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CHEMICAL HAZARD ASSESSMENT VERIFICATION PROGRAM

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1 Introduction

The Chem*FORWARD* (CF) Verification Program helps to ensure the quality of, and confidence in, chemical hazard assessments (CHAs) contained in the CF repository. Quality assessments begin with well qualified Assessors (refer to the CF Assessor Qualification Process). In an effort to provide the highest quality assessments and to promote harmonization, all assessments are subject to CF's third-party verification step whereby expert toxicologists are enlisted to provide peer review of the CHAs.

The Verification Program is designed to ensure that shared chemical hazard assessments contained in CF are current, comprehensive, and credible in order to support their use in decision-making for product design, development, and procurement. In addition, the Verification Program includes a process for technical challenges (refer to the Continual Improvement Technical Challenge Process) to allow for transparent dialogue and additional data review.

Verified CHAs will be:

- Complete. According the CF GHS-based input method and guidance;
- Current. Updated regularly according to CF program requirements;
- Based on data that are as relevant, reliable and adequate as feasible;
- Accurate in applying classification or rating criteria to existing data;
- Transparent and appropriate in applying expert judgment in the evaluation of existing data, especially when various data streams differ; and
- Transparent and appropriate in supplementing test data with New Approach Methods (NAMs) for filling data gaps for hazard classification needs.[1]

CHAs will not be posted to the CF platform until Verification is complete. Verified CHAs will be labeled as VERIFIED and include expiration dates.

Verified CHAs that are undergoing a technical challenge will be labeled as **Challenged** and the specific endpoint(s) or other items being challenged will be identified.

[1] https://www.epa.gov/sites/production/files/2018-06/documents/epa_alt_strat_plan_6-20-18_clean_final.pdf

2 Definitions

Chemical – a substance designated by a single CASRN or other unique identifier

Assessor – an organization with expertise in chemistry and toxicology that meets the requirements outlined in the CF Assessor Qualification Process. Assessors are licensed to perform chemical and material assessments for CF. Assessors are familiar with criteria in the following programs, including but not limited to the Globally Harmonized System of Classification and Labeling of Chemicals (GHS), Cradle to Cradle Certified (C2C) Products Program, Greenscreen for Safer Chemicals (GS), US EPA Safer Choice (SC) Program and the European REACH regulatory program and compliance requirements.

Chemical Hazard Assessment (CHA) – process of assessing and classifying hazard endpoints associated with individual chemicals

Hazard Endpoint – a potential outcome associated with physical properties, human health, environmental health, or fate indicators. May also be called 'hazard trait'.

New Approach Methods (NAMs) – Use of predictive tools and methods to assess chemical hazard endpoints. Examples include models for structure activity relationships (SARs), quantitative structure activity relationships (QSARs), in-vitro test methods, read across and more.

Evidence Integration (Weight of Evidence (WoE)) – A weight of evidence approach may combine information from disparate sources to generate sufficient evidence to fulfill an information requirement taking into consideration study design and data quality. A WoE approach is especially useful when information from any single authoritative source is not sufficient to fulfill an information requirement whether due to deficiencies in data quality or conflicting conclusions.[2]

CF Verification Program – A set of procedures developed to ensure high quality of Material Wise CHAs. Verification ensures that Individual CHA reports are verified for data quality and best professional practices for data interpretation, integration, application of classification criteria and communication of results.

CF Verifier – Toxicology experts qualified by CF to apply the CF Verification Program.

[2] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/weight-of-evidence

Continual Improvement Technical Challenge Process – A fair and transparent process developed to handle challenges to elements of existing CF CHA reports

3 Verification Process Flow

3.1 Triggers

The Verification process is triggered when a new CHA is submitted to CF.

3.2 Verification Step 1: Data Completeness Check

The Completeness Check is intended to ensure that:

1. The substance is clearly defined including mandatory information on chemical identification, physical properties and physical forms as appropriate.
2. A data search has been performed on every endpoint and the approach to data search and results are clearly documented and summarized. Data includes original scientific publications, literature reviews, test results, modeling results and hazard list screening.
3. Justification is provided for the appropriateness of any NAMs (i.e., read-across, SAR models, etc), used to supplement data or to fill data gaps.
4. Hazard classification levels and justification for hazard classification levels including data gaps (Classification Not Possible) are provided.
5. Level of confidence in the classification results is provided.
6. Data sources are accurately referenced.
7. All mandatory input requirements are provided.

Completeness checks occur within a week of receiving a CHA from an Assessor. If elements of the CHA are incomplete, the Assessor will be informed and a request for completion will be initiated. Once all completeness issues are resolved the CHA will be moved to the Data Evaluation Check.

3.3 Verification Step 2: Data Evaluation Check

The Verification Data Evaluation Check focuses on data quality and professional best practices in data interpretation, data integration, use of NAMs, and application of CHA method criteria. Different quantities and types of data may be available and needed to make a hazard classification (or rating) decision. For example, certain authoritative or regulatory data sources may be available and sufficient to classify a chemical for a specific hazard endpoint. In that case, additional data will not change a hazard classification and are not needed. In other cases,

complexity or lack of definitive results may dictate the need for a more comprehensive data set to support decision-making using all available evidence.

Data are evaluated for relevance, reliability and adequacy following ECHA guidelines:

- **Relevance** refers to the extent to which the data, tests/study design, and modeling approach selected are appropriate for a particular hazard identification and classification.
- **Reliability** refers to the inherent quality of the study design including clarity in the way the experimental procedure and results are described to give credibility to the findings. Reliability may include consideration of Klimisch scores. However, studies with no Klimisch ratings or high ratings (not reliable or not assignable) may still be included as part of an evidence-based approach to hazard evaluation.
- **Adequacy** refers to the usefulness of data for hazard identification and evaluation purposes. When there are multiple studies for an endpoint, the greatest weight is assigned to those studies that are best designed. For some hazard endpoints, designated authoritative sources are considered adequate without additional information.[3]

Data are evaluated and classified for hazard using an evidence-based approach. An evidence-based approach may integrate various streams of available information from guideline and non-guideline tests, research, models, analogs, etc. The relative values or weights of different types of information gathered for assessment are considered and used to make a judgment. An evidence-based approach allows for the use of professional judgment in evaluating different types and quality of data streams. The rationale for judgments made using a weight of evidence approach must be clearly and transparently provided. Comprehensive and high quality data, consistency of results and the severity of effects support definitive judgment in a weight of evidence approach.[4]

[3] https://echa.europa.eu/documents/10162/13643/information_requirements_r4_en.pdf
[4] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/weight-of-evidence

The Verification Data Evaluation Check includes the following steps:

1. Verifier reviews the hazard endpoint and the data summarized in support of the hazard classification/rating.
    a. Verifier determines if the classification/rating is supported by an authoritative source that may not be overridden with additional data.
        i. If so, the accuracy of the citation and rating are verified and accepted. If not, the Verifier goes to the next step.
2. Verifier assesses data quality (relevance, reliability, adequacy) to determine if data are sufficient for the classification/rating.
    a. Verifier checks the comprehensiveness of the data provided by spot-checking external sources for additional data not included.
    b. Verifier determines if additional data not included in the CHA are consistent with data included in the CHA report.
        i. Verifier may recommend expanding the data search
    c. Verifier reviews the use of any predictive data from NAMs. For example, if read-across is used then the Verifier reviews the justification provided by the Assessor for the selection of analogs/surrogates used to fill data gaps to ensure that they are appropriate for the chemical and hazard endpoint (hazard trait) of interest. For Q/SAR models, the Verifier reviews the use of the model used to ensure that the chemical is in the domain of applicability for the model.
3. Verifier confirms the classification/rating decision is based on acceptable data.
    a. Classification categories are checked against the requirements of the classification scheme being applied.
    b. The rationale for the classification/rating is clearly articulated and justified, based on the summarized data and reflects professional best practices.
        i. Modeling results are integrated with the other data streams according to professional best practices.
        ii. Read-across results are integrated with the other data streams according to professional best practices.
    c. The data summary identifies differing data and implications for applying weight of evidence evaluation.

The CF Verifier will apply all elements of the Data Evaluation Check and will document all non-conformances with requirements and/or disagreements with interpretation of data or application of the criteria via the Feedback and Resolution step.

3.4 Feedback and Resolution

1. All issues related to results from the CF Verification Data Evaluation Checks will be documented by the Verifier and shared with the Assessor directly via the commenting functionality of the CF application.
2. The Assessor will respond to each issue in a timely manner. The Assessor will document each response and any modifications made to the CHA in response to Verifier comments.
3. The Verifier will review responses and modifications to determine if each issue is resolved.
    a. If an issue is resolved, the Verifier will mark the comment as resolved
    b. If the issue is not fully resolved, the Verifier may submit a follow up comment.
        i. The Assessor will respond to the next round of comments and document all responses and modifications.
        ii. The Verifier will review the next round of comments to determine if the issue is resolved.
        iii. Repeat as needed.
4. If the issue is not resolved because of disagreement in interpretation, the issue will move to Technical Arbitration (Section 3.5).

3.5 Technical Arbitration

1. If an issue is not resolved, the Assessor or Verifier can request input from CF.
2. The issue will be reviewed by CF staff with toxicology expertise. CF may also enlist external expertise as needed.
3. CF toxicology experts will review the data, perform their own supplementary research as needed and prepare a recommendation.
4. The recommendation will serve as a 'tie-breaker' for resolving the issue being challenged.

4 Fee Structure

1. When a CHA is contracted through ChemFORWARD, the verification costs are included in the initial cost of the CHA.

2. When a CHA is contracted directly with an assessor, there is a $600 verification fee.