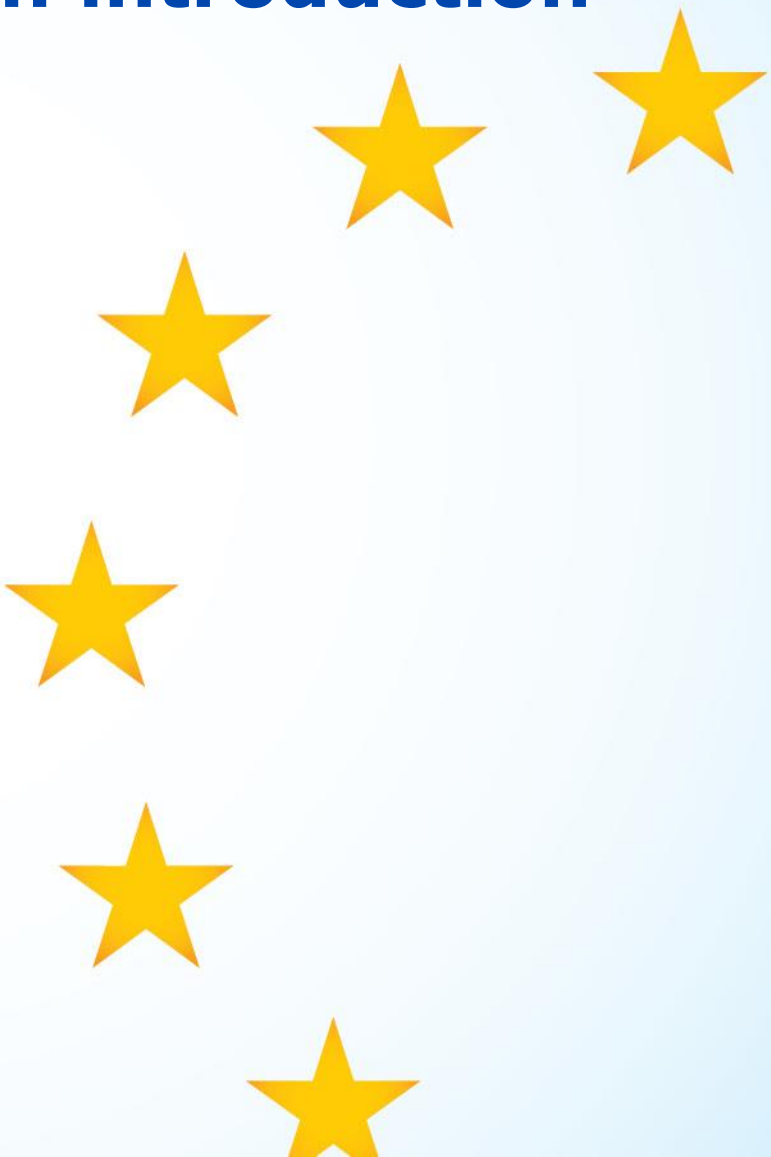
Practical guide

Chiara Perazzolo
Scientific Officer

Ari Karjalainen
Scientific Officer

Konstantinos Prevedouros
Senior Scientific Officer

Practical guide (PG) – an introduction



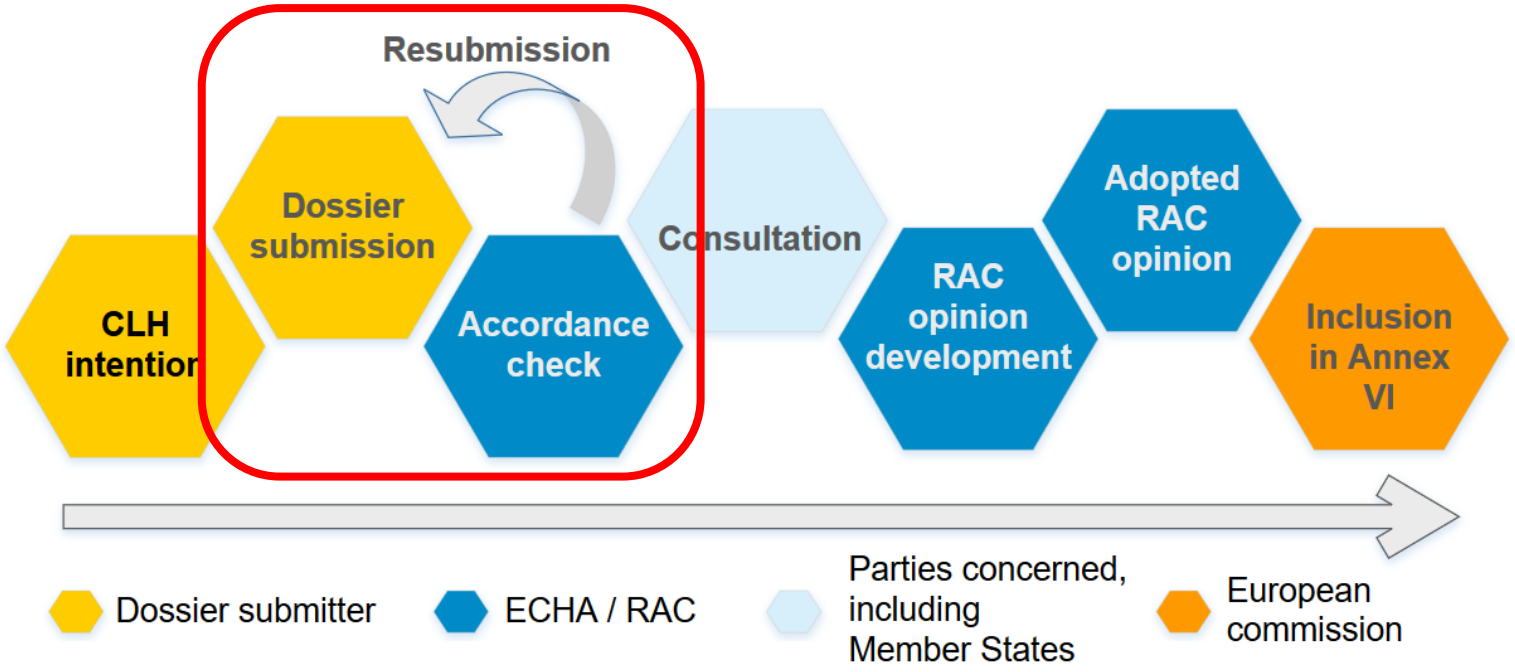
PG how to submit a CLH dossier

- Provides practical tips and advice to the DS
- Contains information from
  - CLP Regulation
  - ECHA guidance
  - Experience gained from the ‘Accordance check’ process
  - Experience gained from RAC discussions
- Does not replace existing ECHA guidance

The text of the CLP Regulation is the only authentic legal reference and the information in the PG does not constitute legal advice

Scope of this practical guide

Steps of the CLH process



Structure of the practical guide

- Follows the structure of the CLH dossier
  - 'Administrative'
    - Classification table
    - Justification
  - Physical hazards…
- … and groups topics which are relevant for several sections
  - Data confidentiality
  - Comparison with the criteria

- Includes references to other documents
- Includes a 'before submission' checklist (Appendix 1)
- Includes an Accordance check checklist (Appendix 2)

Examples

‘General’ topics

- Data availability
  - From all available sources
  - DS can exclude data with a justification

- Comparison with the criteria
  - **Always present and relevant**
  - Criteria for the HC category proposed, e.g. Carc. 2
  - … and for the **more** stringent HC category, e.g. Carc. 1B, 1A
  - … and for the **less** stringent HC category, e.g. No Classification

Accordance check - what is checked 1/2

General
Classification table
Comparison with the criteria is adequate
CLH proposal should be clearly stated also in the conclusion of each HC, even when the proposal is no classification
SCLs, M-factors, and ATEs are part of the proposal and should be included in the HC conclusion and in the CLH table
Hazard classes open for consultation should clearly stated and in line with the content of the rest of the report
If justification for submitting the dossier is required, it is included
Substance identity is clear
Read across is robustly justified
All data from other processes (REACH, BPR, PPP) are considered in the CLH dossier if available
Sufficient information is included in order for the CLH report to serve as a stand-alone document

Accordance check - what is checked 2/2

Physical hazards
Addressed for BPR ad PPP substances
Only and all the hazard classes relevant for that physical state are assessed
Assessment is based on criteria and methods listed on Annex I CLP Regulation
Human health hazards
Unpublished studies have authors names redacted and appropriate referencing
Study summaries include basic information (see section 2.10)
If present, historical control data are included with relevant information (see section 4.1.3)
Data relevant for one HC generated under studies normally considered indicative for another HC are included on the assessment of the latter HC. e.g. sperm data observed on repeated dose toxicity studies are included and evaluated under reproductive toxicity, sexual function and fertility
Environmental hazards
Unpublished studies have authors names redacted and appropriate referencing
Appropriate test protocols used, e.g. Aquatic Toxicity
Study summaries include basic information (see section 2.10)
Clear conclusion on substance properties (rapid degradability, bioaccumulation, ecotoxicity values)

Classification table

Has an established format in Annex VI to CLP:

- H. Class, H. Statement order
- ATE, SCL, M-factors 'spelling'

Existing entry in CLP Annex VI

	Index No	Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATEs	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	WWW-XXX-YY-Z	Substance name: ISO name; EC name/IUPAC name	AAA-BBB-C	DDD-EE-F	Acute Tox. 4* Acute Tox. 4* Eye Irrit. 2 Skin Irrit. 2 Aquatic Chronic 3	H332 H302 H319 H315 H412	GHS08 GHS07 Wng	H332 H302 H319 H315 H412			
Dossier submitters proposal	WWW-XXX-YY-Z	Substance name: ISO name; EC name/IUPAC name	AAA-BBB-C	DDD-EE-F	**Retain** Aquatic Chronic 3 **Add** STOT RE 2 Aquatic Acute 1 **Modify** Acute Tox. 2 Acute Tox. 4 **Remove** Skin Irrit. 2	**Retain** H412 **Add** H373 (blood) H400 **Modify** H330 H302 **Remove** H315	**Retain** GHS08 **Add** GHS06 GHS09 **Remove** GHS07	**Add** H373 (blood) **Modify** H330 H302 H410 **Remove** H315 H412		**Add** inhalation: ATE = 0,27 mg/L (dusts or mists) oral: ATE = 500 mg/kg bw M=10	
Resulting entry in Annex VI if adopted by RAC and agreed by Commission	WWW-XXX-YY-Z	Substance name: ISO name; EC name/IUPAC name	AAA-BBB-C	DDD-EE-F	Acute Tox. 2 Acute Tox. 4 STOT RE 2 Eye Irrit. 2 Aquatic Acute 1 Aquatic Chronic 3	H330 H302 H373 (blood) H319 H400 H412	GHS06 GHS08 GHS09 Wng	H330 H302 H373 (blood) H319 H410		inhalation: ATE = 0,27 mg/L (dusts or mists) oral: ATE = 500 mg/kg bw M=10	

Classification table

Existing entry in CLP Annex VI

Not included in the DS proposal row for **HCs not reassessed**

Automatically present in the final classification

Retain → Reassessment of an existing classification to **confirm it**

Add → Assessment and **proposal** of a classification for **new HCs**

Modify → Reassessment of an existing classification to **modify it**

Remove → Reassessment of an existing classification to **remove it**

					Classification					Specific Conc. Limits, M-factors and ATEs	Notes
					Hazard Class and Category Code(s)	**Hazard statement Code(s)**	**Pictogram, Signal Word Code(s)**	**Hazard statement Code(s)**	**Suppl. Hazard statement Code(s)**		
		name			Acute Tox. 4* ~~Acute Tox. 4*~~ Eye Irrit. 2 ~~Skin Irrit. 2~~ Aquatic Chronic 3	H332 H H H H	GHS09	H332			
Dossier submitters proposal	WWW-XXX-YY-Z	Substance name: ISO name; EC name/IUPAC name	AAA-BBB-C	DDD-EE-F	**Retain** Aquatic Chronic 3 **Add** STOT RE 2 Aquatic Acute 1 **Modify** Acute Tox. 2 Acute Tox. 4 **Remove** Skin Irrit. 2	**R** H412 **Add** 373 (blood) H400 **Modify** H330 H302 **Rem**	 **Add** GHS06 GHS09 **Remove** GHS07	H373 (blood) **Modify** H330 H302 H410 **Remove** H315 H412		Inhalation: ATE = 0,27 mg/L (dusts or mists) oral: ATE = 500 mg/kg bw M=10	
Resulting entry in Annex VI if adopted by RAC and agreed by Commission	WWW-XXX-YY-Z	Substance name: ISO name; EC name/IUPAC name	AAA-BBB-C	DDD-EE-F	Acute Tox. 2 Acute Tox. 4 ~~STOT RE 2~~ Eye Irrit. 2 ~~Aquatic Acute 1~~ Aquatic Chronic 3	H33 H30 H373 (blood) H319 H400 H412	 GHS09 Wng	H373 (blood) H319 H410		mists) oral: ATE = 500 mg/kg bw M=10	

Substance identity

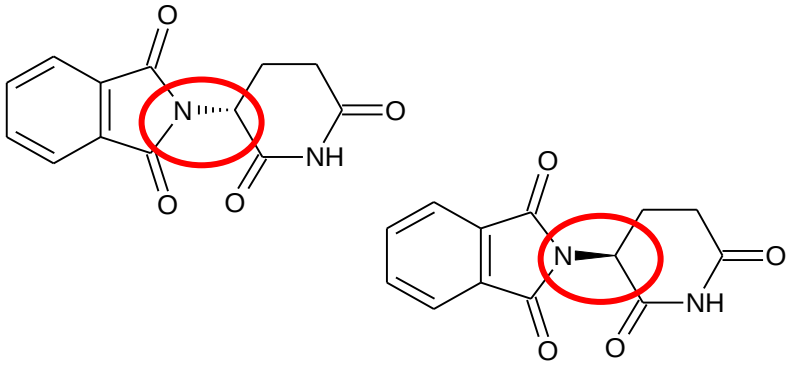
Substance Identity

Early discussion on the appropriate identifiers
(EC N., CAS N., names)

Substance identity tips

Guidance for identification and naming of substances under REACH and CLP

Watch for isomers



Name, EC N. and CAS N.

Structural formula

SMILES notation

Composition

Substance identity tips

EC numbers Vs List numbers

EC Number	Status
2xx-xxx-x	Official
3xx-xxx-x	Official
4xx-xxx-x	Official
5xx-xxx-x	Official
List Number	**Status**
6xx-xxx-x	Not Official
7xx-xxx-x	Not Official
8xx-xxx-x	Not Official
9xx-xxx-x	Not Official

Test material composition

Physical hazards

12th Adaptation to Technical Progress

Changes to existing HCs:

- Explosives
- Flammable gases
- …
- Substances and mixtures, which in contact with water, emit flammable gases

New HC included

Desensitised explosives

12th ATP entered into force in Oct. 2020, not yet included in the consolidated version

Assessed based on UN RTDG MTC

- Depends on their physical state as defined in Annex I, 1.0
- EU methods A.# generally do not provide sufficient information to assess the physical hazards

  - Exceptions are listed in the PG, from other ECHA guidances
- Most of them can be assessed using the 'screening procedures'
- Generally assessed for active substances under PPP and BP Regulation with no existing Annex VI entry

Human health hazards

Human health HCs some generalities

- By default, all effects observed are relevant to humans: non relevance to be demonstrated

- Route of Exposure

  Generally, can be specified when data conclusively show no classification for the other routes of exposure

- Specific concentration limits (SCL)

  SCL are part of the proposal and should (ideally) be evaluated each time and the conclusion included in the CLH dossier

Stand-alone report

- Overview in Section 2.10 of the PG
- Complete dataset (some points)
  - Information from registration dossier and relevant and reliable key data from public sources should be used
  - Balanced – all data, whether supporting the proposal or not
  - Conclusions need to be justified: References to "(not) treatment-related" need to be accompanied by data for independent verification
  - Effects need to be quantified (e.g. "increased/ decreased **by X%**")
  - Additional information in Annexes
  - Unambiguous and consistent proposal
  - Clear weighting of the quality of the data: Guideline/ GLP compliance and deviations

Human health HCs vs 'island'

- Some studies can provide information for more than one human health HC:
  - STOT SE assessment is based also on acute tox. studies
  - STOT RE evaluation should include all data from repeated dose toxicity studies, e.g. 28d, 90d, carcinogenicity…
  - Effects on reproductive organ observed on RDTS are generally evaluated under Reproductive toxicity

Not necessary to include the study results more than once (cross-referencing instead), however comparison with the criteria should include evaluation of all data available

Specific target organ toxicity, single exposure (STOT SE)

Includes three categories:

- STOT SE 1/2

  Assigned for non-lethal 'significant and/or severe toxic effects' on a specific target organ

- STOT SE 3

  Covers 'transient effects' occurring after single exposure, specifically respiratory tract irritation and narcotic effects

Effects observed on RDTS immediately after dosing or on the first days might be of relevance

Issues relating to specific hazard classes

- Acute toxicity
  - Proposal for an ATE to be included
- Skin corrosion/irritation
  - Decide whether category 1A, 1B, 1C or 1 or category 2
  - Correct use of data to address the criteria
- Eye damage/ irritation
  - Correct use of data to address the criteria
  - If data are available, assess despite a Skin Corr classification
- Respiratory or skin sensitisation 1, 1A or 1B
  - Consider whether data are sufficient to rule out 1A
- STOT RE
  - Use of Haber's rule

CMR

- Germ cell mutagenicity
  - Classification vs informing on carcinogenicity
- Carcinogenicity
  - Inhalation route issues relating to fibres and particles
  - MoA data
- Reproductive toxicity
  - Are the findings are relevant to classification for development or fertility?
  - Maternal/ paternal toxicity

Special cases

- Group entries
- Supplementary hazard statement codes
  - EUH0XY (e.g. EUH071, EUH066): Provide justification
- Notes associated with a classification: Justification

Environmental hazards

Information on degradation

- Biotic and abiotic (photolysis of uncertain relevance)
- Relevance of test protocol
- Conclusion on ready biodegradability, but more importantly, on **rapid** degradability
- Conclusion at the end of the respective CLH report section
  - follow decision scheme as in Section 4.1.2.9 of CLP
- Discussion on degradation products (identification, yields, hazard profile, etc.)

Information on bioaccumulation

- An evaluation for CLP purposes is always needed irrespective of available information
  - Experimental studies, QSARs, octanol-water partitioning (K_{OW})
- Relevance of study design and test protocol; related to substance properties
- CLP preference on experimental BCF data
  - in their absence, good-quality experimental K_{OW} data
- Clear conclusion at the end of the respective CLH report section
- Relevant for chronic classification

Information on aquatic toxicity…1/2

- Information on three trophic levels
- Appropriateness of test protocol
- Comprehensive, transparent and detailed reporting
  - Analytical monitoring, test validity criteria
- Study limitations and "assumptions" explained
- Statistical approaches may be followed (SSD)
- Weight of Evidence (number of studies, species, reliability, etc.)
- Independent evaluation for **CLP purposes**

Information on aquatic toxicity…2/2

- Preference of EC_{10} over NOEC for the same study
- Compare with CLP criteria together with conclusion on rapid degradability and bioaccumulation (chronic)
- In the absence of chronic data, the "surrogate" approach should also be used
- Most **stringent** outcome
- Special consideration for test concentrations above water solubility and "true" NOECs

Other best practices and tips

- Refer to previously published RAC opinions, especially on structurally similar substances
- Use relevant practical guides, guidances, templates
- Familiarise with CLH process
- Co-ordinate with pesticidal/ biocidal CAs
- Explore different ways of getting support
- Perform additional editorial checks

Q & A on the Practical Guide

Q&A prior to the info-session

- Who can submit a CLH proposal?
- Can I submit as non EU entity?

CLP Regulation Art. 37: a proposal can be submitted by competent authority (CA), manufacturer, importer or downstream user (MIDU), see REACH definitions → No proposal from non EU entities

Q&A prior to the info-session

- Who can propose a modification of HC on an existing harmonised classification?

  Only CA can "modify, retain or remove" see slide on classification table

- Who can propose additional HC to an existing harmonised classification → CA and MIDU

  Both CA and MIDU can "add" a new HC to an (existing) entry, see slide on classification table

Q&A prior to the info-session

- Proposal for classification of active substances, either plant protection products or biocidal products
- Read across, groups, non animal testing methods

See existing guidance documents on ECHA website

- Endocrine disruptors → not part of CLP … not yet

Data protection and confidentiality

Bo Balduyck
Policy Officer

Valeria D'Agostini
Legal Advisor

Confidentiality

Confidential information in the CLH Report

- CLH report intended to be made publicly available: it must contain all information considered relevant for the classification proposal
- No confidential information (assessment by DS)
- Confidential information to be provided by DS as a separate confidential Annex and clearly marked as such
- Specific reference to the confidential Annex in the CLH report
- Confidentiality criteria provided in REACH (Article 118(2) and Article 119)

REACH Article 119(1)

Information always published, no possibility of confidentiality claims:

- *the name in the IUPAC Nomenclature for substances which fulfil the criteria for any of the hazard classes set out in Article 58 (1) of the CLP Regulation17 16 , 17 without prejudice to paragraph 2(f) and (g);*
- *if applicable, the name of the substance as given in EINECS;*
- *the classification and labelling of the substance;*
- *physicochemical data concerning the substance and on pathways and environmental fate;*
- *the result of each toxicological and ecotoxicological study;*
- *any derived no-effect level (DNEL) or predicted no-effect concentration (PNEC) 24 established in accordance with Annex I;*
- *the guidance on safe use provided in accordance with section 4 and 5 of Annex 26 VI;*
- *the analytical methods if requested in accordance with Annexes IX or X which 28 make it possible to detect a dangerous substance when discharged into the 29 environment as well as to determine the direct exposure of humans.*

REACH Article 119(2)

Information published unless claimed confidential with a justification accepted as valid by ECHA as to why the disclosure is potentially harmful for the commercial interests of the party concerned

- *If essential to classification and labelling, the degree of purity of the substance and the identity of impurities and/or additives which are known to be dangerous;*
- *the total tonnage band (i.e. 1-10 tonnes, 10-100 tonnes, 100-1000 tonnes or over 1000 tonnes) within which a particular substance has been registered;*
- *the study summaries or robust study summaries of the information on physicochemical data concerning the substance, on pathways and environmental fate as well as on toxicological and ecotoxicological studies;*
- *certain information contained in the safety data sheet as defined in Article 119(2);*
- *the trade name(s) of the substance;*
- *the name in the IUPAC Nomenclature can be claimed confidential for a substance 14 that fulfils the criteria for any of the hazard classes set out in Article 58(1) of 15 Regulation (EC) No 1272/2008, but only for a period of six year and if the 16 substance is not one of the substance defined in Article 3(20) of REACH, e.g. 17 substances listed in the European Inventory of Existing Commercial Chemical Substances ('EINECS');*
- *the name in the IUPAC Nomenclature for a substance that fulfils the criteria for any of the hazard classes set out in Article 58(1) of Regulation (EC) No 1272/2008, if the substance is only used as one or more of the following: (i) as an intermediate; (ii) in scientific research and development; (iii) in product and process orientated research and development*

REACH Article 118(2)

Information whose disclosure is normally deemed to undermine the commercial interests of the concerned person:

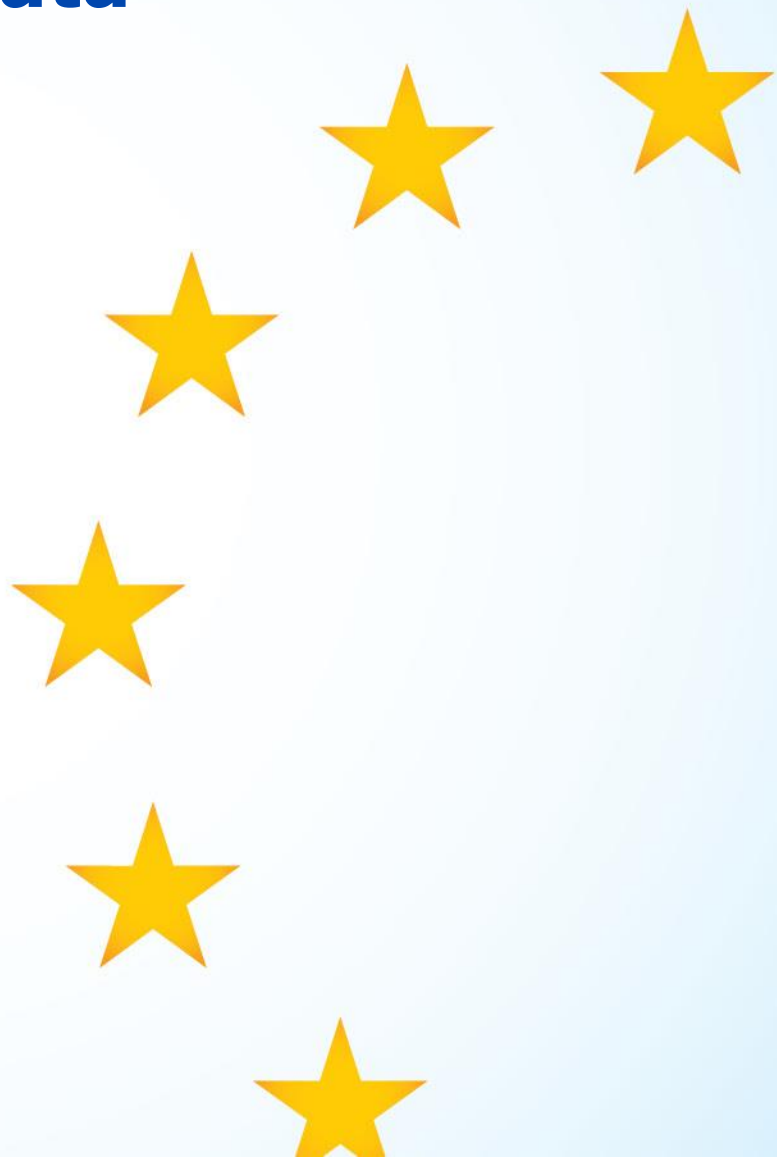
- *details of the full composition of a mixture;*
- *without prejudice to Article 7(6) and Article 64(2), the precise use, function or application of a substance or mixture, including information about its precise use as an intermediate;*
- *the precise tonnage of the substance or mixture manufactured or placed on the market;*
- *the links between a manufacturer or importer and their distributors or downstream users*

Examples of information that can be inserted in the confidential Annex

- *Degree of purity of the substance*
- *Identity of impurities and additives or concentration range*
- Information on the composition and manufacturing process of a UVCB substance

N.B. : if impurities and additives are confidential it is sufficient to state whether they contribute to the classification and labelling

Protection of personal data



Definition of personal data

- *”Any information relating to an identified or identifiable natural person”*
- E.g. name, contact information of natural persons (not legal entities/companies)

Personal data in CLH Report to be redacted

- Names of authors of unpublished studies
  - both vertebrate and
  - non-vertebrate studies
- Report number and name of testing laboratory if they allow to deduce author's name
- DS responsible for the redactions

- ECHA is striving to align its transparency/personal data protection policy with EFSA (see new EFSA Transparency Regulation)

RAC & CLH Dossiers

Tim Bowmer
RAC Chairman

Committee for Risk Assessment

Committee for Risk Assessment (RAC)

Art. 85, 87 and 88 of REACH

- RAC provides ECHA and the Commission with scientific advice in the form of opinions
- Members are nominated by Member States but appointed by the ECHA Management Board in their independent capacity
- No policy role
- REACH (authorisation, restriction), CLH, OELs
- RAC agrees the vast majority of opinions by consensus, with only occasional majority recommendations

Committee composition and operation

- As of March 2021, 50 members
  - Includes 2 EEA, 5 co-opted
- Members are expected to give >50% of their time to the work of RAC
- RAC meets 4 times a year for (25-30 meeting days per year)
- The CLP process is managed by the ECHA Classification Team (Unit C1)
- Meetings are organised, membership and participation managed by the Committees Secretariat (in the case of RAC, Unit D3)

Accredited stakeholders

- All stakeholders are now accredited to ECHA and not to individual Committees
- RAC meetings are not public but are open to stakeholders
- Only in exceptional circumstances are RAC sessions closed (e.g. appointment of rapporteurs)
- Strict adherence to confidentiality is required while dossiers are being processed

See Code of Conduct for ECHA Stakeholders:
https://echa.europa.eu/documents/10162/13559/conduct_code_stakeholder_observers_en.pdf

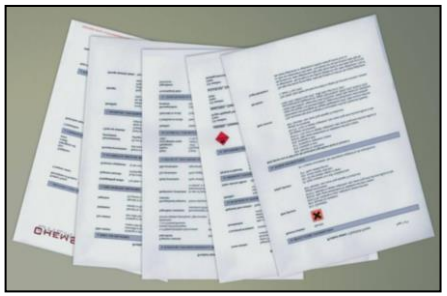
Members, Advisers and Invited Experts

- *Members may be accompanied by advisors*
- *RAC may invite experts*
- *Up to 5 co-opted members*

Observers

- *Case owners (e.g. dossier submitters, lead registrants)*
- *Stakeholders: Industry, civil society (regular & occasional) plus their experts*
- *International Organisations (e.g. UN bodies and OECD)*
- *COMMISSION representatives and other Community bodies*
- *ECHA staff*

RAC and ECHA procedures



Committee for Risk Assessment

- Rules of procedure
- Several Committee procedures governing the work of RAC

Harmonised Classification & Labelling

- Framework for RAC opinion development
- Procedure for agreement seeking
  (fast-track agreement)

Link to RAC web page https://echa.europa.eu/about-us/who-we-are/committee-for-risk-assessment

A-listing agreement

- Specific endpoints can be fast-tracked through RAC for agreement without plenary debate – called an 'A-list'
- Criteria have to be met related to the adequate scrutiny of the hazard classes proposed
  - The Dossier Submitter and the Rapporteurs are in agreement
  - The members providing written comments on the dossier have been given notice of the intention to propose fast-track for particular hazard classes
  - Those members agree with the DS and Rapporteurs
  - No substantial arguments against the proposals during general consultation
- Any member can request discussion
- The agreed classification is read into the record in plenary

Recent changes to RAC

- At its March 2021 meeting RAC, in support its activities set up a standing working group on CLH
- The working group will:
  - operate under the RAC rules of procedure
  - meet ahead of each plenary meeting of RAC
  - be open to Stakeholders in the same way as RAC
- Its purpose is to:
  - provide a substantial part of the necessary scrutiny of RAC opinions
  - discuss technical detail
  - recommend actions to RAC, including A-listing
  - remove up to 70% of the debating time from plenary

By WG-3 in October 2021 the full agenda for each RAC plenary will go through the working group

Other changes: consultations

- According to the EU Ombudsman consultations intended for the public should be translated into the EU official languages and accept replies in the same languages
- Consultation on ECHA dossiers are seen as technical consultations, to gather scientific information and not generally intended for the public
- Therefore, ECHA continues to perform these specifically technical consultations in English, while consultations intended for the general public will be translated into all EU official languages

Track record & workload

RAC Track record and workload - CLH

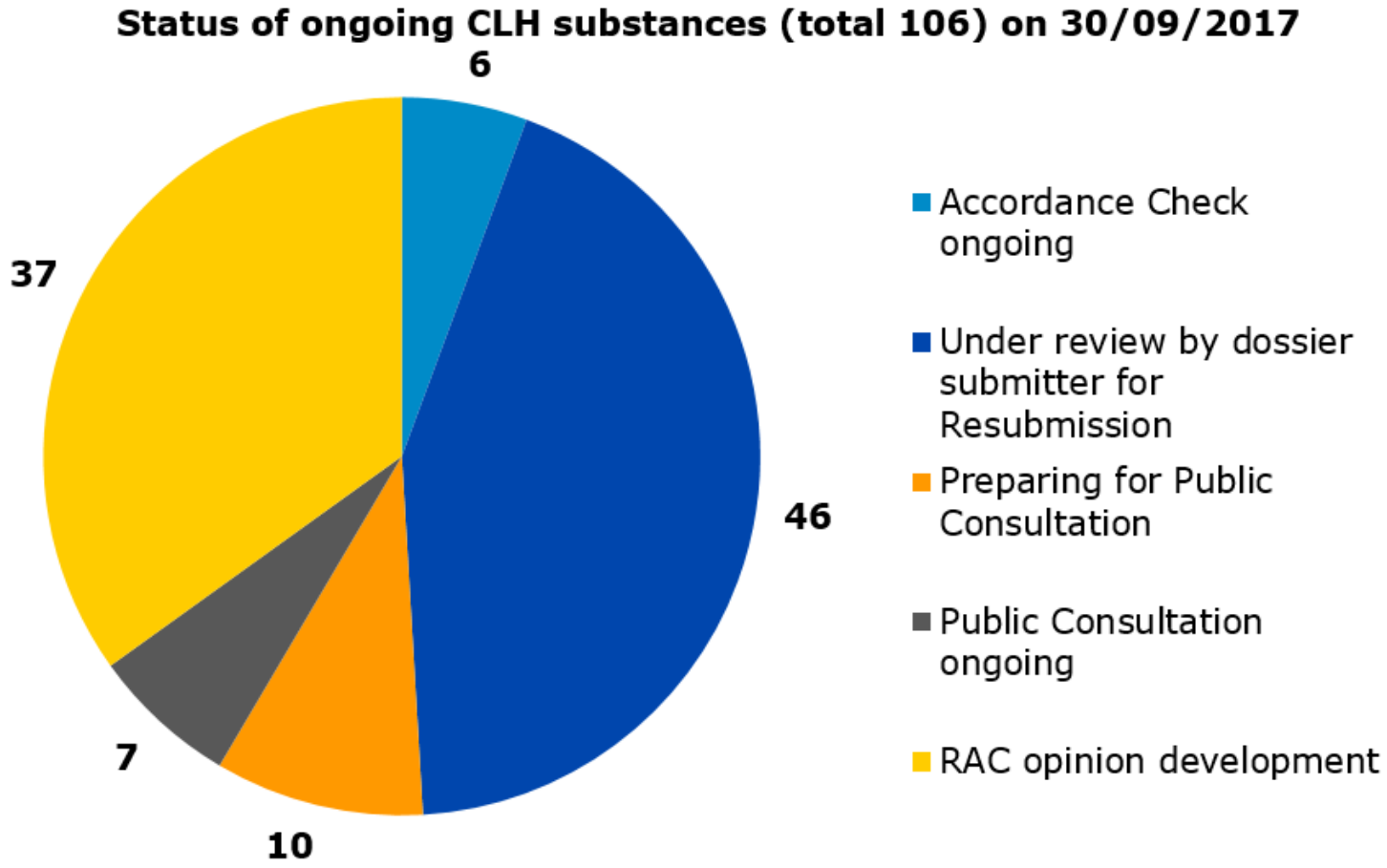
Progress since 2010 (first full year of RAC opinion-making)

- Dossiers submitted **620**
  - MSCA 601
  - Industry 19
- Opinions adopted **447**
- There are roughly 100 dossiers in process at any one time

Further increase in workload expected

50-60 opinions per year since 2017

Dossiers in process – March 2021



Some advice on preparing for RAC

RAC evaluation of CLH proposals

What is taken into account……

- Explicit classification criteria
  - supported by extensive guidance
- The (intrinsic) hazardous properties of a chemical
- The available data (the CLH dossier and general consultation submissions)
- The weight of the evidence
  - Studies/data are given a greater or lesser weighting
  - Klimisch is a guide to quality not a reason to dismiss

RAC evaluation of CLH proposals

What it not taken into account……

- The risks from using the substance
- Socio-economic aspects
- Down-stream legislative consequences (especially risk management)

Such issues, raised either in submissions, position papers or in plenary cannot be dealt with by RAC

Attending RAC discussions

- Dossier Submitters and Stakeholders may attend plenary (and working group meetings)
  - They may bring an expert
- The Committee may ask questions to clarify details of the dossier
  - Accompanying experts should really understand the dossier and have access to the study documentation
- Interventions should be short and to the point under discussion
  - The chair allows members to speak first, then fits in the Dossier Submitter and Stakeholders into the discussion
- Most proposals for harmonised classification are decided in one meeting

Why do we need good dossiers?

- RAC carries out a straightforward scientific assessment of the evidence using:
  - the classification criteria and ECHA Guidance
  - the available data (CLH report and consultation submissions)
- There are many dossiers running in parallel to yours
- Level of detail
  - are the study summaries really adequate?
  - if not, can you access the original study reports?
- Missing data can have a significant impact, e.g.
  - relevant studies, incl. negative outcomes
  - historical control data

What happens if RAC can't conclude?

- Classification in the hazard classes, categories and differentiations stipulated by CLP is not the only possible outcome
- Hazard classes which cannot be evaluated or for which the data are 'inconclusive' are taken as 'not classified' based on Annex VI of CLP
- If RAC cannot resolve the data because key parts are missing, then this undesirable situation may occur

No classification due to inconclusive data

No classification due to lack of data

Historical control data

Chiara Perazzolo
Scientific Officer

Historical Control Data (HCD)

- **The concurrent control is normally the most relevant comparator**
- HCD may be used to assess unexpected increases or decreases of incidence in the concurrent control
- HCD may be used to assist with the interpretation of rare tumours
- HCD should be used as additional WoE

HCD variability

- HCD are influenced by laboratory, breeder, species, strain, route of administration, vehicle, feed, housing, changes in pathology practices, etc.

Genetic drift may influence tumour incidence, some tumours appear to be stable over time

All these parameters should be considered when selecting and reporting the HCD

HCD – CLP guidance 1

- *HCD provide useful information on the normal pattern and range of tumour types and incidences for a particular strain/species, which may not be reflected by the tumour findings in the concurrent controls in any individual study*
- *HCD should be use to check the validity of the concurrent control*
- *HCD can also be useful to judge the biological significance of marginal increases in uncommon tumours*

HCD – CLP guidance 2

- *Use of HCD should be on a case by case basis with due consideration of the*[ir] *appropriateness and relevance*
- *HCD must be from the same animal strain/species, and ideally, be from the same laboratory*
- *HCD should be contemporary to the study being evaluated (e.g. within a period of up to around 5 years of the study)*

HCD – in CLH dossier

- ~ Used to check the validity of the concurrent control
- ✓ Used to check increase of uncommon tumours
- ✗ Due consideration of appropriateness and relevance

HCD must be …

- ✓ same animal strain/species
- ✓ ideally from the same laboratory

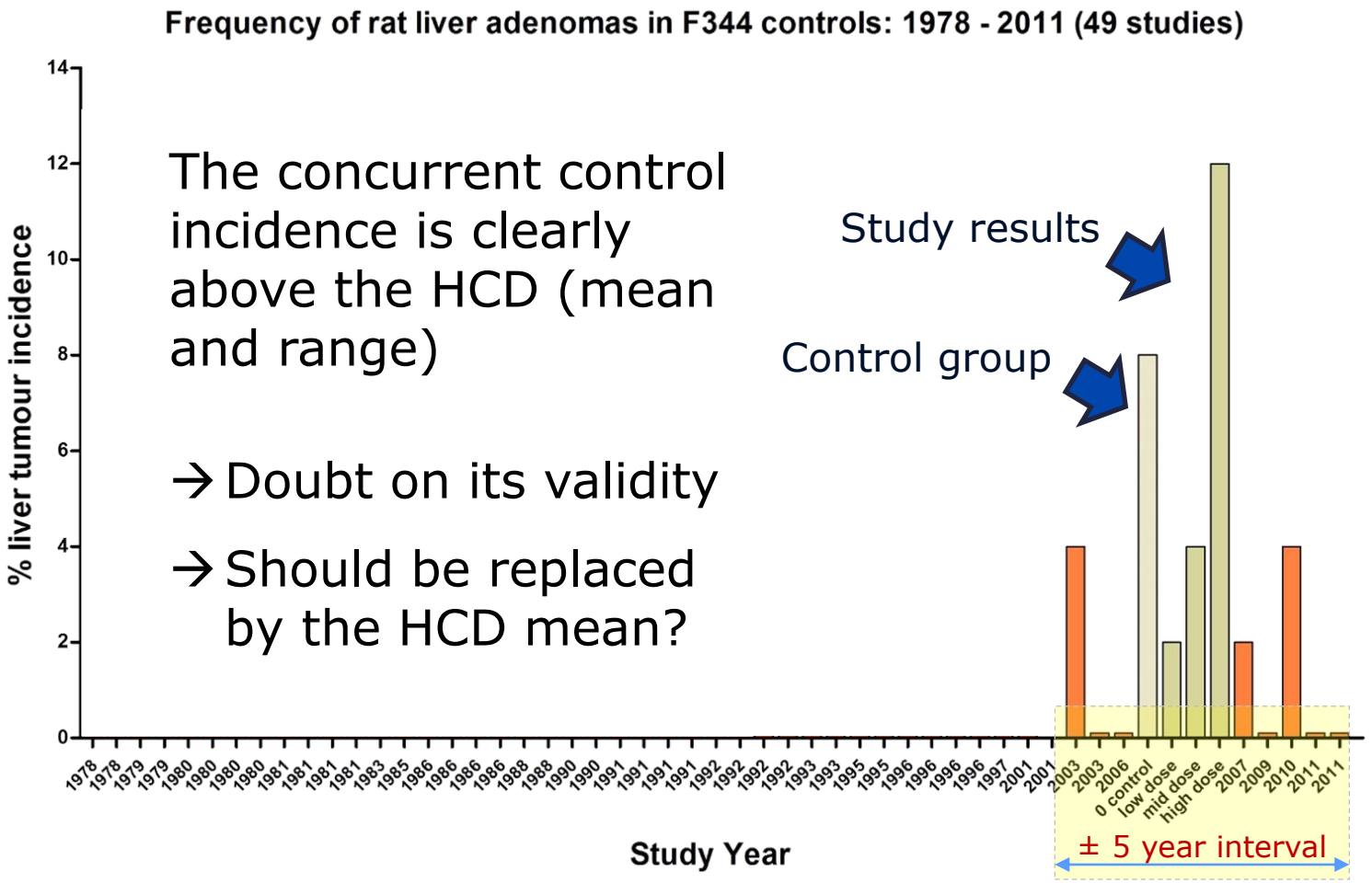
- ~ HCD should be contemporary to the study being evaluated (e.g. within a period of up to around 5 years of the study)

Example:

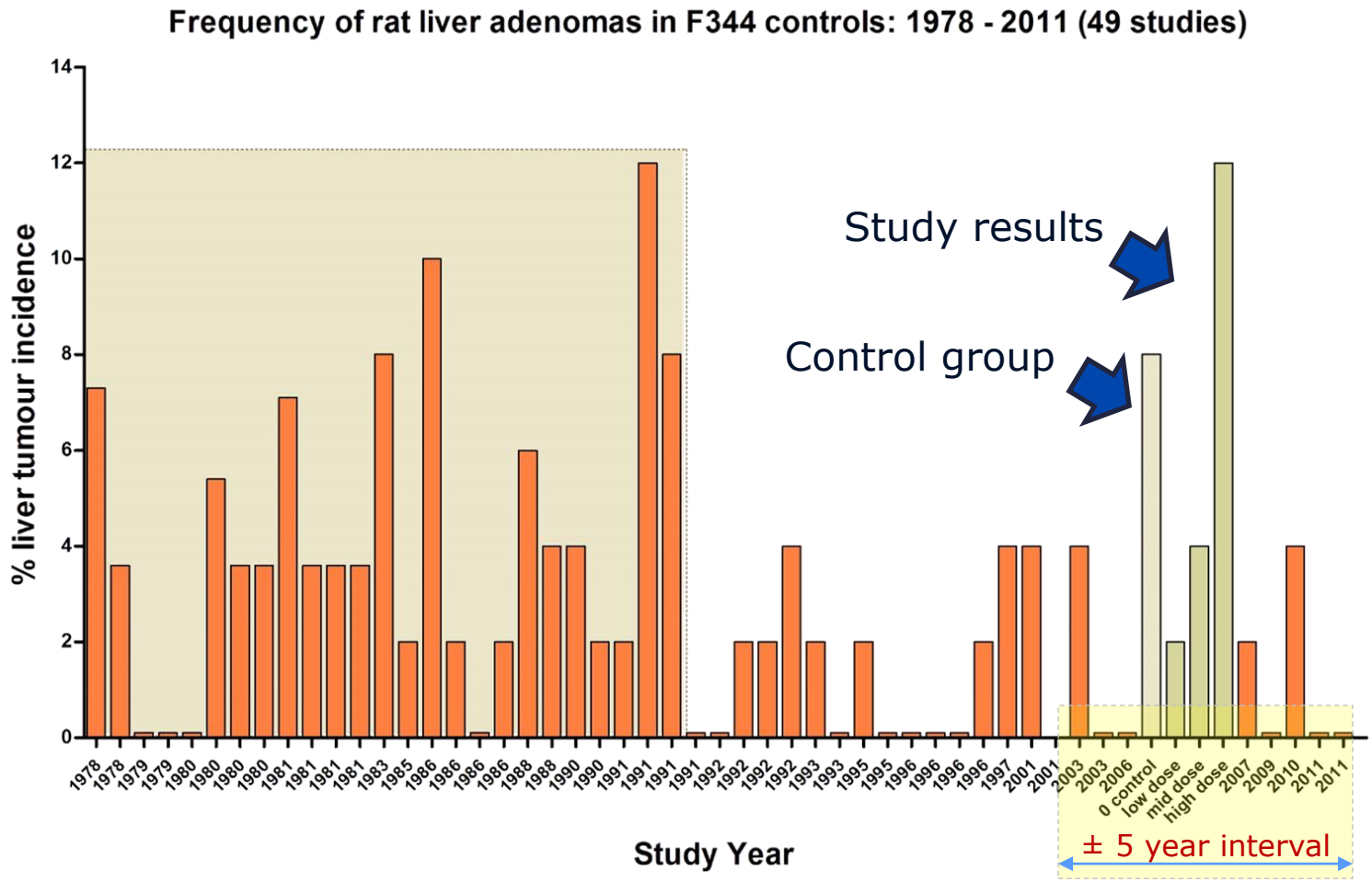
Checking the validity of the concurrent control

Importance of contemporary
… or the 5 years interval

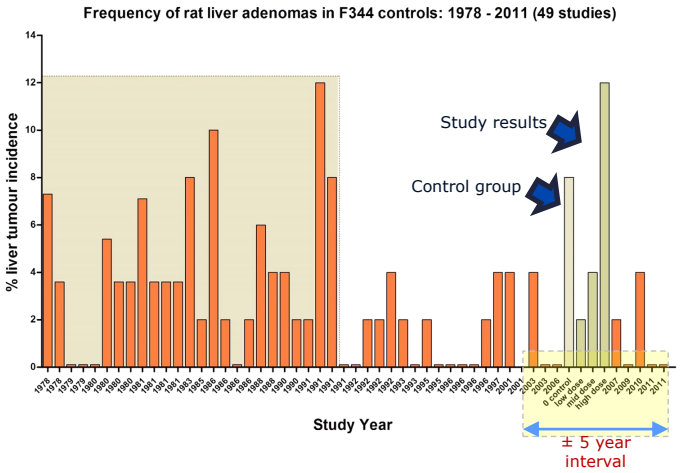
Checking concurrent control



Importance of time interval for HCD



HCD and time interval



	5 years HCD	Full HCD range (1978-2011)
# studies	10	49
Mean	1.25%	2.7%
Range	0-4%	0-12%

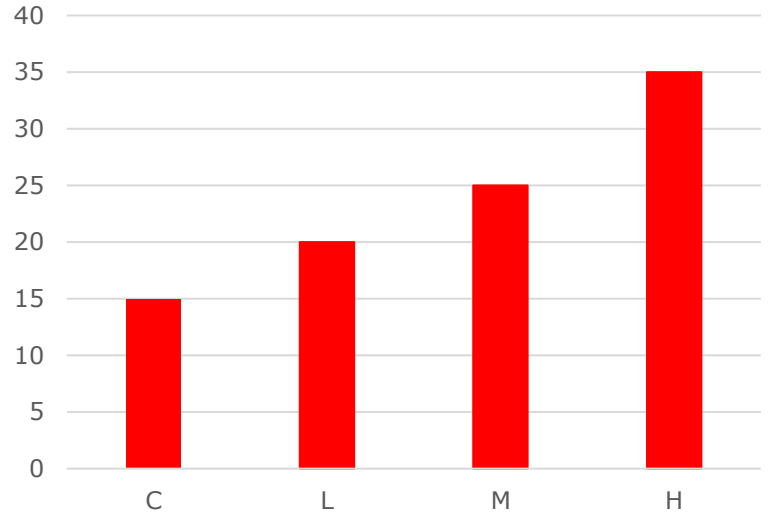
HCD of the full time span (1978-2011) are not representative of the conditions at the time of the study → provide inaccurate information

Example:

HCD range

‘Study’ results

- The incidences follow a dose-response relationship



Control	Low dose	Mid dose	High dose
15	20	25	35

Disclaimer: the data were generated for the purpose of this example and do not represent real data

‘Study’ results and HCD range

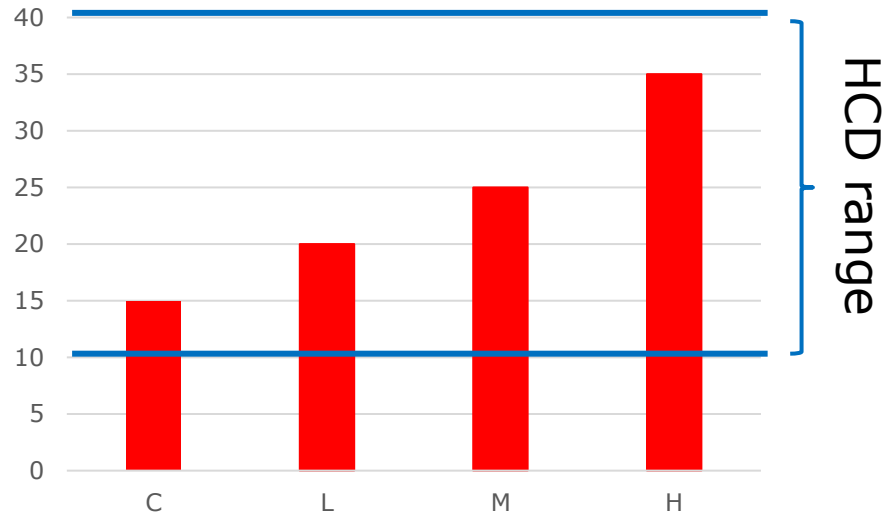
Control	Low dose	Mid dose	High dose	HCD 1	HCD 2
15	20	25	35	10 - 40	10 - 40

- Tumour incidences are within the range HCD 1 and HCD 2
- Should the tumour be considered ‘relevant’ for classification or not due to HCD ranges (10 - 40)?

Disclaimer: it is not possible that 2 HCDs have the same relevance and reliability, however for the sake of the this theoretical example they are considered equally relevant and reliable

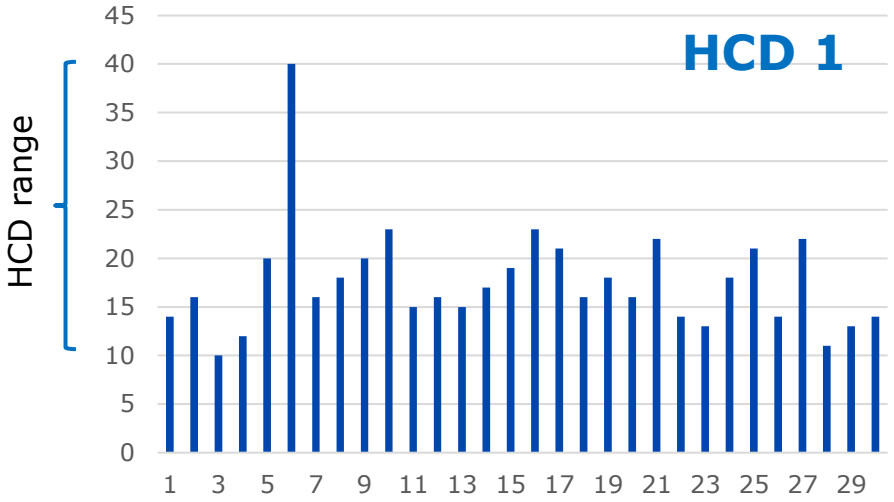
Graphical view

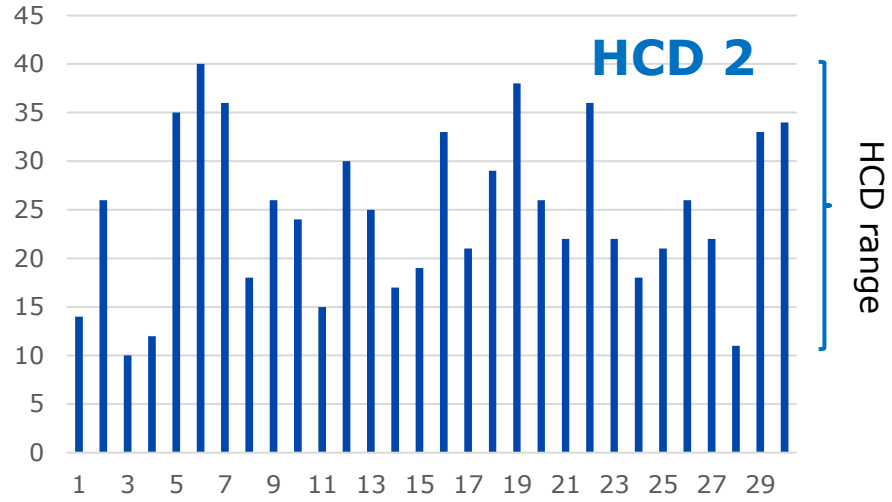
- Should the tumour be considered ‘relevant’ for classification or not due to HCD (10 - 40)?



Control	Low dose	Mid dose	High dose	HCD 1	HCD 2
15	20	25	35	10 - 40	10 - 40

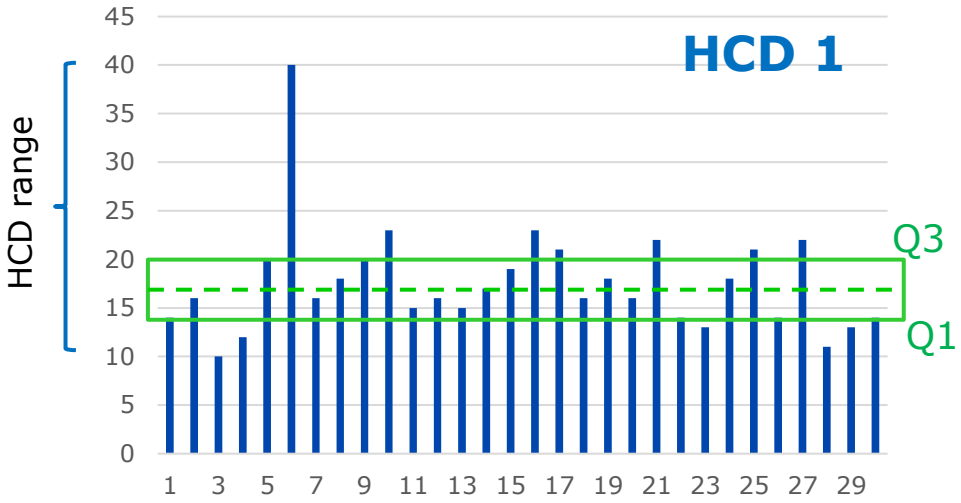
HCD 1 and HCD 2 in detail (10 – 40)

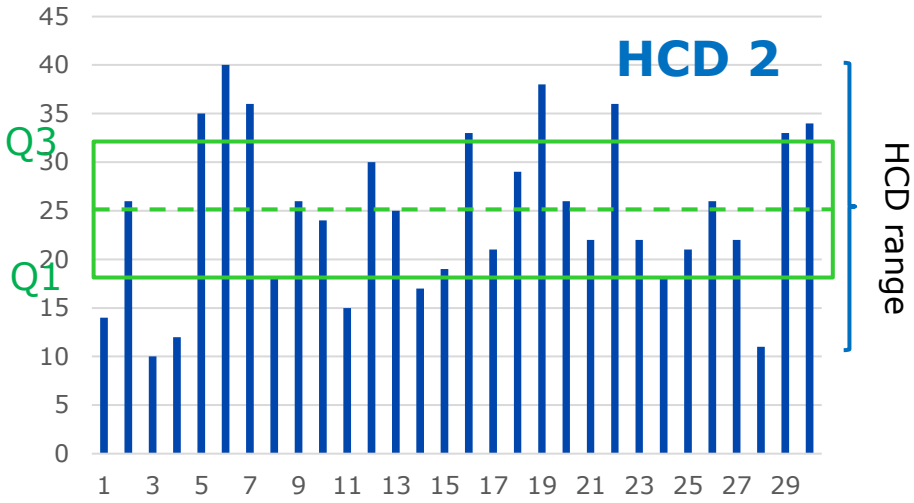




	min	Q1	Median (Q2)	Average	Q3	max
HCD 1	10	14	16	18	20	40
HCD 2	10	18	25	25	32	40

HCD 1 and HCD 2 in detail (10 – 40)





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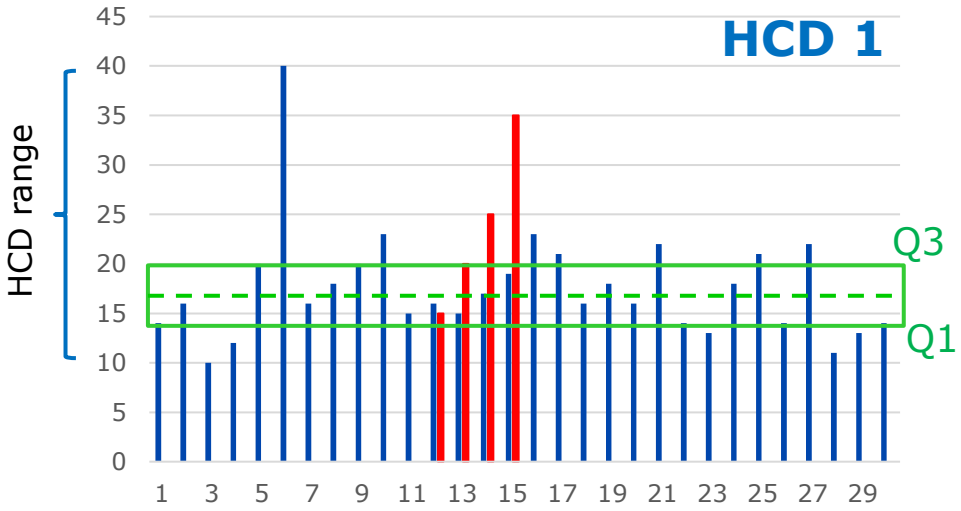
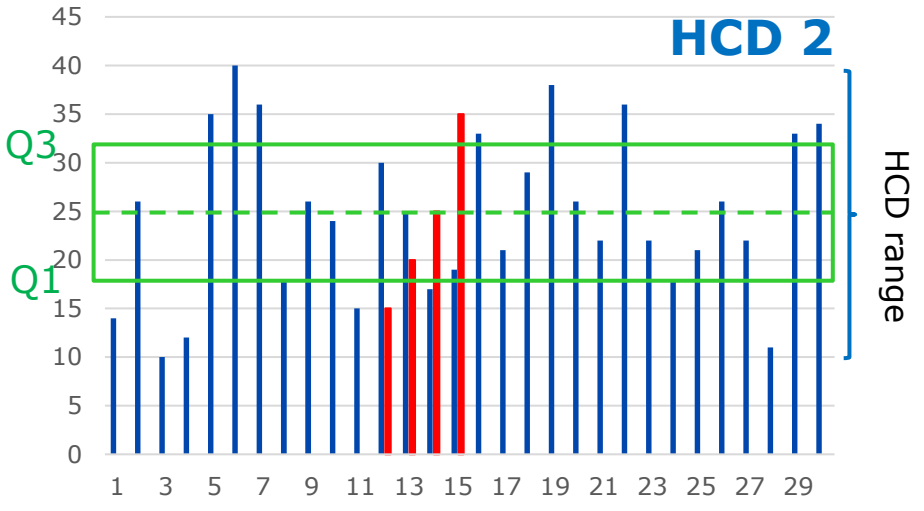
HCD 2	10	18	25	25	32	40

HCD 1 and HCD 2 in detail (10 – 40)





Control	Low dose	Mid dose	High dose	HCD 1	HCD 2
15	20	25	35	10 - 40	10 - 40

	min	Q1	Median (Q2)	Average	Q3	max
HCD 1	10	14	16	18	20	40
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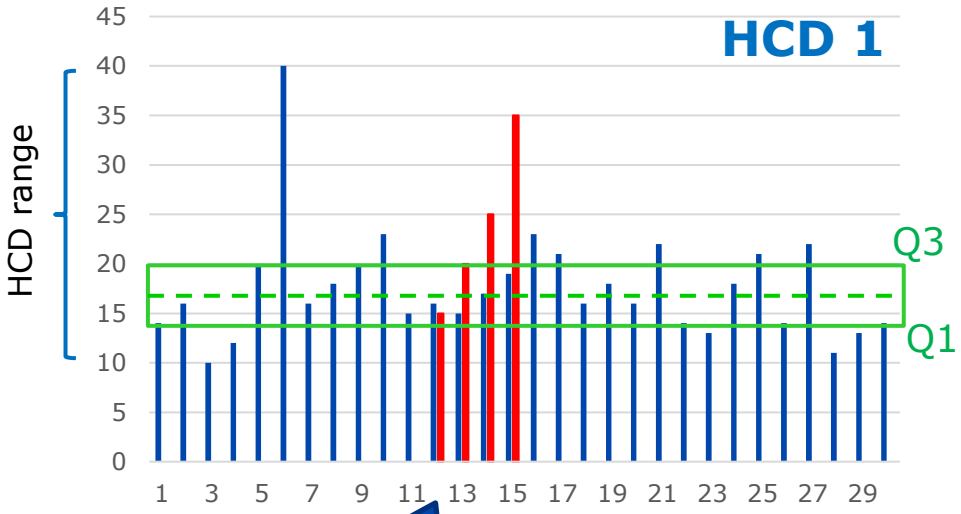
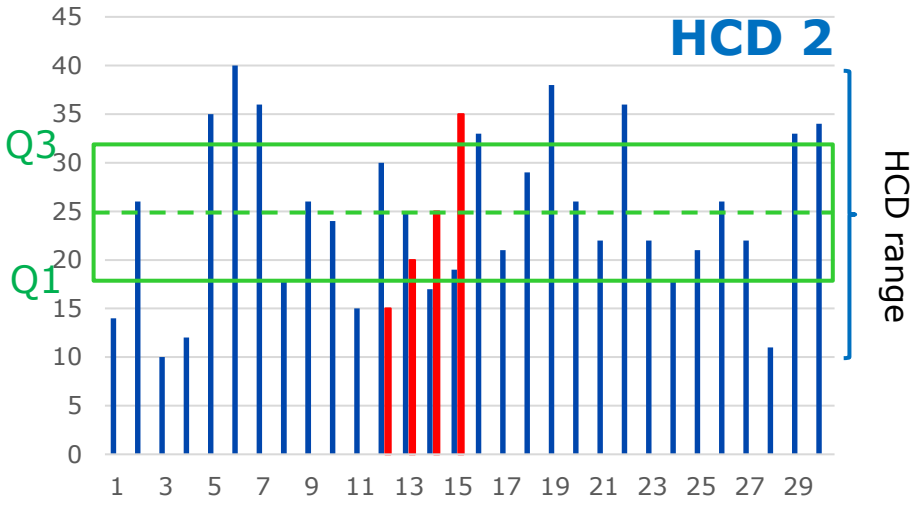
HCD 1 and HCD 2 in detail (10 – 40)





- Control: no unexpected increase or decrease

  C: 15 vs HCD 1: Q1-3 14-20

- 'Study' results may justify classification

- Control: possible decrease in incidence

  C: 15 vs HCD 2: Q1-3 18-32

- 'Study' results may not justify classification

HCD - Summary

- Provide useful information
- Concurrent control is normally the most relevant
- HCD must be contemporary to the study (5 years)
- HCD range alone is not sufficient because without information about the mean/median it may give disproportionate weight to outliers
- Useful references:
  - Commission Regulation (EU) No 283/2013
  - Best practices for use of HCD of proliferative rodent lesion, Keenan *et al.*; Toxicol. Pathology 2009; 37:679

Presentation of the survey and the follow-up information session

Pia Korjus
Senior Scientific Officer

Survey

… launch in June 2021

Survey - objective

Survey – why? …. and what is it?

- The reasons for doing a survey:
  - To replace some aspects of the planned Workshop in Helsinki
    - Q & A sessions
    - Coffee break networking
  - To capture the information we would have collected from ”one-to-one” sessions
- The survey is:
  - A tool for us to collect information to improve the submission of CLH dossiers
  - For ECHA/C1 to understand better the Dossier Submitter’s tasks
- The survey will collect information on:
  - Your current experience with submitting dossiers
  - The key obstacles you come across
  - Ideas and suggestions for additional sections in the Practical Guide
  - What would help you?

Before starting the survey

- Get familiar with the the Practical Guide **”How to submit a CLH dossier”** and briefly remind yourself of the already existing ”Guidance on the preparation of dossiers for harmonised classification and labelling”
- Tell us:
  - Is there something that is missing, but would be a necessary piece of advice?
  - Is there something that is not clear enough for how to implement in the preparation of a CLH-dossier?
  - Does the new Practical Guide meet your needs?

Some sample questions …

Q: Do you think the Practical Guide provides useful advice on how to prepare a dossier?

Q: Overall did you find the Practical Guide

- Understandable and easy to apply?
- Somewhat understandable and applicable?
- Difficult to understand and to apply?
- Other, please specify?

Q: Do you think the Practical Guide is missing important topics?

- If yes, which ones?
- No

… a flavour of what is included

Q: Do you encounter obstacles when preparing the CLH dossier?

- Lack of qualified resources and time available
- I don’t know how to use the CLH template
- I don’t know where to find the relevant guidance
- I don’t know how to apply the CLH criteria to study results
- Other, please specify

Q: Are you/your organisation aware of the importance to submit a notification to Registry of Intentions (RoI) prior submitting the CLH dossier?

- Yes
- No

Accordance check

- Dossier submitters get ECHA's feedback after "accordance check" (passed or failed) as:
  - A letter
  - Track changes/comments in the draft CLH-dossier
- Has it been useful to you, did it help you to get the CLH-dossier (and the future ones) into a good shape?
- Survey question:

Q: If the CLH dossier did not pass the accordance check by ECHA and the CLH dossier is sent back to you for review, do you find the comments you received from ECHA clear and constructive?

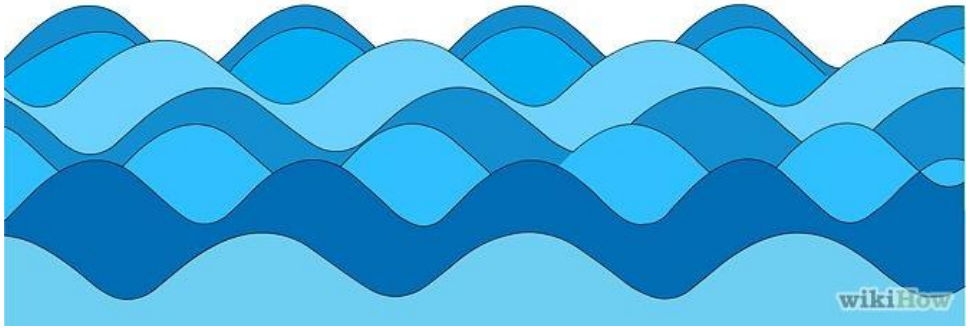
- Overall yes
- Somewhat clear and constructive
- Overall not
- If not, how could ECHA improve the feedback given

Replying to the survey

- The survey will be available at the ECHA webinar site, and registered participants will get a link to a webropol survey
- It will start at the beginning of June
- You may wish to talk to your colleagues to get the internal feedback from the organisation
- Responding will take approx 15-30 min
- There will be the possibility for free text feedback
- It will run for 2-3 months

ECHA
EUROPEAN CHEMICALS AGENCY

Help us to get useful information that is important to you! Let’s get into the same rhythm.



Follow-up information session

… Autumn 2021

What next?

- Based on the feedback ECHA will...
  - Review the comments from the survey and update the Practical Guide accordingly
  - Review the ECHA Guidance on preparation of dossiers and to update/align with the Practical Guide (including revisions from the survey)
  - Review the ECHA Classification website sections and update accordingly

and ECHA will …

- organise a follow up Information Session in autumn 2021 to:
  - Present findings from the survey
  - Address any revisions in the Practical Guide
  - Focus on any specific issues for additional explanation

- and present any plans for updating ECHA Guidance
  a. Practical Guide – How to submit a CLH dossier
  b. ECHA Guidance on the preparation of dossiers for harmonised classification and labelling

Conclusions and closing

Stella Jones
Head of Unit
Hazard I

Conclusions

- Summary of today’s event
- How did the Slido go?
- What’s next?

Thank you!

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