Study on the role of Robust Study Summaries in hazard assessment

Survey and interviews report

Final Report delivered under contract ECHA/2021/46[1]

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[1] https://echa.europa.eu/-/study-on-the-role-of-the-robust-study-summary-in-hazard-assessment-with-practical-suggestions-on-the-improvement-of-the-oecd-harmonised-templates-conc

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Executive Summary

Background

According to the EU REACH Regulation[2], article 3(28), 'a Robust Study Summary (RSS) is a detailed summary of the objectives, methods, results, and conclusions of a full study report, providing sufficient information to make an independent assessment of the study, minimising the need to consult the full study report'.

The OECD has developed Harmonised Templates[3] (OHT) to report the relevant information in the context of the risk assessment of chemicals, including Robust Study Summaries for different regulatory endpoints. IUCLID 6[4], a software tool developed by the European Chemicals Agency[5] (ECHA), in collaboration with the OECD, serves as the reference implementation for the OHTs, and provides data entry screens for users to provide the relevant information on chemicals in an agreed format, within a regulatory context.

As part of an OECD project, ECHA commissioned a study on the role of Robust Study Summary (RSS) in hazard assessment. One of the key drivers for conducting this study is related to concerns raised by some stakeholders regarding the reliability of RSS. Stakeholder engagement activities were conducted, including a survey and semi-structured interviews, to capture the comments and suggestions of RSS users. This report is part of the first work package (WP) of the study and will be used along with other work packages to inform the formulation of final recommendations to improve the usefulness of and trust in RSS.

Stakeholder engagement with authors, evaluators and other users of RSS was conducted in October and November 2021. Over the course of the consultation period, 160 participants responded to the survey and the project team interviewed 15 participants. The data collected during the surveys and interviews were analysed using quantitative and qualitative methods, and the results are presented in this report. The data was grouped into five thematic codes, which form the basis of the report:

- User Profile
- RSS Purpose
- Use of RSS
- RSS Content
- Areas of Improvement

User Profile

RSS users who participated in the surveys and interviews included authors, evaluators and other users, namely researchers and NGOs. We are confident that the survey captures the major users of RSS. The most engaged user type in responding to the survey and interview invitations were authors.

[2] https://eur-lex.europa.eu/legal-content/en/TXT/HTML/?uri=CELEX:02006R1907-20220301
[3] https://www.oecd.org/ehs/templates/introduction.htm
[4] https://iuclid6.echa.europa.eu/
[5] https://echa.europa.eu/

Most survey respondents work in the European Union (EU) and, consequently, the most common regulations reported were from the EU. The stakeholders who completed the survey were very experienced with RSS as the majority of respondents had over 10 years of experience. They also used RSS across multiple subject areas, and many reported working with RSS outside of their primary area of expertise.

RSS Purpose

Study participants confirmed that the purpose of the RSS is to summarise the information contained in study reports to be used for hazard and risk assessment. They also indicated that RSS were prepared to fulfil regulatory requirements, derive hazard assessment information, and communicate information on hazards and chemicals.

Use of RSS

Stakeholders used RSS as the *de facto* standard to report and submit data to regulators, as they felt that RSS are preferred by evaluators in the EU regulatory context. Stakeholders also felt that when RSS are completed correctly, they are fit-for-purpose. When RSS are not completed correctly, users trust that evaluators flag this, thus ensuring quality.

However, one major exception was identified when using RSS for EU Biocidal Products Regulation (BPR[6]) and Plant Protection Products (PPP[7]). In those contexts, respondents identified that they are not seen as fit-for-purpose due to difficulties with the format and an uncertainty that the RSS are read by evaluators since the full study reports are also required to be attached with the RSS.

From an evaluator's standpoint, RSS were viewed as sufficient to perform hazard assessments without the full study reports, when the RSS are correctly completed. Further, most evaluators did not typically need to refer to the full study report when evaluating RSS for EU REACH purposes, if the RSS was correctly completed. This is an important finding for the goals of this research.

Strengths of RSS are that they save time and resources, they are valued for their standardised structure both for submitting data to the authorities and they aid evaluation. Several weaknesses and challenges were mentioned frequently, such as:

- The ability of authors to determine what information is relevant for RSS
- Complex or higher-tier studies and endpoints are difficult to summarise
- Uploading tables and special characters in IUCLID may lead to missing important information, mistakes, inaccuracies
- Lack of knowledge about the quality and reliability of data leads to needing to refer to the full study report
- Older study reports were often mentioned as not containing the relevant information for the current RSS structure

Despite these issues, users agreed that RSS are an important source of information.

[6] https://echa.europa.eu/regulations/biocidal-products-regulation/understanding-bpr
[7] https://www.efsa.europa.eu/en/topics/topic/pesticides

RSS Content

Overall, respondents shared that RSS quality can vary based on several factors, including the author, endpoint complexity, substance, and study type. One of the key reasons specified for poor RSS quality is the lack of data, specifically tabulated data. Despite its limitations, most respondents indicated that RSS are at least *'somewhat reliable'* for conducting hazard assessment.

The complexity of certain human toxicology, ecotoxicology, and environmental fate endpoints came up in the survey and interview as challenging elements that were highlighted as affecting the quality of RSS.

The usefulness of RSS guidance for authors to prepare RSS is debated. While some authors say that there is plenty of guidance on the ECHA website for example[8], others say that they do not use the guidance as it is difficult to find the relevant information needed.

Areas of Improvement

While suggestions for improvement were made, respondents emphasised that RSS is meant to be a *summary* of study objectives, methods, results, and conclusions and that including too much detail in the RSS would be counterproductive. Similarly, several respondents felt that the information requirements for RSS are sufficient so changing those requirements would not result in improvements.

However, there were several recommendations made to improve various aspects of RSS, specifically around the following aspects:

- Functionality of the RSS template
- Methods to evaluate RSS and study reliability
- Author experience and training
- Improvement of RSS guidance

The various recommendations for improvement shared by stakeholders are summarised in Section 3.5 of the report. One key suggestion frequently made is to develop a series of guidance videos that could be embedded in the IUCLID Help function.

Conclusion

As a result of the data collected from stakeholders, we can conclude that RSS are found to be a reliable source of information for hazard assessment purposes. Furthermore, when they are completed correctly, there is a good level of confidence that they are fit-for-purpose. However, RSS limitations are a key indicator of their reliability. Some of the limitations of RSS lie in the quality and type of information that they contain, the nature of the study they summarise, their author and the endpoint they cover.

The key strengths of RSS are the consistency of the format, as well as the time and resources savings that result from using the summary data. RSS are identified as an important source of information when there is no access to the full study. Although many of the strengths are

[8] https://echa.europa.eu/practical-guides

associated with the fact that RSS are summaries, many weaknesses are also related to this. For instance, evaluators identified that insufficient explanation of the study methods and results is the most frequent weakness when evaluating an RSS.

Future work that could be done to improve the reliability and quality of RSS would be to improve the RSS guidance by adapting it to a more user-friendly and interactive format. Furthermore, the development of completed RSS templates to be used for reference purposes and author training are other areas identified that could directly contribute to an improvement of RSS quality.

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Glossary

Acronym	Definition
AICIS	Australian Industrial Chemicals Introduction Scheme
BPR	Biocidal Products Regulation
CEPA	Canadian Environmental Protection Act
ChemSec	Chemical Secretariat
CHESAR	Chemical Safety Assessment and Reporting Tool
CLP	Classification, Labelling and Packaging Regulation
CRO	Contract research organisation
ECHA	European Chemicals Agency
EEB	European Environmental Bureau
EFSA	European Food Safety Authority
GDPR	General Data Protection Regulation
GLP	Good Laboratory Practice
ICS	International Chemical Secretariat
IUCLID	International Uniform Chemical Information Database
Japan CSCL	Japan Chemical Substances Control Law
K-REACH	Korean REACH
NGO	Non-governmental organisation
OECD	Organisation for Economic Co-operation and Development
OHT	OECD Harmonised Templates
PPP	Plant Protection Product Regulation
QSAR	Quantitative structure-activity relationship
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RSS	Robust study summary
TG	Testing guidelines
UK HSE	United Kingdom Health and Safety Executive
US EPA	United States Environmental Protection Agency

1. Introduction

1.1 Background information (provided by ECHA)

According to the EU REACH Regulation[9], article 3(28), 'a Robust Study Summary (RSS) is a detailed summary of the objectives, methods, results, and conclusions of a full study report, providing sufficient information to make an independent assessment of the study, minimising the need to consult the full study report'.

The OECD has developed Harmonised Templates[10] (OHT) to report the relevant information in the context of the risk assessment of chemicals, including Robust Study Summaries for different regulatory endpoints. IUCLID 6[11], a software tool developed by the European Chemicals Agency[12] (ECHA), in collaboration with the OECD, serves as the reference implementation for the OHTs, and provides data entry screens for users to provide the relevant information on chemicals in an agreed format, within a regulatory context.

1.2 The project

As part of an OECD project, ECHA commissioned a study on the role of Robust Study Summary (RSS) in hazard assessment. One of the key drivers for conducting this study is related to concerns raised by some stakeholders regarding the reliability of RSS. As a result, stakeholder engagement activities were included in the scope of the study to capture the comments and suggestions of users. The stakeholder engagement activities and results complement other data gathering tools, including a literature search and RSS technical assessment. This work is part of Work Package 1 (WP1), which aims to assess the role of Robust Study Summaries in hazard assessment. During WP2, there will be an analysis of the accuracy of RSS (by comparing existing RSS with newly generated RSS based on the relevant source of information). Finally, WP3 will combine the findings of WP1 and WP2 to make recommendations to improve the usefulness of and trust in RSS.

The stakeholder engagement process was designed to achieve the following goals:

- Identify and define groups of stakeholders who are engaged in the use of RSS
- Understand how RSS are currently used by hazard assessors and what factors influence the assessor's confidence in the quality of the RSS
- Contribute to the evaluation of the current limitations of the RSS

[9] https://eur-lex.europa.eu/legal-content/en/TXT/HTML/?uri=CELEX:02006R1907-20220301
[10] https://www.oecd.org/ehs/templates/introduction.htm
[11] https://iuclid6.echa.europa.eu/
[12] https://echa.europa.eu/

This report provides an overview of the stakeholder engagement activities related to WP1 and a summary of the feedback received from stakeholders in relation to the role of RSS in hazard assessment. The feedback was received through an electronically administered survey and semi-structured video interviews. The input collected is summarised and discussed in this report, by theme, as follows:

- User profile
- RSS purpose
- Use of RSS
- RSS content
- Areas of improvement

2. Stakeholder Engagement Methodology

The stakeholder engagement process was conducted in October and November 2021 by Yordas Group. Over the course of the consultation period, 160 participants responded to the survey and the project team interviewed 15 participants. A description of the methodology used in the stakeholder engagement activities is provided below.

2.1 Stakeholder Groups

Stakeholder engagement with authors, evaluators and other users of RSS was conducted. The key stakeholder groups included in this study are listed in Table 2.1 and include relevant representatives from regulatory organisations, industry and non-governmental organisations (NGOs). The objective was to reach out to many RSS users, to get a broad range of responses. Yordas anticipated that different stakeholders, who play different roles in relation to RSS, would bring a range of insights. The list of stakeholder groups and detailed list of stakeholders was agreed with ECHA. These groups are representative of the key RSS users.

Table 2.1 Stakeholder groups relevant to this project

Stakeholder Group	Details
EU Regulatory Organisations	Representatives from ECHA and Technical Committees
Non-EU Regulatory Organisations	Non-EU regulatory agencies, such as the OECD Secretariat, UK Health and Safety Authority (HSE), US Environmental Protection Agency (EPA), Health Canada, Australian Industrial Chemicals Introduction Scheme (AICIS)
National Member State Competent Authorities	Experts in RSS from National Agencies
Industry	Including both large organisations and SMEs. Business types included testing laboratories, consultancies and chemical manufacturers
NGOs	Environmental NGOs, such as ChemSec, CHEM Trust, EEB, ICS

2.2 Stakeholder Engagement Activities

The stakeholder engagement activities conducted as part of this project included electronically administered surveys and semi-structured video interviews. The methodology used to carry out these activities is described in the following subsections.

2.2.1 Survey

The survey was prepared based on our understanding of the key issues associated with RSS, and some of the preliminary findings from a literature search. The survey was reviewed and approved by ECHA before being encoded into the EUSurvey platform. The survey was piloted

by the project team, using staff members not working on the project, but who are familiar with RSS. ECHA also piloted the survey and provided comments, after which final changes to the survey were made. A total of seven individuals tested the survey before its release.

Structure

The survey began with an introduction to the study, the purpose of the consultation, and a set of instructions for completion. We included contact details of the study team for any questions and logistical requests. One survey participant contacted the study team to share PhD studies and accepted papers that they had conducted on RSS. Some of these studies had already been included in the literature search, but others were subsequently integrated into the report.

The survey was divided into four sections:

- Background information on participants
- Jurisdictions/regulations/endpoints for which participants use/write RSS
- Key elements to consider when using/writing RSS
- Reliability of RSS

The survey was configured to adapt the questions visible to a respondent depending on their RSS user type (‘author’, ‘evaluator’ and ‘other types of users’). It was structured to take between 15 to 20 minutes to complete, and respondents were able to edit their responses until they submitted the survey.

All data collected in this survey was handled in compliance with the General Data Protection Regulation (GDPR). The survey data is reported only in anonymised aggregate form or in a manner that does not allow individual responses to be identified. Survey results are presented in this report in accordance with GDPR and other data sharing laws for the stated purpose of improving hazard assessment.

Survey Distribution

The survey was open for a period of 30 days, from the 18th of October 2021 until the 18th of November 2021. The survey was promoted by ECHA and Yordas on a regular basis over the course of the response period, as documented in the communication summary (Table 2.2). Overall, the survey was shared with more than 10,000 individuals via email and through social media posts on LinkedIn and Twitter. The rate of opening of emails sent as part of the email campaigns ranged from 18 to 35 percent, which varied depending on the target audience included in the mailing list. The rate of clicks to the survey portal from the emails ranged from six to ten percent. Social media posts received less interest than emails as the audience was not as narrowly selected. The most successful social media platform was LinkedIn, with impressions (the number of times the post was displayed on LinkedIn feeds) between 100 to 500 for each post, and engagement rates ranging from 2.8 to 5.0 percent. Based on these results, we can infer that we received more survey participants from the email campaigns than the social media posts. The key reason is that the email campaigns were targeted at individuals that we know use RSS, whereas social media posts were targeted at the overall audience of ECHA or Yordas, of which only a small proportion may be users of RSS.

Table 2.2 Survey communication summary

Communication Type	Date (2021)	Details	Audience
Email	18 Oct.	Survey launch email sent by ECHA to RSS users	10,000 stakeholders included in mailing list ● 2,636 opened emails ● Open rate: 26%
Social Media Post*	18 Oct.	Invitation to survey shared on the Yordas social media channels	Impressions: 505 Reactions: 13 Clicks: 4 Shares: 8 Engagement rate: 5.0%
Email	21 Oct.	Initial email sent by Yordas to stakeholder list	764 stakeholders included in mailing list ● 165 opened emails ● 72 clicked the survey link ● Open rate: 22% ● Click rate: 9%
Social Media Post	22 Oct.	Invitation to participate in the survey shared on the Yordas social media channels	Impressions: 107 Reactions: 2 Clicks: 0 Shares: 1 Engagement rate: 2.8%
Social Media Post	28 Oct.	Invitation to participate in the survey shared on the Yordas social media channels	Impressions: 276 Reactions: 6 Clicks: 3 Shares: 1 Engagement rate: 3.6%
Social Media Post	2 Nov.	Invitation to participate in the survey shared on the Yordas social media channels	Impressions: 269 Reactions: 4 Clicks: 2 Shares: 1 Engagement rate: 2.6%
Email	8-9 Nov.	Reminder to participate in survey sent by Yordas to stakeholder list	764 stakeholders included in mailing list Opens: 140 Clicks: 76 Open rate: 18% Click rate: 10%
Email to NGO stakeholders	9 Nov.	Invitation to key NGO stakeholders to participate in the survey	17 stakeholders included in mailing list Opens: 6 Clicks: 1 Open rate: 35% Click rate: 6%
Social Media Post	12 Nov.	Invitation to participate in the survey shared on the Yordas social media channels	Impressions: 109 Reactions: 1 Clicks: 1 Shares: 0 Engagement rate: 1.8%

*__Note:__ Data for social media posts was extracted from the results on the LinkedIn platform as engagement on Twitter was minimal.

Response Rate and Validity

The overall response rate for the survey communication activities was 1.5 percent. The highest levels of engagement were from direct emails with open rates ranging from 18-35 percent indicating that the real level of participation is likely to be slightly higher, perhaps around 5 percent. While this is low, internet survey response rates of under 10 percent are not uncommon and do not necessarily indicate that results are invalid[13]. In cases of low response rates, it is helpful to do a nonresponse bias analysis to ascertain why rates are low and whether there would be significant differences between those who responded and those who did not. The risk to validity is if respondents were not representative of the surveyed population in some way. For example, if there were not a broad sampling of different user types, or if the survey only had highly divergent responses.

There are several reasons why we might have anticipated a low response rate. External surveys (i.e., surveying participants from outside of one's own organisation, in this case, ECHA) tend to have lower response rates. It is also well-known that internet surveys tend to have lower response rates with little information about non-respondents (see footnote 13). Furthermore, issue relevance has been found to have a strong correlation with response rate, where relevance is defined as timeliness and importance of a topic. Researchers observed that if a person has low interest in the topic of the survey, it is unlikely to respond[14]. Thus, we can assume that individuals with the highest interest in RSS responded to the survey, and as it is a niche topic, the number of respondents was bound to be limited.

There is also significant survey fatigue in the population in general due to a sharp rise during the Covid-19 pandemic.[15] In fact, survey response rates overall have declined significantly in recent years, in some cases by as much as 40 percent. This trend can be observed across different types of surveyors (academic, NGO, private) and subject matter.

Conversely, we know that there are methods to maximise response rate, but these are not always possible to be applied. For example, providing an incentive to respondents to complete a survey generally elicits a higher response rate. Incentives can range from some kind of

[13] See van Mol, C. (2007) 'Improving web survey efficiency' in *International Journal of Social Research Methodology*, 20(4): 317-327.; Bose, J. (2001) 'Nonresponse bias analysis at the National Center for Education Statistics' in the *Proceedings of Statistics Canada Symposium 2001, Achieving Data Quality in a Statistical Agency*.;Berg, Nathan. (2005) 'Non-response bias' in *Encyclopedia of Social Measurement*, 865-873.; Alvarez, R. Michael, Van Beslaere, C. (2005) 'Web-based Survey' in *Encyclopedia of Social Measurement*, 955-962.

[14] Sheehan, K.B. (2001) Email survey response rates: a review. Journal of Computer-Mediated Communication. Volume 6, issue 2; Sheehan, K.B. and McMillan, S.J. (1999) Response variation in email surveys, an exploration. Journal of Advertising Research, 39, 45-54

[15] Dillman, D. A., Smyth, J. D., & Christian, L. M. (2014). *Internet, phone, mail, and mixed-mode surveys: the tailored design method*. John Wiley & Sons.;National Research Council. National Research Council. (2013). *Nonresponse in social science surveys: A research agenda*. National Academies Press.; De Koning, R., Egiz, A., Kotecha, J., Ciuculete, A. C., Ooi, S. Z. Y., Bankole, N. D. A., ... & Kanmounye, U. S. (2021). Survey Fatigue During the COVID-19 Pandemic: An Analysis of Neurosurgery Survey Response Rates. *Frontiers in Surgery*, 326.; Field, A. (2020) 'Survey Fatigue and the tragedy of the commons' in *Evaluation Matters*: 6; 1-11; Galea, S., Tracy, M. (2007) 'Participation Rates in Epidemiological Studies.' *Ann Epidemiol*: 17, 643-53.

compensation (payment, a voucher, a discount), to less tangible incentives, for example when respondents feel their input will result in a positive impact on their everyday life (e.g., an internal survey of employees about a change to working practices). In this case, respondents may have felt that there was little incentive for them to complete the survey because they were not compensated for their time, and/or because they were not confident that their input would have an impact.

Other well-known low response rate factors, such as demographics affected by access to the internet, lower education rates, or class differences, are not significant to this set of stakeholders. However, time pressure is a significant factor in response rate. Surveys of populations who are busy people, as in this case, tend to have much lower response rates.

We can speculate that the technical nature of the topic, which may not be directly relevant to all stakeholders included in the stakeholder engagement list, may have also lowered the response rate. For example, ECHA emailed the survey to anyone who submitted a REACH registration dossier between October 2017 to October 2021. We thus have a portion of the surveyed population whose eligibility is unknown. We also know that while duplicate email addresses were removed, emails may have been sent to multiple individuals in the same organisation, many of whom may not deal with RSS directly, or may simply have been out-of-date contact details. Knowing this untraceable rate and eligibility rate from ECHA's participant list would allow us to assess how much this contributed to the response rate. If we were able to factor in these rates (i.e., the real number of relevant people reached by the survey), we might find that the actual response rate was much higher. Importantly, the response rate from Yordas' own stakeholder database was 30 percent, which is in line with what we would expect from an external internet-based survey. Taken together, we surmise that the biggest factor in non-participation may have been untraceability and ineligibility[16].

We are, however, confident that the responses we received do not exhibit response rate bias, a hallmark of which is that respondents are highly divergent from the general stakeholder sample. We received survey responses across all stakeholder groups, and from various geographies and contexts (section 3.1 User Profile). Furthermore, the responses received show a good spread of opinions across the spectrum. These, along with a representative sample and spread of opinions within our follow up interviews, suggest that we have a low margin of error and deviation from the sample.

A final factor increasing the validity of our findings is the experience level of respondents. As we show in detail in section 3.1.3 below, the respondents had a high level of experience with RSS (more than 50 percent had over 10 years of experience). The technical nature of the research topic necessitates a good level of familiarity with RSS. However, we do also see a good spread of user experience with the majority having at least three years of experience.

[16] For a discussion of the difficulties in determining eligibility and untraceability in internet survey populations, see, for e.g., M. Anne Harris. 'Invited Commentary: Evaluating Epidemiologic Research Methods–the importance of response rate calculation.' *American Journal of Epidemiology* 172 (3): 645-647. For a good discussion of the elements to response rates, including ineligibility and unknown eligibility, as well as untraceability, see Survey Research Centre. 'Response Rates'. University of Waterloo: https://uwaterloo.ca/survey-research-centre/survey-services/types-survey-research/response-rates

We thus see a range of experience from relatively new users to long-time and highly experienced users. Taken together, these strongly indicate that we can trust that the findings are valid.

2.2.2 Interviews

The objective of the interviews was to deepen the analysis and to further elaborate on areas from the survey. The survey included a question asking for people's willingness to participate in a follow up interview to expand on their feedback. From this, we generated a list of potential interview respondents.

The main driver of interview participant selection was to ensure a representative sample of those who expressed interest. Overall, 55 of the total number of survey respondents (34 percent) expressed interest in participating in interviews, which demonstrates a high level of engagement amongst the surveyed population. We contacted 24 of these, and 15 individuals agreed to participate in the interview (Figure 2.1). The original scope had included only 10 follow up interviews, but, to ensure a broad representation, it was agreed with ECHA to increase this number to 15. Interview participants were selected from each representative stakeholder group identified in Table 2.1, and we ensured that we covered all RSS user types. Yordas was also aware of the geographical distribution of survey participants and tried to cover a wide geographical range when selecting interview participants. Other criteria that were considered in the interview participant selection were RSS working context, years of experience and subject area.

ECHA highlighted an interest in ensuring the views of regulators were included, so we contacted a higher proportion of respondents from regulatory organisations to address this. The response rate from evaluators was 41 percent, which still demonstrates a high level of engagement (Figure 2.1), although the factors discussed above in 2.2.1 on response rate, such as time constraints or task burdens, may have impacted the rate here. We cannot say for certain what factors may have affected regulator participation, but we can point to common factors: for example, regulators may not have felt sufficiently involved in the process; that is, participation rates in internal surveys are usually higher when stakeholders feel they have been consulted from the design stage.

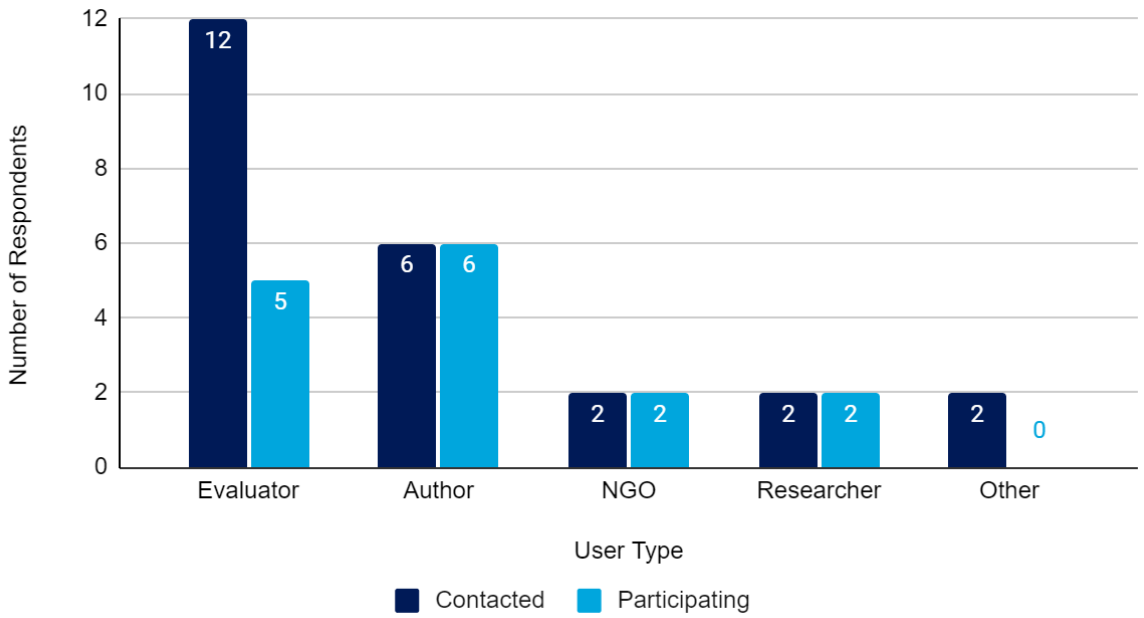

Figure 2.1 RSS user types invited for an interview (n=24) compared to those who accepted

We developed an interview guide divided into six sections, with six key questions and associated sub questions. We recognise that different stakeholders have different roles to play, such as RSS authors or evaluators, as well as different backgrounds, such as whether they come from industry or a regulatory organisation. To address this, questions in the interview were tailored to the role of the stakeholder. This guide was shared with ECHA and the OECD for feedback and agreement. An interview proforma, which included a note-taking template, was also developed to help structure the interview and note-taking. The interview was structured as follows:

- Introduction (All respondents)
- Part A: RSS Alternatives (All respondents)
- Part B: How easy are the RSS to write? (Authors, other users if applicable)
- Part C: How well are RSS written? (Evaluators, other users if applicable)
- Part D: Do RSS achieve their intended goal? (All respondents)
- Conclusion (All respondents)

The semi-structured interviews were conducted by one lead interviewer and one note taker. Guidance was provided to each interviewer and note taker to ensure that interviews were conducted consistently. To achieve optimum use of interview time, interview proforma were used to ensure comprehensive coverage of interview questions and to keep the interview focused on the relevant topics. The questions in the interview guide comprise the core question and many associated questions related to the central question.

To ensure the data has been captured accurately, the interviews were also recorded. A total of 15 interviews were conducted, resulting in a combined total of 352 minutes of recorded dialogue.

After the interview, a third team member, who was not present at the interview, listened to the recording to complete and cross-reference the interview notes to ensure a full and accurate representation of the interview participant's input. This team member is part of the stakeholder engagement team and has knowledge of thematic analysis. As they listened to the interview to complete the notes, they paid attention to patterns and themes that occur in the data and ensured that no general themes were left out of the interview notes. Those interview summaries were then analysed following the methodology described in Section 2.3.2.

2.3 Data Analysis Methodology

Survey responses and interview notes were analysed using quantitative and qualitative methods, which are described in the subsequent sections.

2.3.1 Survey Responses

The survey responses were extracted from the EU Survey[17] platform into an Excel format. Results were then imported into a statistical analysis tool. The closed and semi-quantitative questions were analysed using a frequency approach. The open-ended questions were coded following the qualitative data analysis methodology described in Section 2.3.2.

2.3.2 Interview Data

The data collected from the interviews was assessed using a form of thematic analysis, which is the most common form of analysis within qualitative research. Positivist thematic analysis was used to identify relevant themes or patterns of meaning within data[18].

We grouped the data by question and generated the initial codes through a reflective thematic analysis approach, in which we tagged items of interest in the data with a coding label using the qualitative data analysis software, NVivo. As the coding process is iterative, it was refined through a second round of review to ensure the coding guide captures all the elements of the response.

To determine how well the identified codes could be independently applied to the data and to minimise bias, a second team member reviewed to test for inter-rater reliability. Inter-rater reliability refers to the degree of agreement among independent raters who assess the same data. To achieve this, the second team member coded 20 percent of interviews (n = 3) using the final coding framework to assess the consistency between the coding.

After completing coding, we were able to begin analysing the data. Data analysis is part of coding but ultimately goes much further. Good data analysis involves staying close to the codes, but interrogating their significance, as well as identifying any gaps in the data.

[17] https://ec.europa.eu/eusurvey/

[18] Boyatzis, R. E. (1998). *Transforming qualitative information: Thematic analysis and code development.* Sage Publications; Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology, 3*(2), 77–101.

For example, the first round of coding simply identifies all respondents according to various categories and all subjects discussed. The next round of coding begins to incorporate some data analysis. We ask questions like:

- How can we make sense of the data?
- Can we organise it in particular ways?
- What are the most significant codes from different standpoints?

We might consider one code significant simply because everyone discussed it. In other cases, we might find that, although only a few people pointed a particular element out, the insight was still significant in some way. Triangulating the data together as a team ensured fresh insight and agreement on the thematic codes. We then systematically moved data from their original codes into five overarching themes, as described below. This secondary coding began to show the significance and possible meanings.

Following the inter-rater reliability test, we combined the codes into overarching themes under each question topic to help present and summarise the data. We used various data visualisation tools, including mind maps, to present the results of the interview responses.

Rather than discussing findings using the dozens of codes that emerged from survey and interview questions, we have used the overall thematic codes to organise and present the data. The thematic codes identified are:

- User Profile
- RSS Purpose
- Use of RSS
- RSS Content
- Areas of Improvement

Each thematic code has thematic sub-themes, and we also tease out some of the differences between users. The full codes are presented in Section 3 Data Analysis.

3. Data Analysis

The data analysis provides a summary of the key findings from the surveys and interviews, with the results of the statistical and qualitative data analysis. The discussion below is meant to both report findings and interrogate them for gaps, significance, validity and meaning. We discuss the five themes listed in Section 2.3.2 and summarise each with the above in mind.

3.1 User Profile

Five background questions were included in the survey. These establish the different RSS user types. From here, respondents were directed to fill out the relevant sections of the survey according to user type (e.g., author or evaluator). Since we identified interview participants based on user type, there was less need to establish different types, but we still gave participants the opportunity to discuss who they are and the type of work they do in interview questions A1 and A2.

While this is the most basic of our thematic codes, it sets the scene for our findings by establishing exactly who uses RSS and in which working contexts or expertise. It fulfils ECHA's stated goal of identifying and defining groups of stakeholders who are engaged in the use of RSS.

The theme User Profile includes the following sub-codes (Figure 3.1):

- User type
- Working context
- Demographics
- Regulatory context
- Specialty profile

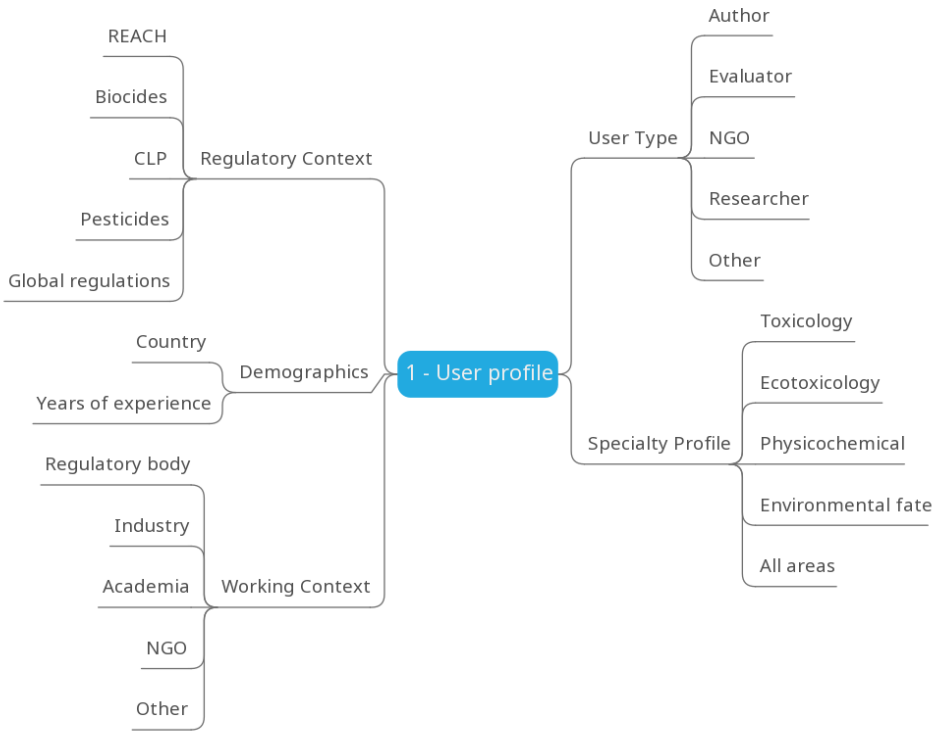

Figure 3.1 Thematic categories in Topic 1 - User Profile

3.1.1 User Type

Survey

Figure 3.2 shows the details of the survey user types. Of the 160 survey respondents, the majority were authors, followed by evaluators, other types of users ('others'), researchers and employees of NGOs. 'Others' included readers of RSS, dossier submitters, users for safety data sheets (SDS) and 'traders'. Traders was a self-identification of two respondents, whom we assume work for trading companies in the chemicals industry.

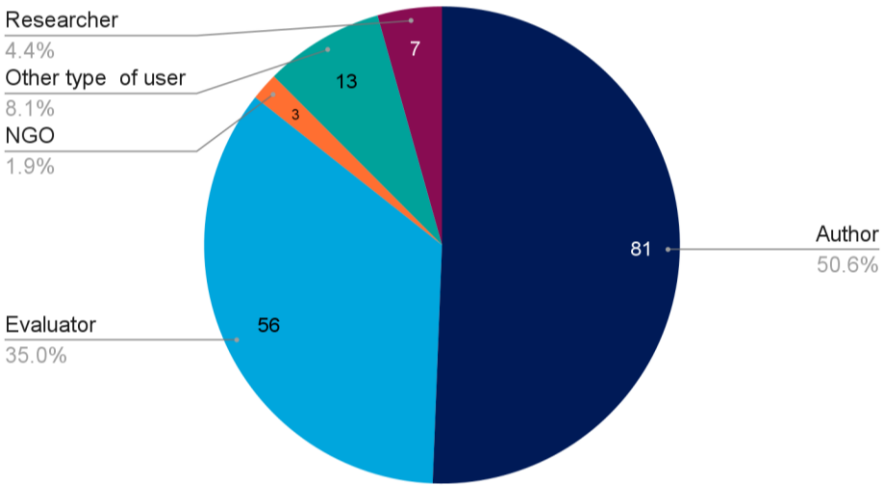

Figure 3.2 RSS user type of survey respondents (n=160) (response to survey question QA2)

The predominance of authors is most likely explained by the first round of direct emails sent by ECHA to their RSS user database, many of whom are likely to be authors. Furthermore, looking at the overall population of RSS users, we can assume that there are thousands of registrants under various regulations who would be RSS authors, compared to tens of evaluators employed by regulatory agencies. Using simple statistical analysis, we would expect to receive responses from more authors than evaluators, assuming that our sample is representative of the population. Although we do not have data indicating which contact method elicited final respondents, the high open rate (26 percent) of this initial email may explain the final percentage here. While the open rate indicates that the ECHA email may have been quite successful in eliciting respondents, it does beg the question as to whether the data is linked to an over representation of authors in the survey respondent population because of this method. Again, future research could tease out whether this is a truly accurate percentage breakdown of user types. However, it is logical that a significant percentage of RSS users would be those who author them.

While we expected to engage with RSS researchers as part of this study, we were contacted specifically by one group of researchers who have conducted their own studies on how RSS are used. As this work is in the public domain, we cite it below but have anonymised these respondents in the data[19]. The data contained in these reports has been analysed as part of the literature search, which was also conducted in WP1 of this study.

While only a small proportion of overall users, the user type 'traders' was unanticipated and is thus an interesting finding. These respondents use RSS for information only, and both were among the least experienced users of RSS of all the respondents (0-2 years' experience). However, since this is quite a different category of user, follow up research with this group might elicit further insight (in how they use RSS, for example).

We are confident that the survey captures the major users of RSS, however, there may be further small sub-groups like the 'traders' and 'researchers' who have either not been captured or sufficiently explored[20].

[19] Ingre-Khans, E., Ågerstrand, M., Beronius, A., & Rudén, C. (2016). Transparency of chemical risk assessment data under REACH. *Environmental Science: Processes & Impacts*, *18*(12), 1508-1518.;Ingre-Khans, E., Ågerstrand, M., Beronius, A., & Rudén, C. (2019). Reliability and relevance evaluations of REACH data. *Toxicology research*, *8*(1), 46-56.;Ingre-Khans, E., Ågerstrand, M., Rudén, C., & Beronius, A. (2020). Improving structure and transparency in reliability evaluations of data under REACH: suggestions for a systematic method. *Human and Ecological Risk Assessment: An International Journal*, 26(1), 212-241.;Ingre-Khans, E., Ågerstrand, M., Beronius, A., & Rudén, C. (2019). Toxicity studies used in registration, evaluation, authorisation and restriction of chemicals (REACH): How accurately are they reported?. *Integrated environmental assessment and management*, *15*(3), 458-469.;Ingre-Khans, E. (2018). *Transparency within REACH?: Regulatory risk assessment of industrial chemicals* (Doctoral dissertation, Department of Environmental Science and Analytical Chemistry, Stockholm University).

[20] The following paper is a case in point, making the case that academic users of RSS are unaware of regulatory reporting requirements. Academic stakeholders are thus potentially a sub-group for whom future research is needed. Ågerstrand, M., Christiansen, S., Hanberg, A., Rudén, C., Andersson, L., Andersen, S., ... & Beronius, A. (2018). A call for action: Improve reporting of research studies to increase the scientific basis for regulatory decision-making. *Journal of Applied Toxicology*, *38*(5), 783-785.

Interview

As described in Section 2.2.2, we conducted 15 follow-up interviews with survey respondents who had been selected based on a set of criteria. As Figure 3.3 details, the interviews consisted of the following user types: authors (6), evaluators (5), industry and academic researchers (2) and consultants working with NGOs (2).

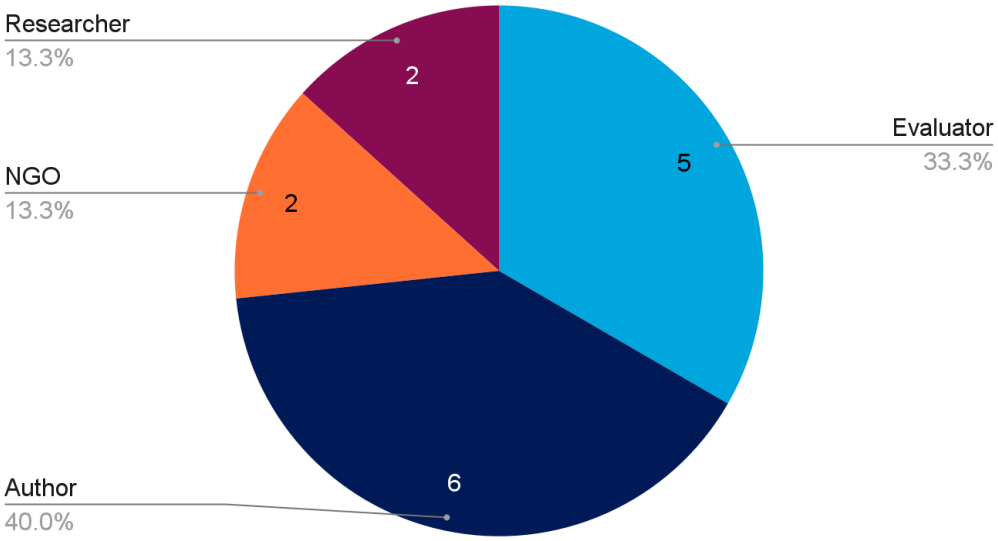

Figure 3.3 RSS user type of interviewees (n=15)

3.1.2 Working Context

This sub-code overlaps somewhat with user type in that we would expect evaluators, for example, to have a regulatory body as their working context and that authors might be found in several working contexts. Indeed, the findings in Figure 3.4 show a high proportion of those working in a regulatory context (32.5 percent), which bears out our assumption.

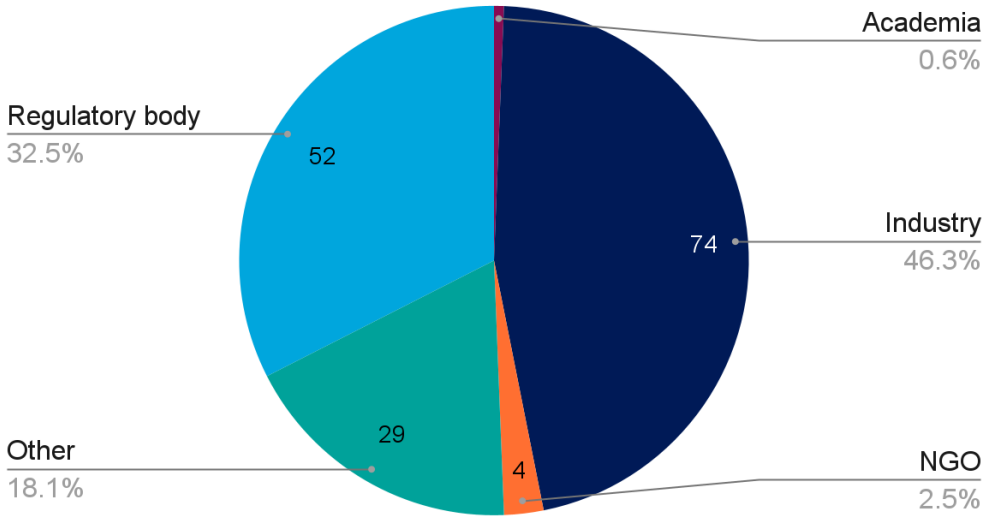

Figure 3.4 Working context of survey respondents (n=160) (response to survey question QA1)

Similarly, it is perhaps unsurprising that the most frequent working context was industry (46.3 percent), since it is usually the persons in industry who will submit regulatory dossiers to regulatory agencies. The survey did not ask respondents to identify in which industry they worked, but for those who indicated they would consent to an interview (55/160) we know that the top industries were oil & gas, chemical manufacturing (especially specialty chemicals), chemical regulatory consulting and biotechnology. Interestingly, we also saw some participation by industry associations.

That almost one-fifth of users come from other working contexts, such as consultancies and other service providers is an important finding in terms of who uses RSS[21]. It suggests first that our pilot of the survey internally within Yordas was a good place to test questions (see Section 2.2.1). More importantly, however, it indicates a depth of specialist expertise amongst consultants and other service providers and an important ECHA stakeholder category. It would be interesting to see if this percentage grows in future years.

Five interviews, each with stakeholders from regulatory bodies and industry, were completed, with other interviewees from academia, NGOs and consultancies (see Figure 3.5). A representative sample of stakeholder types who responded to the survey was selected for an interview.

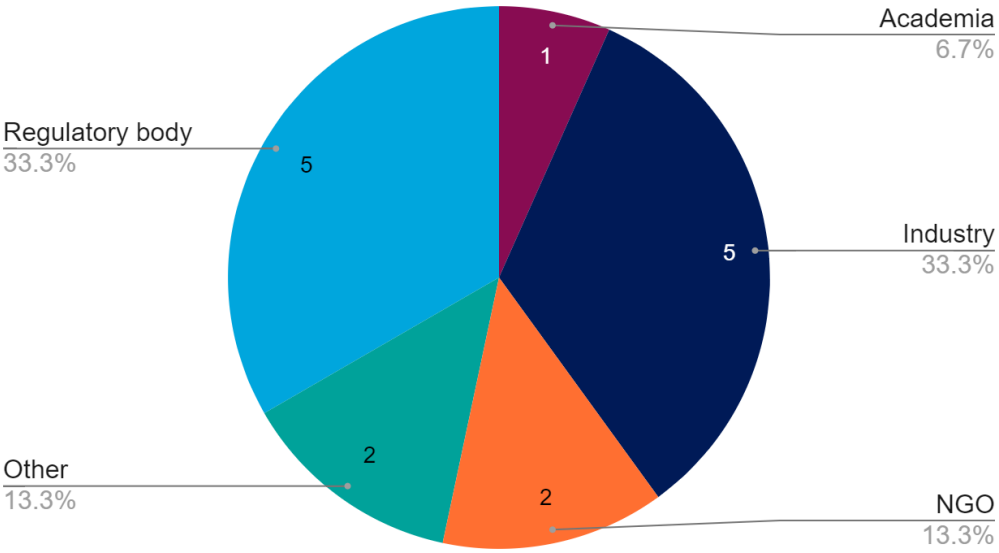

Figure 3.5 Working context of interview respondents (n=15)

3.1.3 Demographics

Of relevance to this study was that more than 50 percent of respondents to the survey had over 10 years of relevant experience working with RSS. The next highest cohort of respondents had 6-9 years of experience (see Figure 3.6). Similarly, most stakeholders interviewed had 10+ years of experience, followed by those with 6-9 and 3-5 years of experience. As we have discussed above, this means that the typical profile of an ECHA

[21] The category of 'others' here includes consultants, other service providers, Only Representatives (who may also be consultants or service providers), and the traders mentioned above.

stakeholder RSS user is well experienced and likely to be at least mid-career. We think it is likely also safe to assume that there was more participation from those with long experience of using RSS simply because they had lots of experience and opinions to share. However, the survey also shows that about a quarter (24.4 percent) of users have between 0-5 years of experience.

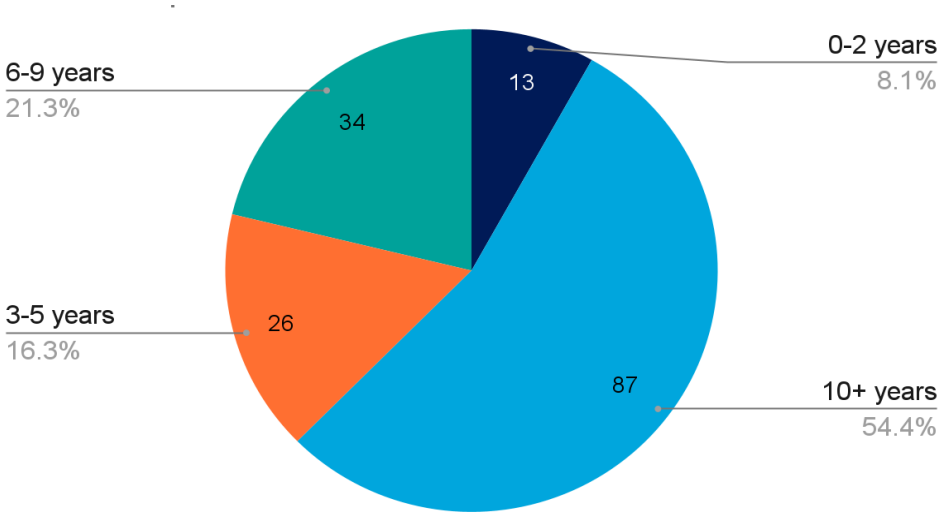

Figure 3.6 Years of experience of survey respondents (n=160) (response to survey question QA4)

Most survey respondents originated from the European Union, though there was a good diversity of users from other regions, including the OECD member countries of the United Kingdom, United States, Canada, Australia, Iceland, Switzerland, Korea and Japan. There was, further, one respondent from the non-OECD member country Brazil (see Figure 3.7). We are thus confident that the survey reflects the experience of a wide variety of RSS users from a geographic standpoint.

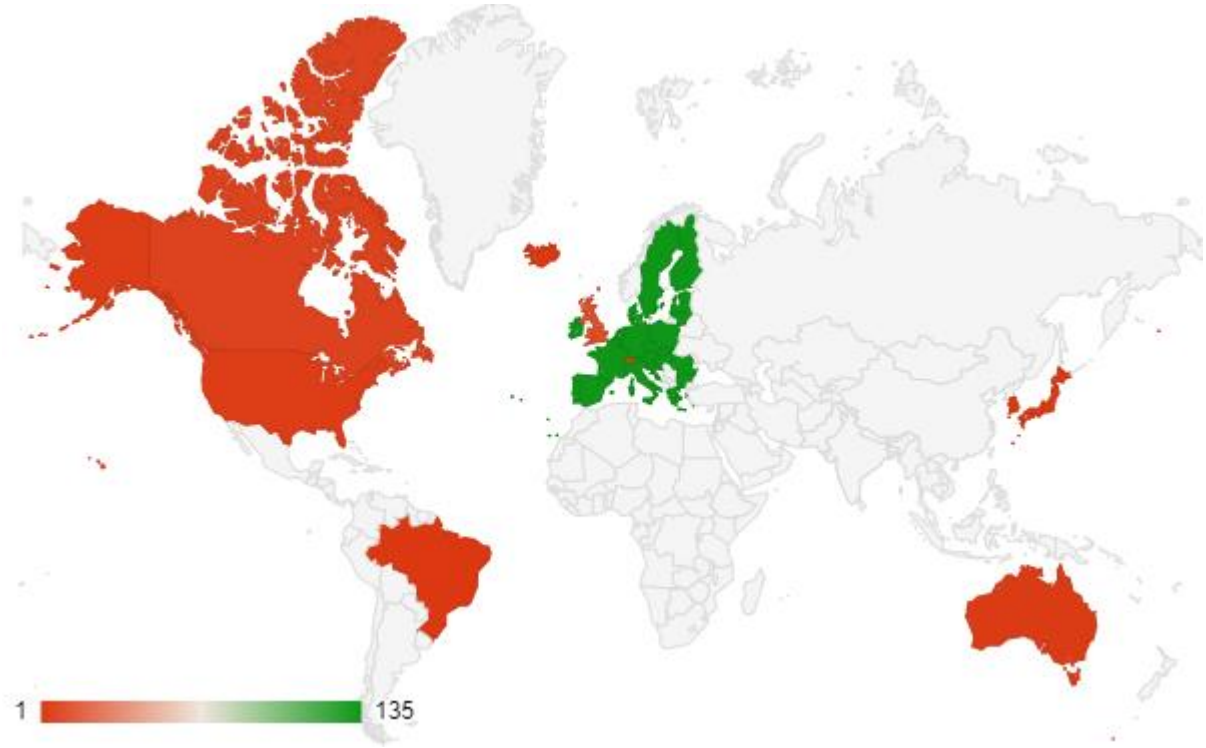

Figure 3.7 Main working regions of survey respondents (n=160) (response to survey question QB2)

By design, all participants in the follow-up interviews worked in the EU, except for one who worked in Canada. We attempted to include interviews with participants from other countries, but the volunteers either did not respond to our requests for an interview, or we were not able to arrange a mutually suitable time for volunteers in Australia.

3.1.4 Regulatory Context

Perhaps more interesting for the remit of this project is the regulatory context of respondents (see Figure 3.8). As expected, EU REACH was the most popular working context for survey respondents as 65 percent work with this regulation. Other EU regulations, such as the Biocidal Products Regulation (BPR), Classification Labelling and Packing (CLP) and Plant Protection Products (PPP) were also frequently selected. There were also a range of global regulations used by individual respondents, such as the Canadian Environmental Protection Act (CEPA), Korea REACH (K-REACH) and Japan Chemical Substances Control Law (CSCL). When we match up the geographic context with the regulatory context, however, we still find that the most popular regulatory context for using RSS around the globe is in connection with EU, and more latterly UK, regulations. It is difficult to draw a firm conclusion about this since the respondent pool was largely drawn from ECHA's REACH registration database, which may therefore be causative.

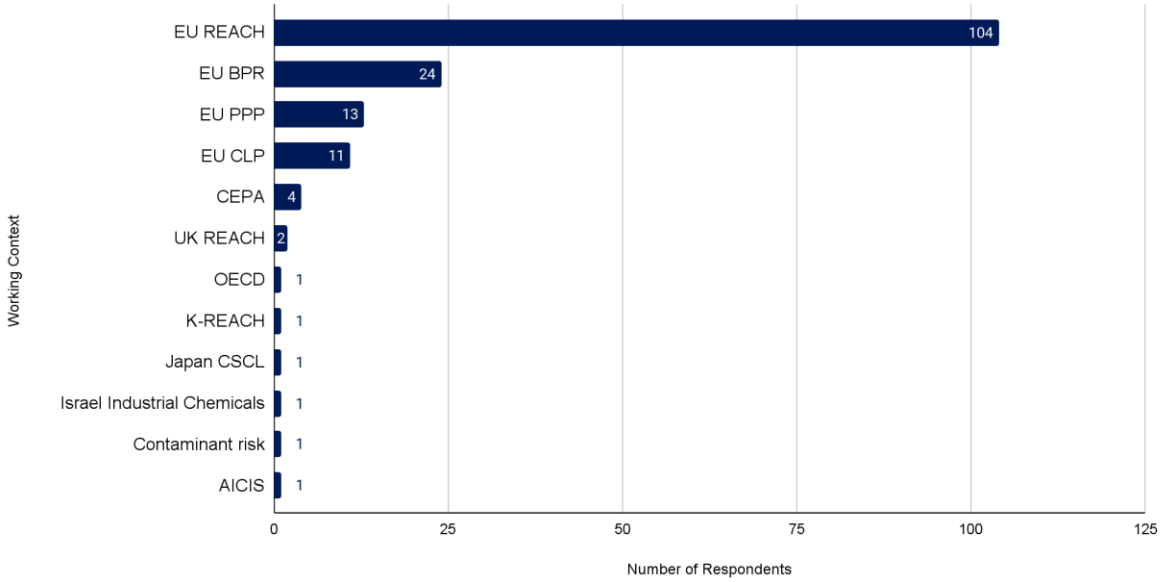

Figure 3.8 Regulatory context of survey respondents (n=160) (response to survey question QB3)

Of those interviewed, participants mainly worked with EU REACH, EU BPR, EU CLP and recently UK REACH. Although we had hoped to have a broad spread of respondents for the interviews, we found that those from the EU were the most engaged. This is unsurprising given that most stakeholders contacted came from the EU REACH registration database (Section 2.2.1).

3.1.5 Specialty Profile

It is an important finding that most respondents (62.5 percent) use RSS across multiple subject areas. About one third (36.3 percent) only use RSS in one subject area and 1.3 percent only work with a single endpoint (see Figure 3.9). Similarly, about one-third of respondents (30.4 percent) work with RSS outside of their primary area of expertise more than half of the time.

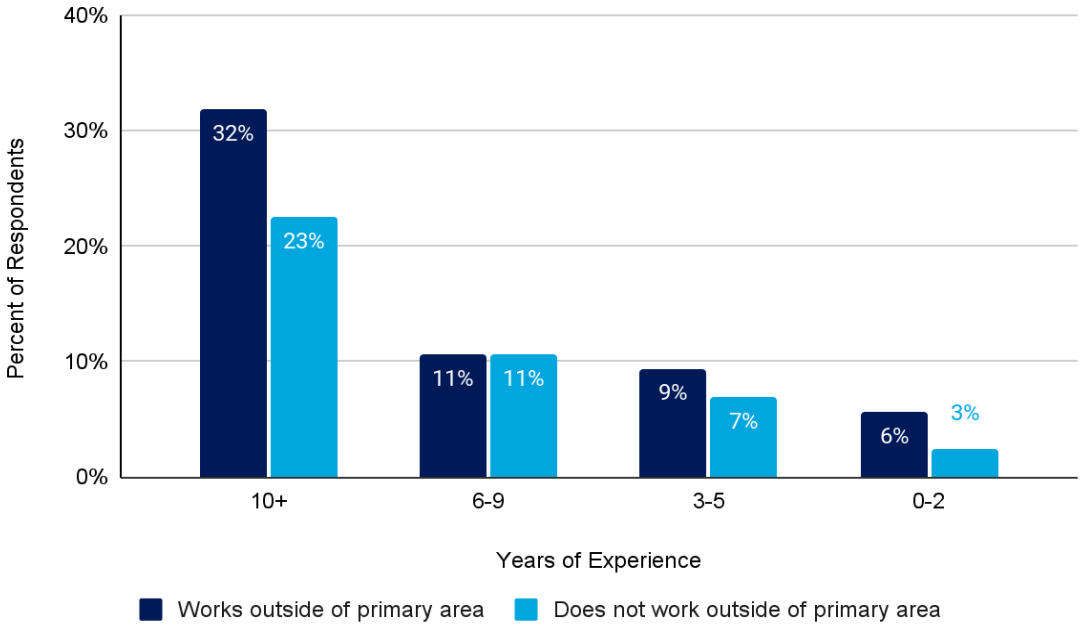

Figure 3.9 Respondents' (n=160) working context with their primary subject area grouped by years of experience (responses to survey questions QA4 and QA5)

Several questions arise from these findings:

1. How much can the high percentage of respondents who use RSS across multiple subject areas and outside of their primary area of expertise be attributed to the fact that respondents tended to be highly experienced users?
2. Similarly, could the working context of a respondent be another reason for the use of RSS across multiple subject areas?
3. Could issues related to quality and reliability be associated with certain subject areas being outside the expertise of respondents?

We cannot answer questions one or two definitively, but we can surmise that it may be the case that with increasing experience, users feel confident to apply RSS across different subject areas and even outside of their primary areas of expertise. Furthermore, as regulatory submissions requiring RSS can be an expensive requirement for companies, registrants might want to meet regulatory requirements in the most cost-effective manner, which may mean that RSS for different areas of expertise are filled in by "non-experts". By the same token, we can surmise that there may be something about the working context of respondents that dictates the way they use RSS (in the context of consultancy, for example, or for evaluators). We will return to question three in our sections below on data regarding the quality, reliability, and strength of RSS.

It is important to note that the data shows that the most common areas of specialist expertise of respondents to the survey were (see Figure 3.10):

- Human toxicology
- Ecotoxicology
- Physicochemical
- Environmental fate

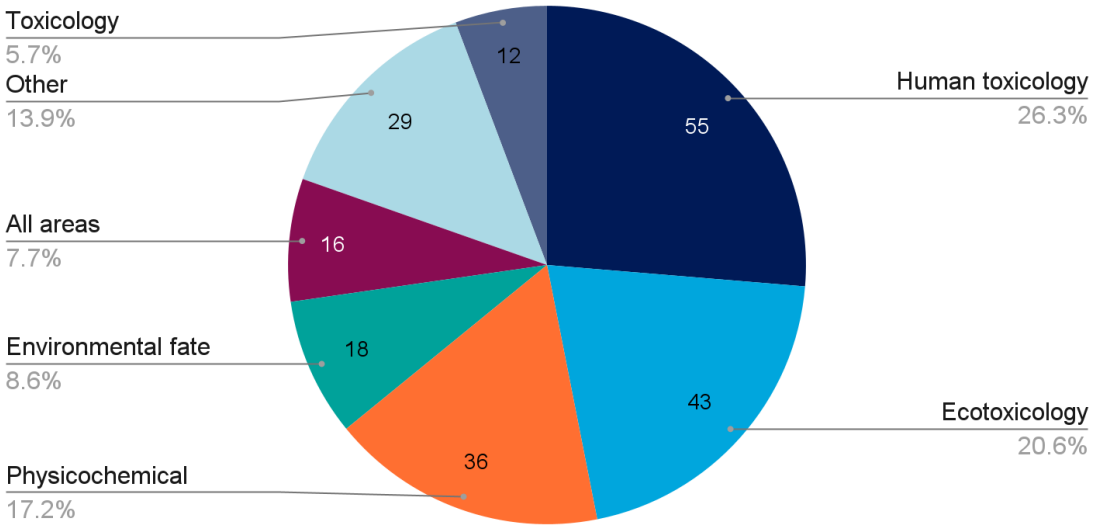

Figure 3.10 Common areas of speciality (n=160) (response to survey question QA3)[22]

35.9 percent of respondents do not frequently work with RSS outside of their primary area of expertise (Figure 3.11). Again, we cannot state definitively why this is the case. Although less experienced respondents do occasionally work with RSS outside their subject area (6 percent of those with 0-2 years' experience), it is predominantly those with more experience who use RSS in this way (32 percent for those with 10+ years of experience). Similarly, there may be working contexts (in academia, for example, or as evaluators) that necessitate the user to stay more closely to their primary area of expertise.

Interestingly, the authors and NGO employees who were interviewed commonly use RSS in the subject of toxicology.

[22] Other specialties mainly include food, efficacy, risk assessment, pesticides and toxicokinetics.

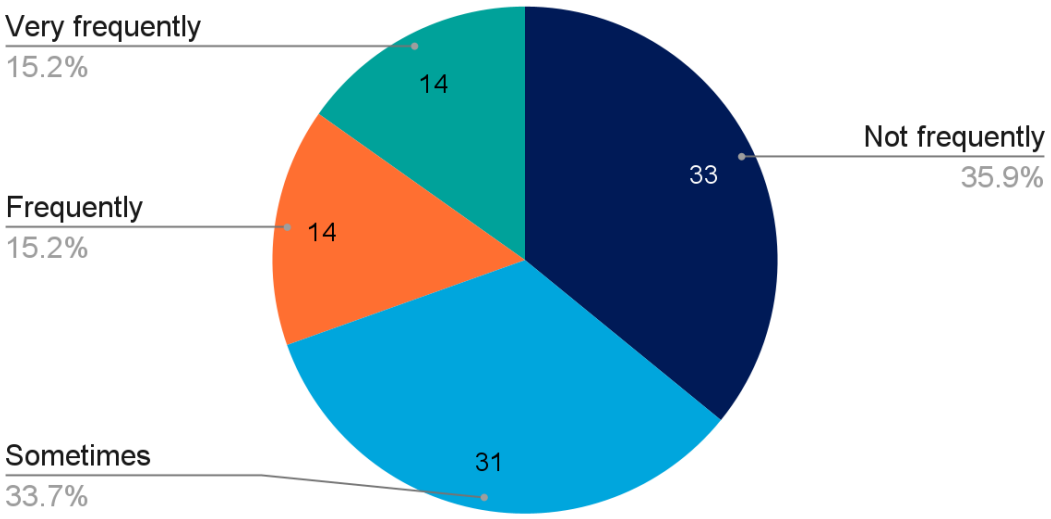

Figure 3.11 How often respondents (n=160) work with RSS outside of their primary area of expertise (response to survey question QA5)

3.1.6 Summary and Analysis

We are confident that the survey captures the major users of RSS. However, as highlighted in Section 3.1.1 above, there may be small sub-groups that were not captured in this study. The most engaged user type in responding to the survey and interview invitations were authors (50.6%) and evaluators (35%), which is likely linked to the stakeholders included in the mailing lists as it directly targeted more RSS authors and to the close contacts ECHA approached from the regulatory body community.

Survey respondents were mainly those who work in industry, which explains why the most common user types were authors followed by regulatory bodies and thus, evaluators. An important finding was that almost one-fifth of users come from working contexts such as consultancies and other service providers. This likely indicates a depth of specialist expertise amongst consultants and other service providers, which could be added as a standalone stakeholder category in future research.

Most survey respondents work in the EU and so the most common regulations used were those in the EU. The stakeholders who completed the survey are very experienced with using RSS as the majority of respondents had over 10 years of experience. It was interesting to note that approximately one-third of respondents work mostly with RSS outside of their primary area of expertise. Most respondents use RSS across multiple subject areas, an interesting finding that could be further investigated.

3.2 RSS Purpose

In the survey we asked respondents to choose which purpose(s) best fit their understanding of the purpose of RSS. User understanding of the purpose(s) of RSS, helps us to understand how RSS are used and potentially affects their reliability, both stated goals in conducting this research. Respondents in the survey could choose from multiple options from a list but were also invited to write in any other understandings of RSS purpose. Participants in the follow up

interviews were asked to confirm if they believe RSS achieves its purposes and explain their answer from the survey. In this way, there was increased scope for them to speak further on the subject. The key purposes identified by respondents are shown in Figure 3.13.

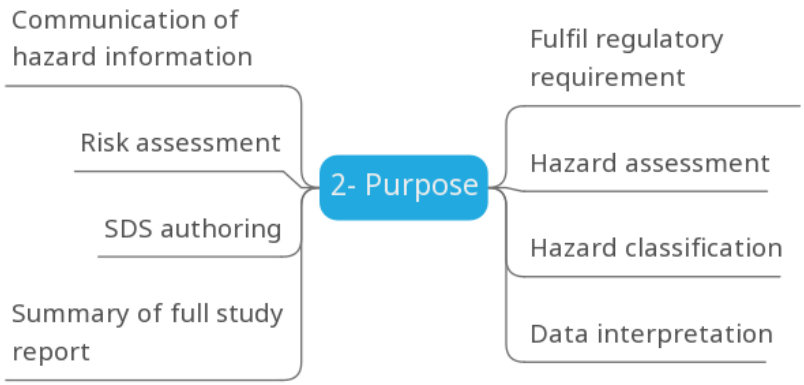

Figure 3.12 Thematic categories in Topic 2 – Purpose

In the survey, the top three RSS purposes identified by all respondent groups are to:

- Fulfil regulatory requirements (compiling dossiers for submission to authorities)
- Derive information on hazard assessment
- Communicate information on hazards of chemicals (see Figures 3.13 and 3.14).

Most researchers and evaluators also identified the derivation of hazard classification as a main purpose of RSS (Figure 3.13). A high number of NGOs and researchers also identified SDS authoring as a key RSS purpose.

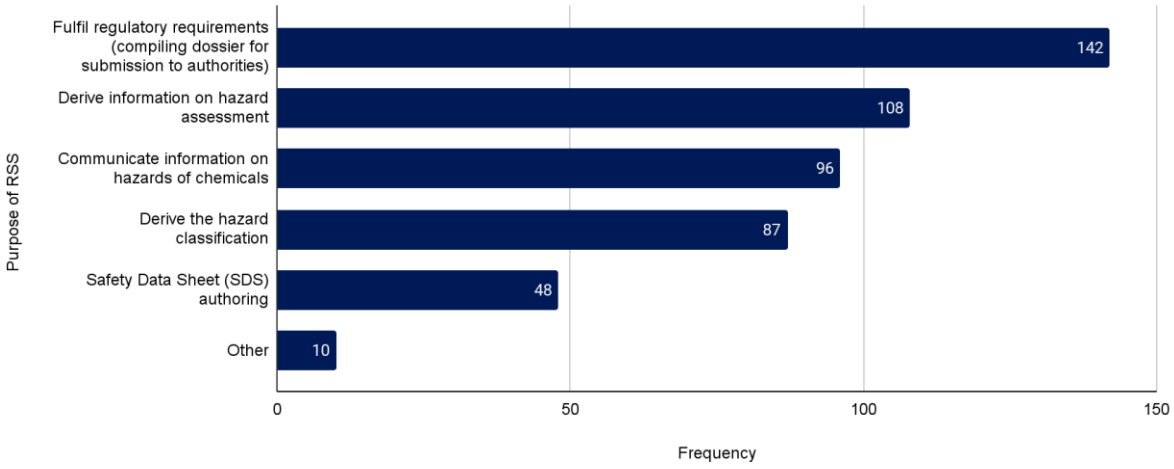

Figure 3.13 Frequency of main purposes for RSS identified in survey responses (n=160) (response to survey question QB1)

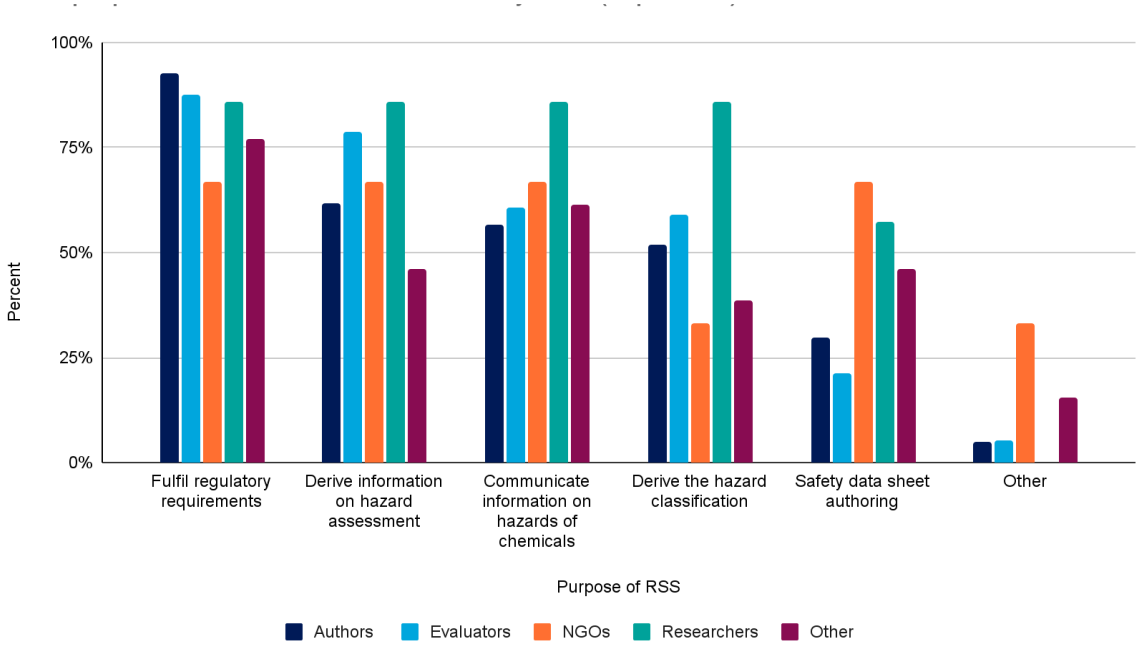

Figure 3.14 Main purposes for which RSS are used by role (n=160) (response to survey question QB1)

Ten respondents identified other purposes for RSS. The key "other" purposes identified were related to the derivation and extraction of data for risk assessment, and the reduction of time required for the review of technical studies for researchers and regulators.

Importantly, when the question was asked during the interviews, the responses were aligned with those identified during the survey. Interview respondents emphasised that RSS is a *summary* of study reports that is used for hazard and risk assessment. In fact, as we show below, the understanding of RSS as a summary is key since it underpins respondent understandings of both the strengths and weaknesses of RSS and dictates how respondents use RSS. The understandings of RSS presented here give us a good sense of how RSS are used.

3.3 Use of RSS

The theme of this section begins to dive more deeply into user experience of applying RSS in different contexts. Here we discuss the following sub-codes (Figure 3.15):

- When and how respondents use RSS
- Are RSS fit-for-purpose and what are their strengths?
- Weaknesses and shortcomings of RSS
- The importance of RSS use
- Identified challenges in the use of RSS

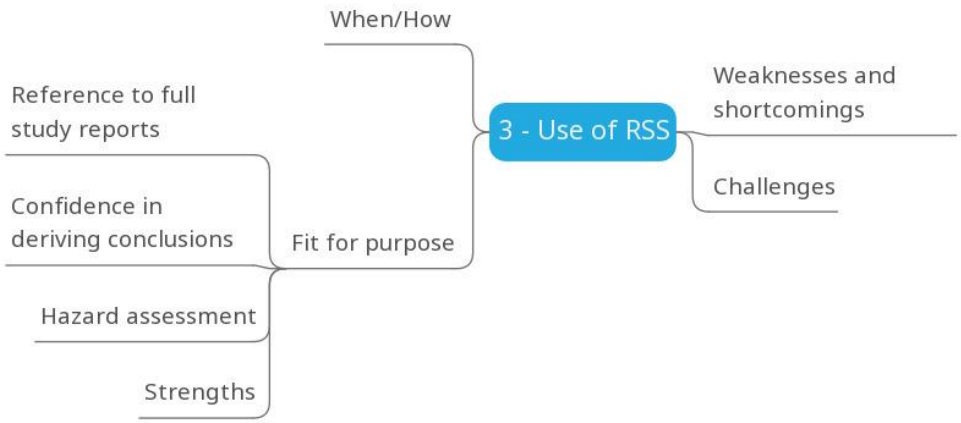

Figure 3.15 Thematic categories in Topic 3 - Use of RSS

Here we can begin to dive more deeply into the use of RSS, as well as begin to evaluate the current limitations of RSS, both goals stated by ECHA for this research. The limitations found feed into conclusions as to the reliability of RSS.

3.3.1 When and How

The various user categories outlined above differed slightly in when and how respondents use RSS. These differences may be understood as on a continuum from the highly functional, to part of a process of evaluation and judgement of data, to a more abstract use aimed at understanding the thought processes of users (Figure 3.16).

Figure 3.16 RSS Use Continuum

Authors and users of RSS specifically said they write, use, and submit RSS using IUCLID. We can thus place them at the highly functional end of the continuum, though there will be differing levels of complexity to their use.

Evaluators validate the regulatory compliance of the information provided in the RSS. They check that the submitted information meets guidelines and requirements and make the final judgement as to whether the data in the RSS is reliable enough to make an assessment. This set of respondents, unsurprisingly, use RSS as part of a process of evaluation and judgement. Authors of RSS feed into this process.

On the abstract side of the continuum, researchers use RSS differently. Amongst our respondents, this group is interested in investigating reported results and in understanding how assessments have been made by registrants. That is, they have a complex, but a more abstract approach to RSS as well as investigating the transparency and reliability of reported data under REACH.

However, importantly, interviewees do not usually submit data in ways other than RSS. Respondents frequently said that if data were to be submitted via other methods, they would not be certain as to how the data would be evaluated by the regulators. In other words, RSS is the *de facto* standard method.

In the REACH context, registrants have the option to include an electronic report as an attachment. These attachments are not made available on the public database, with instead a reference to an 'attachment' in the original RSS. In other regulatory contexts (for example, Canada and K-REACH), printed copies of full study reports and IUCLID data can be used for submitting data. However, despite this possibility, these methods are not regularly used by interviewees. In other global regulatory contexts (such as Japan and the USA), one may use RSS, but may report results via pdf file.

While participants noted that data can, of course, be reported in the full study report, participants pointed out that full study reports take users longer to read as they are more comprehensive. Therefore, one benefit of RSS is that it saves time for users, specifically evaluators, researchers, and NGOs.

Other participants also noted that study summaries had previously been used in PPP regulations before the use of RSS, so it is interesting that RSS are now the standard. Respondents noted that the study summaries used in PPP had issues with quality and lack of standardisation. We will come back to this in our section on the strength of RSS below.

Participants also pointed out that the OECD High Volume Production (HPV) chemicals database and the German MAK Commission have ways of reporting which follow a similar format to RSS.

In all these additional cases, these are methods that respondents are aware of, but they are not primarily used by any of the interviewees.

3.3.2 Fit for Purpose

Figures 3.13 and 3.14 illustrate the purposes of RSS that respondents identified. The most frequently selected purposes were that RSS are meant to fulfil regulatory requirements

(compiling dossiers for submission to authorities), derive information on hazard assessment and communicate information on hazards of chemicals.

Interviewees generally felt that RSS achieve these aims when correctly completed in the standardised format. However, they cautioned that in cases where they do not contain the information requirements, they cannot be safely used for hazard assessment because of incorrect or incomplete data.

For EU PPP and BPR, RSS are not seen as achieving their aims by some interviewees. For EU BPR, this was indicated as being due to the format of IUCLID being difficult to read in comparison to a product assessment report. Additionally, some authors speculated that authorities do not fully read the RSS when the full study report is attached.

Reference to Full Study Reports

The reliance on RSS for different user types was plain. When available, they are the go-to standard for all users in most cases.

- Most evaluators require full study reports less than 50 percent of the time for physicochemical, environmental fate, ecotoxicology, and toxicology endpoints when the RSS is available, as seen in Figure 3.17 (below).

- Of those who use RSS in NGOs and for research, 52 percent prefer to use RSS and 48 percent prefer full study reports. Of those who selected that they use full study reports, the majority rely on them 75-100 percent of the time for hazard assessment and classification.

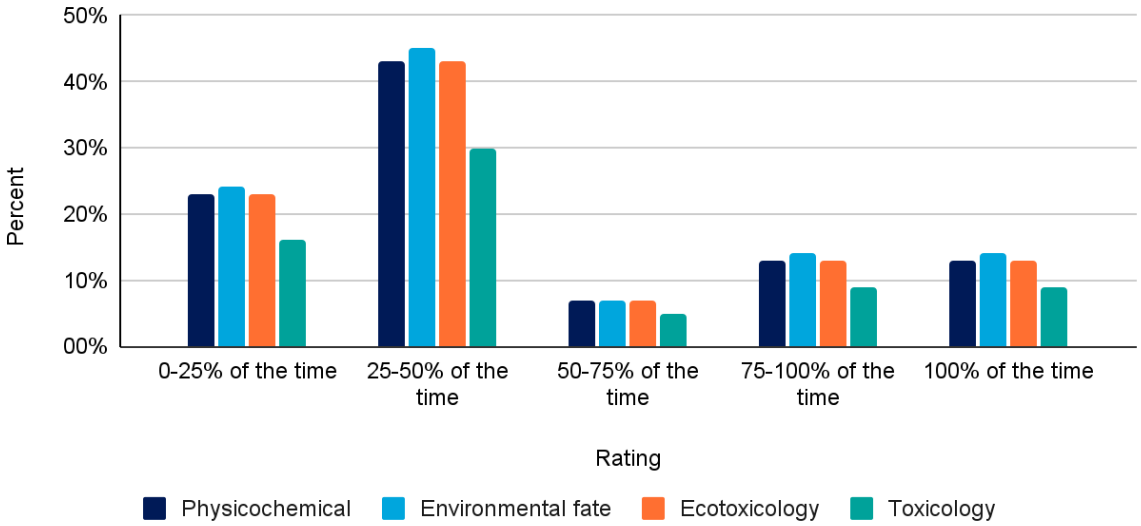

Figure 3.17 How often evaluators (n=56) require reference to the full study report whilst evaluating RSS for endpoint groups (response to survey question QB4 for evaluators)

Authors used RSS and full study reports equally. When assessing and classifying hazards, 50 percent of authors prefer to use the RSS if it is available, and the remaining 50 percent use full study reports. The preference to use full study reports may be due to authors feeling the

need to check original data. It is also because authors usually have access to both RSS and full study reports. If an expert had to choose between referring to the RSS or the full study report, we expect that one would choose the study report as it contains all the study details.

Confidence in deriving conclusions

As seen in Figure 3.18 below, evaluators have the most confidence in using RSS to derive conclusions on physicochemical hazards. However, they have the least confidence in drawing conclusions using RSS for systemic human health and environmental hazards. One of the possible reasons for this is due to the complexity of those endpoints, which can lead to lack of trust in the author to understand and report the data correctly if they are a non-expert.

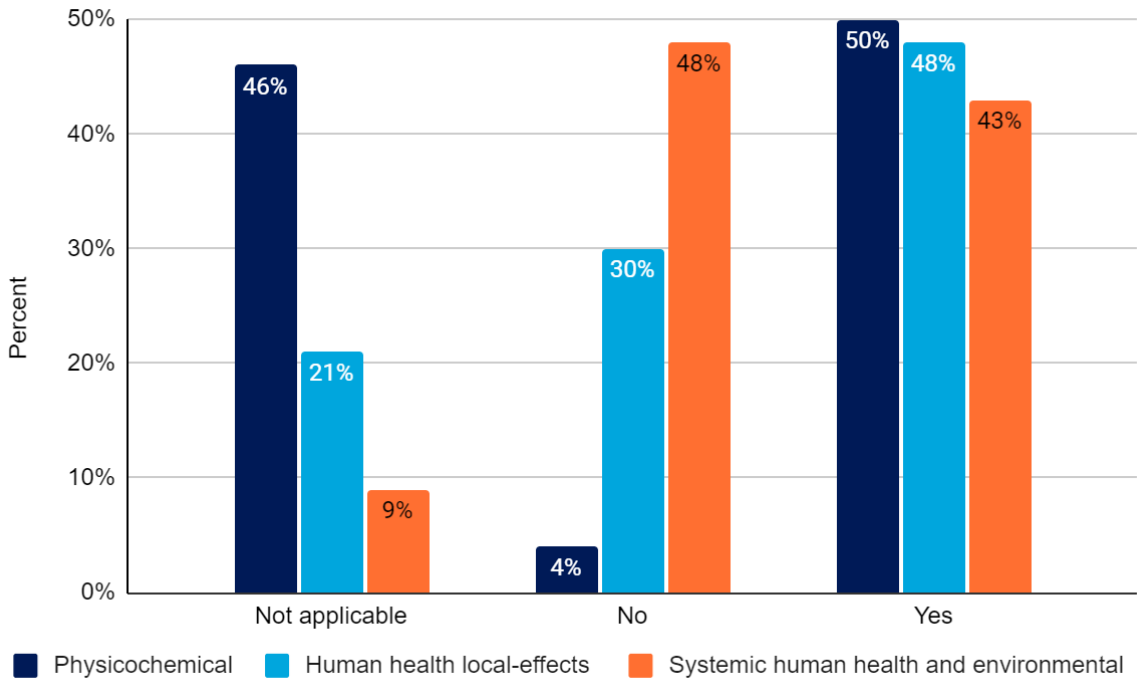

Figure 3.18 Whether RSS are sufficient for evaluators (n=56) to derive conclusions from by hazard group (responses to survey questions QB5,6,7 for evaluators)

When asked about their confidence in using RSS to identify correct relevant dose descriptors and assessment factors to derive safe exposure levels in the absence of full studies, 42 percent of evaluators said they were somewhat confident. Only 4 percent of evaluators are completely confident in doing this, with 21 percent being not at all confident (Figure 3.19). We see this as a key challenge and the general low level of confidence that evaluators have in using RSS for these purposes is an important finding.

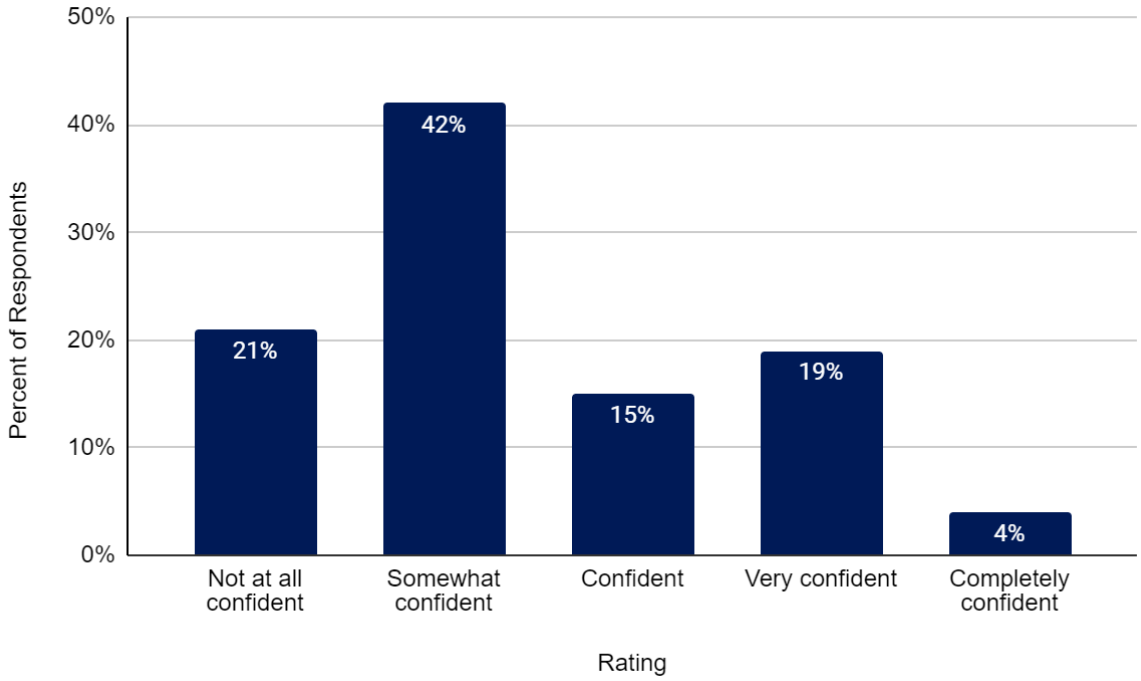

Figure 3.19 Evaluator's (n=56) confidence in using RSS to identify correct relevant dose descriptors and assessment factors to derive safe exposure levels in the absence of the full study report (responses to survey question QB8 for evaluators)

Hazard Assessment

Both authors and evaluators found RSS suitable for hazard assessment purposes, at least some of the time.

Forty percent of authors find RSS sometimes (1-25 percent of the time) suitable to summarise results in hazard assessment from peer reviewed articles. However, 11 percent say that RSS are unsuitable for this purpose. The main reasons why authors identified peer reviewed articles as insufficient is because they do not usually include all the compulsory fields in the RSS format, and typically do not include enough details about the study set up and results.

Similarly, evaluators generally view RSS as sufficient to perform hazard assessment without referring to the full study. However, evaluators cautioned that this could depend on the quality and type of information included in the RSS. Evaluators stressed that, in theory, RSS should be sufficient, but that, in practice, they are not perfect and may not be completed accurately, depending on the author, endpoint and type of study. This is a key finding of this study: RSS has been designed well, but in practice, it is down to human error in completing the templates. Evaluators are aware of this, so it equates to a trust issue that lowers confidence.

Strengths

Respondents named several strengths of RSS, which contribute to whether they view them as fit-for-purpose. Some of these strengths depend on RSS being summaries and thus on the quality of the information in, or authorship of, the summary. The top strengths mentioned had to do with the RSS format or template, and their level of consistency.

The very fact that they are summaries was also often mentioned as both useful and a valuable way of saving time and resources.

As RSS have a standardised format, respondents appreciate the mandatory fields and free text areas in the template as this makes it easy for them to understand what information needs to be filled in. Respondents generally feel that this structure provides enough information for assessment, if completed correctly. Respondents especially singled out the helpfulness of certain elements, such as the test guidelines followed and any deviations.

Respondents viewed current RSS as more consistent compared to the previously used study summaries for PPP regulations. The respondent stated that “there used to be issues with summaries for PPP regulations, and since RSS has been introduced (circa 2007) these are an improvement from the previous unstandardised study summaries used.” Specifically, they appreciate the defined structure and conciseness of RSS, as well as the ability to submit in an electronic format.

Overall, respondents identified RSS as an important source of information when there is no access to the full study. They also provide a common denominator to assess data provided to the authorities.

3.3.3 Weaknesses and Shortcomings

Again, in discussing whether RSS are fit-for-purpose, respondents often singled out what they felt were weaknesses or shortcomings of RSS (Figure 3.20). As above, many of these are, at root, since RSS are summaries. For example, evaluators identified that insufficient explanation of the key study is the most frequent weakness when evaluating effect level calculations in RSS. Similarly, there may be an insufficient explanation of key information from the full study. Again, the confidence level of a user in an RSS also has to do with how much confidence they have in assessing content or interpretation and this is very often to do with the fact that RSS are summaries.

Other frequently mentioned weaknesses were study deviations and problems with the endpoint chosen. Generally, issues surrounding dose conversion were less frequent.

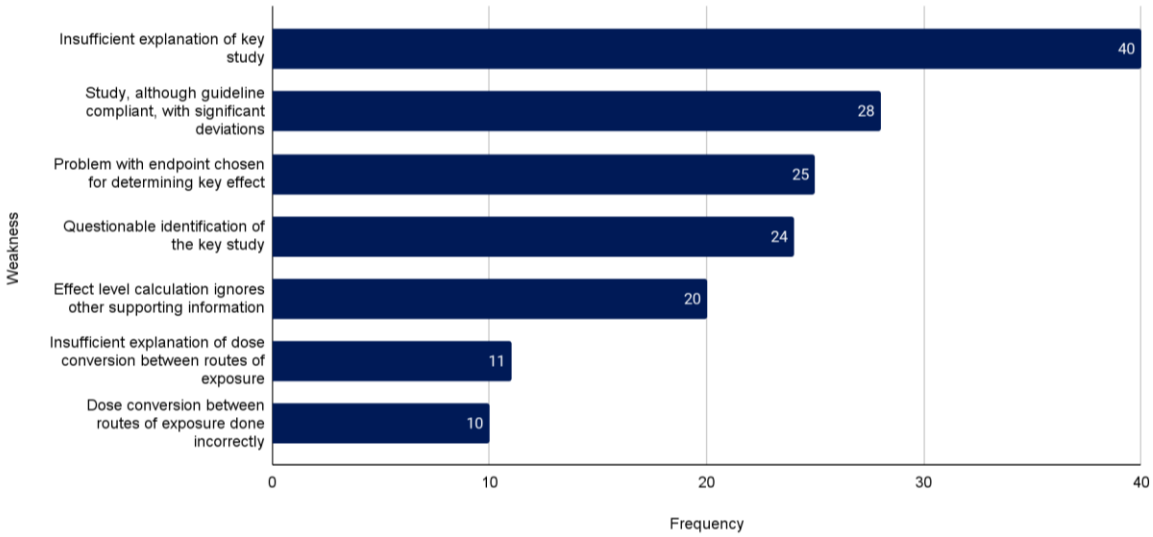

Figure 3.20 Weaknesses most frequently observed when evaluating effect level calculations (n=56) (responses to survey question QB9 for evaluators)

Other weaknesses and shortcomings of RSS had to do with the confidence levels of the user in assessing both the content of and interpretation of RSS. In assessing content, respondents mentioned that:

- It can be difficult to tell if information has been left out or misinterpreted
- There can be a lack of information or incompleteness (either in the template, but also due to insufficient fields)
- Sometimes there are translation errors and misunderstandings of the text
- For certain studies (more complex human health and extended reproduction studies), it is not possible to include all the relevant details and so access to the full studies are systematically requested
- More complex endpoints, such as developmental toxicity and bioaccumulation, require detailed and important information which is not generally completed well or is missing
- Non-disclosure of the full study report
- RSS are too long and detailed, so the full study might as well be used

In cases where respondents had compared the RSS with the full study report, they sometimes found that the content of the full study was reported insufficiently and not to the guideline standard.

In assessing their confidence levels in the interpretation of RSS, respondents highlighted the following:

- Summarising sometimes means that assumptions are made with blanket assertions
- There are variations in the amount of information reported by companies
- There are no/insufficient fields to help understand the reliability and relevance of data
- Critical findings are sometimes not reported as authors decide what details are important to include in the summary
- There is no way to tell if the data is valid or reliable, many evaluators still must read the full study report to ensure that the RSS is correct
- In publicly disseminated RSS, the identity of the test material can be difficult to determine, either because it is confidential or insufficiently completed

Respondents highlighted a few weaknesses of the format for writing RSS, particularly in terms of their implementation in the OECD Harmonised Templates and in IUCLID:

- The picklist options are not well described, particularly the options which ask users to add other information
- The current format is intended to act as a one size fits all, but cannot display complex tables or special characters
- The transition from different template (and IUCLID) versions led to information not being fully migrated or updated which caused manual work
- It was suggested to include more flexibility in the IUCLID templates, such as adding custom options for non-standard data

Finally, respondents stressed that there is an issue when using older study reports that lack details now required for RSS.

3.3.4 Challenges

We have separated out the sub-theme of ‘challenges’ from ‘weaknesses and shortcomings’. Although these sometimes overlap, they are not always the same and they may differ with the perspectives of different types of users. That is, what is a weakness in RSS for evaluators may be a challenge for authors. For example, one weakness identified above is the lack of conciseness or inappropriate information (or lack of appropriate information). From an author’s point of view, a major challenge in writing RSS is the difficulty of being concise when summarising a lot of data and in identifying which information is appropriate from a comprehensive study report.

Alongside the above challenges, authors report the following additional ones:

- A lack of information on the quality and reliability of full study report data, particularly if it is not compliant with test guidelines
- Difficulty in using old studies (e.g., those which precede Good Laboratory Practice (GLP) guidelines) due to outdated information and a lack of details that are now relevant, so recalculating is needed to determine the hazard assessment or classification

- Interpreting results in the full study reports if there were deviations or complex results
- Difficult to include tables
- Interface navigation can be difficult and non-intuitive. Authors experience difficulties in integrating multiple RSS for hazard assessment due to the functionality of IUCLID. Inputting data into small-sized text boxes can make amendments difficult leading to errors.

We are reassured by the fact that the different types of users are identifying the same issues as this indicates that these are genuine weaknesses/challenges for RSS or for their technical implementation in software applications.

Researchers and those who work with NGOs also identified several further challenges that again focused on the worry about leaving out important data in the summary and the need to rely on full study report data when the reliability of an RSS is uncertain. However, they also highlighted the high costs associated with RSS for documentation and to meet regulatory and IT requirements. The identification of confidential information under data sharing has also been identified as a challenge. Interestingly, these users sometimes felt that RSS can be too detailed which makes it difficult to extract the wanted data points. In other words, NGOs think that, when there are too many details in RSS, they can fail their purpose of being summaries.

In the other Data Analysis sub-sections below, we will dive deeper into some of these issues, as well as pull out some suggestions for improvement based on these strengths and weaknesses of RSS.

3.3.5 Summary and Analysis

In summary, stakeholders use RSS as the *de facto* standard to report and submit data to regulators. Users feel that RSS are preferred by evaluators, especially when RSS are completed correctly as they are fit-for-purpose. Users seem to trust that when RSS are not completed correctly, evaluators would flag this, thus ensuring quality.

One major exception was in the case of using RSS for EU BPR and PPP where they are not seen as fit-for-purpose due to difficulties with the format and uncertainty that the RSS are read by evaluators.

From an evaluator's standpoint, RSS was viewed as sufficient to perform hazard assessments without the full study reports, when the RSS are correctly completed. Similarly, there is not a significant difference in the number of authors and users of RSS for research and NGOs who must use the full study reports over RSS for hazard assessment and classification. Further, most evaluators do not typically need to refer to the full study report when evaluating RSS for EU REACH purposes. This is an important finding for the goals of this research.

However, evaluators have the least confidence in drawing conclusions using RSS for systemic human health and environmental hazards. In fact, they are split on this issue with 48 percent saying they are insufficient for this use and 43 percent saying that they are sufficient (Figure 3.18).

Strengths of RSS are that they save time and resources, they are valued for their standardised structure both for submitting data to the authorities and they aid evaluation. The fact that RSS are summaries is seen to be both a strength and a source of weakness or challenge.

Several weaknesses and challenges were mentioned frequently:

- As a summary, blanket assumptions can be made by authors which leads to bias and errors (but is not always the cause of).
- The ability of authors to determine what information is relevant for RSS (and thus potentially leaving out important information) is a weakness for some users and a challenge for authors.
- Similarly, complicated studies and endpoints are difficult to summarise for authors and may lead to not enough relevant information in the RSS. This may be an underlying issue with the template.
- Authors often face challenges in uploading tables and special characters in IUCLID and/or may have trouble with the IUCLID interface in general (e.g., with dropdown lists). The above may lead to missing information, mistakes, inaccuracies.
- A lack of knowledge about the quality and reliability of data (both in the RSS and full study report) leads to needing to refer to the full study report.
- Older study reports were often mentioned as not containing the relevant information for current RSS.

Finally, despite these issues, users agreed that RSS are an important source of information.

3.4 RSS Content

Several questions throughout the survey and interview were targeted to get insights on RSS content. As shown in Figure 3.21, the questions and responses related to RSS content have been grouped into four broad categories: quality, information availability, authoring and regulatory context. Here we dive deeper into comments on RSS content than those in the findings in the previous section. The findings are summarised in the following subsections.

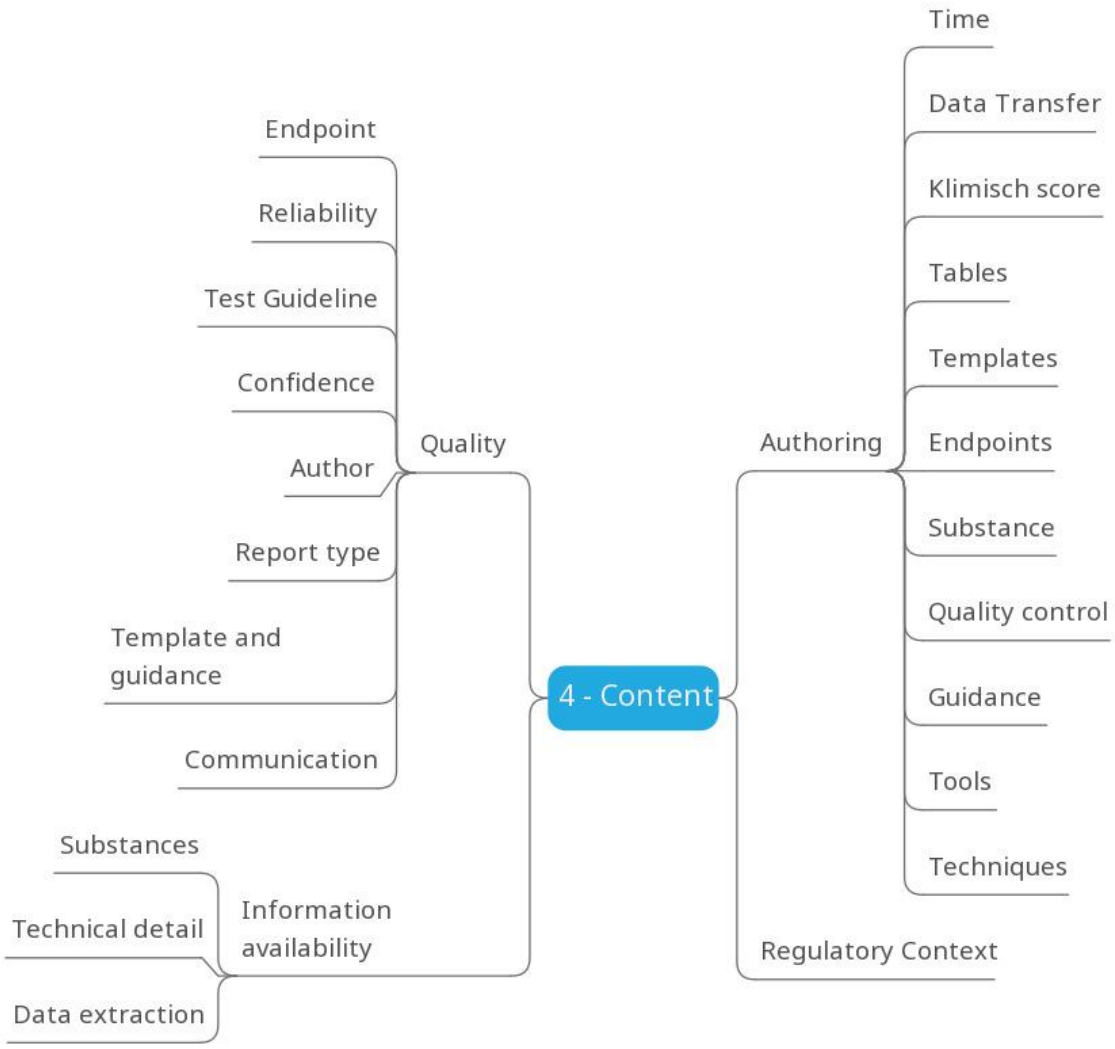

Figure 3.21 Thematic categories in Topic 4 - Content

3.4.1 RSS Quality

Respondents shared that RSS quality can vary based on several factors, including the author, endpoints, study type and methodology. They observed that some registrants are very diligent about producing good quality RSS, while others frequently submit incomplete information. Furthermore, RSS quality can vary depending on the endpoint complexity. As a general observation, the less complex the endpoint is, the better the RSS quality observed. One of the

limitations identified by evaluators is that in many instances, it is not possible to understand how the RSS data has been assessed, which makes it challenging to use.

Endpoint

Nearly 60 percent of evaluators shared that, in their opinion, RSS quality is dependent on the endpoint while 40 percent said they are not related (survey question QC2). Some of the examples that were shared to illustrate the links are summarised in Table 3.1 below.

Table 3.1 Evaluator comments on RSS quality based on endpoints (summary of responses to survey questions QC2 and QC3)

Endpoint Type	Comments
Environmental endpoints	• Typically, worse quality than human health endpoints • Environmental fate and ecotoxicology endpoints usually have more deviations from the guidelines and need to reference the full study report more often • Long-term aquatic toxicity RSS generally have insufficient information to make a full assessment • Algal studies and associated algal toxicity endpoints need to report data for each of the control, but typically lack data in the RSS • Bioaccumulation studies and bioconcentration factor (BCF) endpoints can be difficult to assess from RSS if lipid normalisation data is not provided • Adequate RSS for endpoints that need less information for evaluation, such as aquatic invertebrate studies and associated LEC50 endpoints • Acute aquatic toxicity is usually less detailed than RSS for chronic studies • Simulation studies and BCF studies are challenging to summarise to get good quality RSS
Toxicology endpoints	• Prenatal developmental studies, reproductive toxicity studies, carcinogenicity, and skin sensitivity studies are generally poorly reported • Complex study design such as in vitro or long-term studies are not typically well reported in RSS and require a full study report • Studies with subjective criteria (e.g., reproductive toxicity) are more likely to be less well reported than other studies (e.g., irritation or acute toxicity) • Histopathology is often compared to historical controls, which are often not specified • Chronic studies are often reported poorly, especially with endocrine disruption. Should include all dose-dependent results, but they are typically not included in the RSS • Study report for a toxicology endpoint may exceed 1,000 pages, so the amount of information to summarise is very large, and makes it challenging to report in the RSS format, therefore affecting RSS quality
Physicochemical endpoints	• RSS for physicochemical endpoints are often less detailed than others

Endpoint Type	Comments
	● RSS more likely to follow guideline ● RSS more likely to be sufficient (i.e., no need to reference full study report)
OECD Tests	● OECD 301 (Ready biodegradability): typically, sufficient RSS ● OECD 106 (Adsorption): RSS is rarely sufficient as there is typically relevant information missing
Other	● RSS not well adapted to efficacy testing for BPR

Researchers, NGOs, and other users also reported that RSS quality can be dependent on the endpoint. The examples provided to illustrate this were aligned with those identified by evaluators in Table 3.1 above, such as long-term and higher tier studies being more challenging to report in an RSS.

A total of 56 evaluators identified the frequency at which they need to refer to full study reports for human health and environmental endpoints (Figures 3.22 and 3.23). Of all the endpoints listed in the survey questions, the following endpoints were identified as the ones that *frequently* require evaluators to refer to the full study report:

- Human health endpoints
    - Carcinogenicity
    - Multigenerational, extended one-generation reproductive and developmental toxicity
    - Prenatal developmental toxicity
    - Chronic repeated dose toxicity study
- Environmental endpoints
    - Simulation biodegradation tests in water
    - Bioaccumulation studies

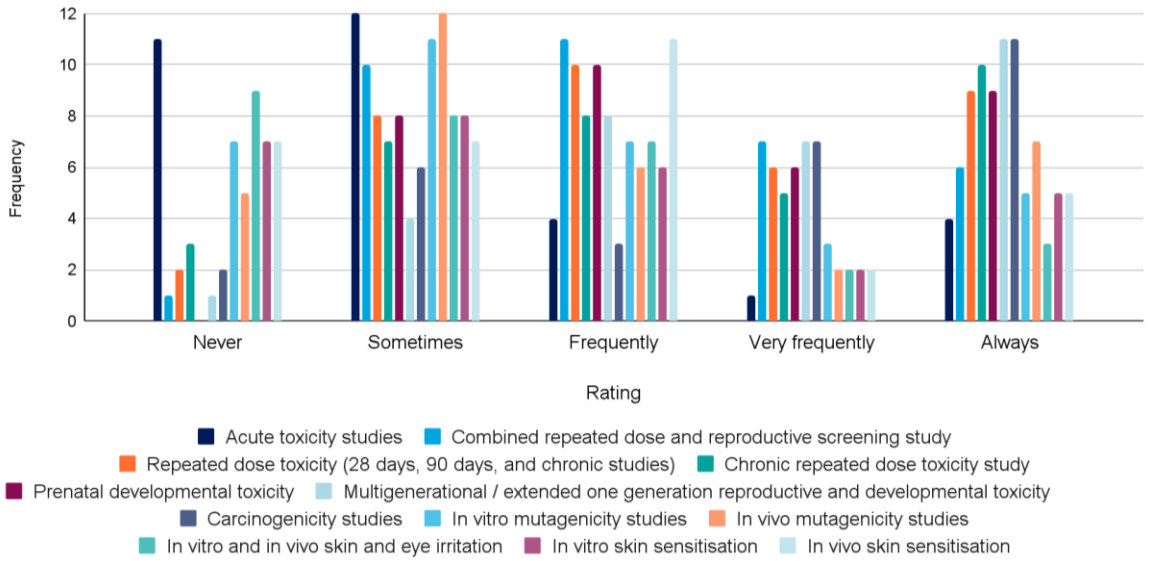

Figure 3.22 Frequency of evaluators (n=56) who report the need to refer to full study reports for human health endpoints (response to survey question QC3)

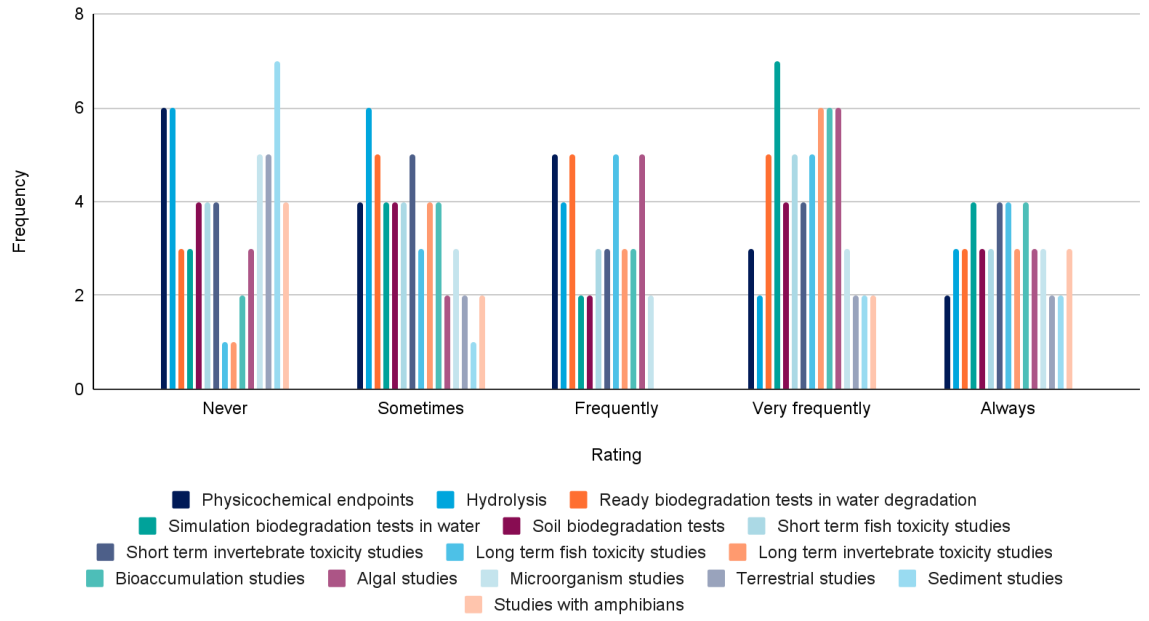

Figure 3.23 Frequency of evaluators (n=56) who report the need to refer to full study reports for environmental endpoints (response to survey question QC4)

Of all the endpoints listed in the survey questions, the following endpoints were identified as the ones that *rarely* require evaluators to refer to the full study report:

- Physicochemical endpoints
- Human health endpoints
    - In vitro and in vivo mutagenicity studies
    - In vitro and in vivo skin and eye irritation
- Environmental endpoints
    - Hydrolysis
    - Aquatic toxicity studies

Reliability

All survey respondents were asked how reliable RSS are for hazard assessment, in line with the goals of this study. As stated above, most respondents felt that RSS were at least 'somewhat reliable' (Figure 3.24) for this use, with only 5 respondents (3 percent of survey respondents) feeling they were 'completely unreliable'. The key reliability concerns identified by respondents include:

- RSS author: expert judgement, interpretation, bias, error
- Endpoint complexity
- Type of substance
- Level of detail: amount and relevance of data provided
- Study report: alignment with study report, alignment with guidance, quality of study report

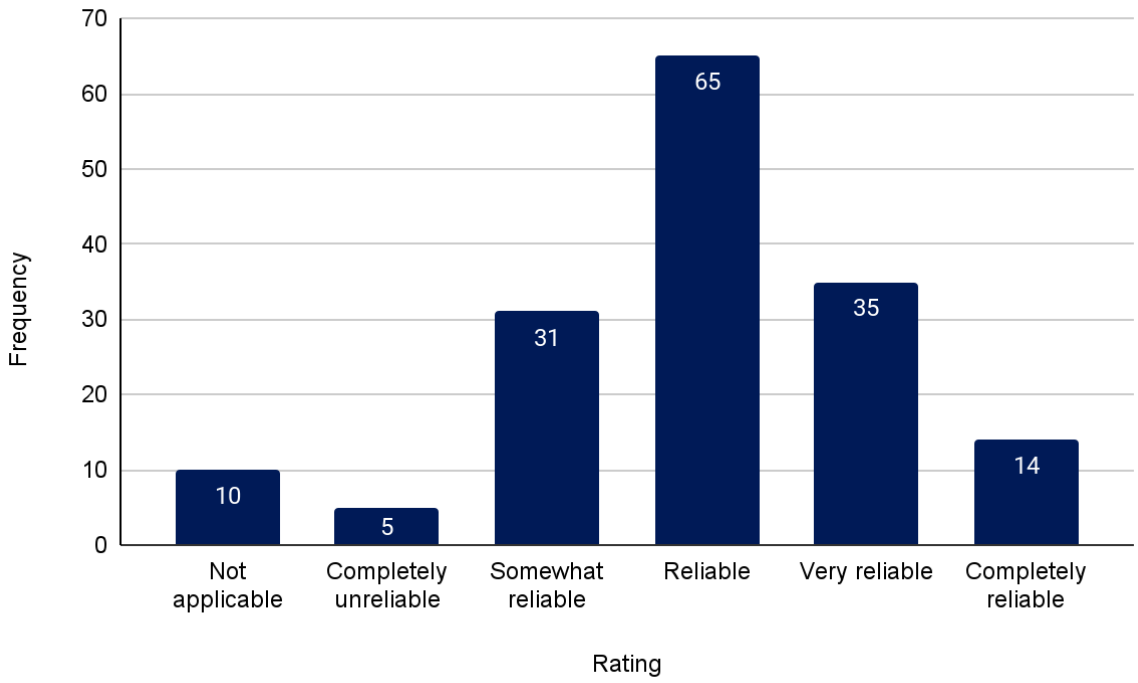

Figure 3.24 Frequency of rating given by survey respondents (n=160) in relation to the reliability of RSS for hazard assessment (survey question QD1)

In the survey, 86 percent of evaluators reported that RSS quality is dependent on the type of report from which it was created. For instance, full study reports, especially those that follow test guidelines and GLP, usually have all the information needed to produce high-quality RSS. However, reports based on secondary information, such as peer reviewed academic publications or literature studies, often have more limited data available which can impact the overall RSS quality.

With regards to the reliability score assigned to a study in RSS, most evaluators disputed the use of the Klimisch[23] score, in 1 to 60 percent of the RSS they assess (Figure 3.25). The reliability score is typically disputed when it is either too high (e.g., Klimisch 1 given to a Klimisch 2 study) or too low (e.g., Klimisch 2 given to a Klimisch 1 study). Indeed, 22 percent of evaluators find they dispute a reliability score assigned to a study in the RSS, 'frequently', 'very frequently', or 'always'.

The types of studies that are reported as most associated with a disputed reliability score are old study reports that predate OECD and GLP guidelines, peer reviewed academic publications and study reports that are not guideline compliant. Reliability scores of OECD test guidelines and GLP compliant study reports generated by contract research organisations (CROs) are less frequently identified as having a disputed reliability score. Furthermore, most evaluators said that endpoint type is not linked to the fact that a reliability score is disputed.

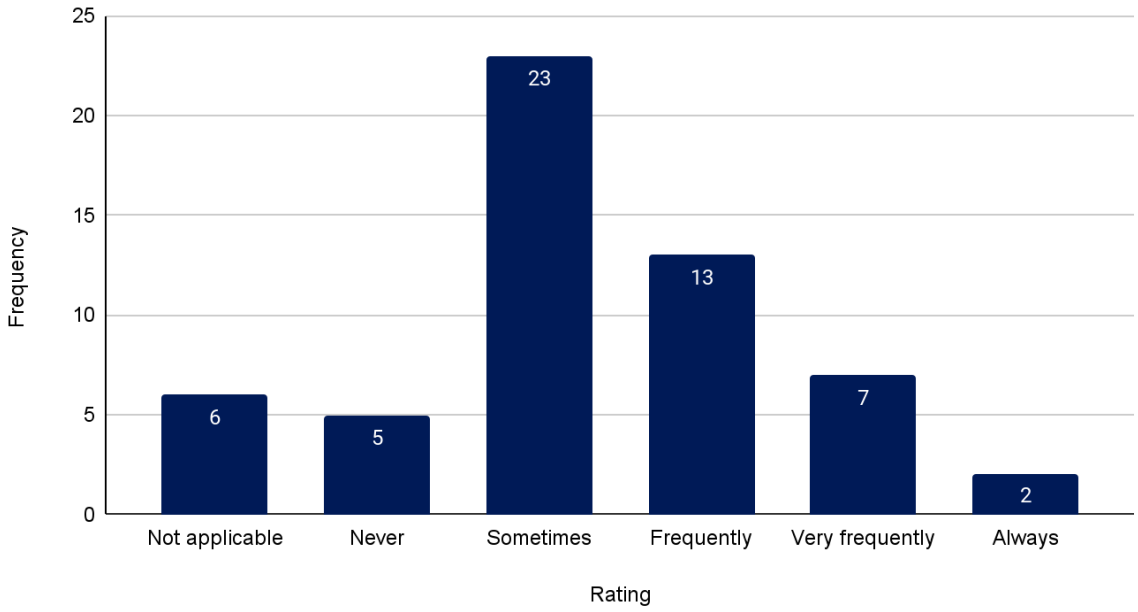

Figure 3.25 Frequency at which evaluators (n=56) dispute a reliability score assigned to a study in the RSS (survey question QC7)

In contrast, it is interesting to note that researchers, NGOs and other RSS users more frequently assign a Klimisch score of 1, 2 or equivalent to peer reviewed academic publications. When a study reliability score is given to a study in the RSS, most of the

[23] Klimisch HJ, Andreae M, Tillmann U. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regul Toxicol Pharmacol. 1997 Feb;25(1):1-5. doi: 10.1006/rtph.1996.1076. PMID: 9056496.

researchers, NGOs and other RSS users infrequently dispute the score. However, this still means that 26 percent claim to dispute the reliability score frequently or always. When the scores are disputed, it is for the same reasons as indicated by evaluators, meaning that the score is either too high or too low. Similarly, this user group stated that there are no specific endpoints commonly associated with a disputed reliability score, but it is rather dependent on the study type, such as peer reviewed publications and older studies.

As shown in Figure 3.26, researchers, NGOs and other RSS users identified ecotoxicology, environmental fate and exposure assessment studies as more frequently requiring references to the full study report due to incomplete information reported in the RSS. On the other hand, physicochemical and human toxicology studies were reported as requiring reference to the full study report less frequently, likely due to the nature and motivations for their investigations.

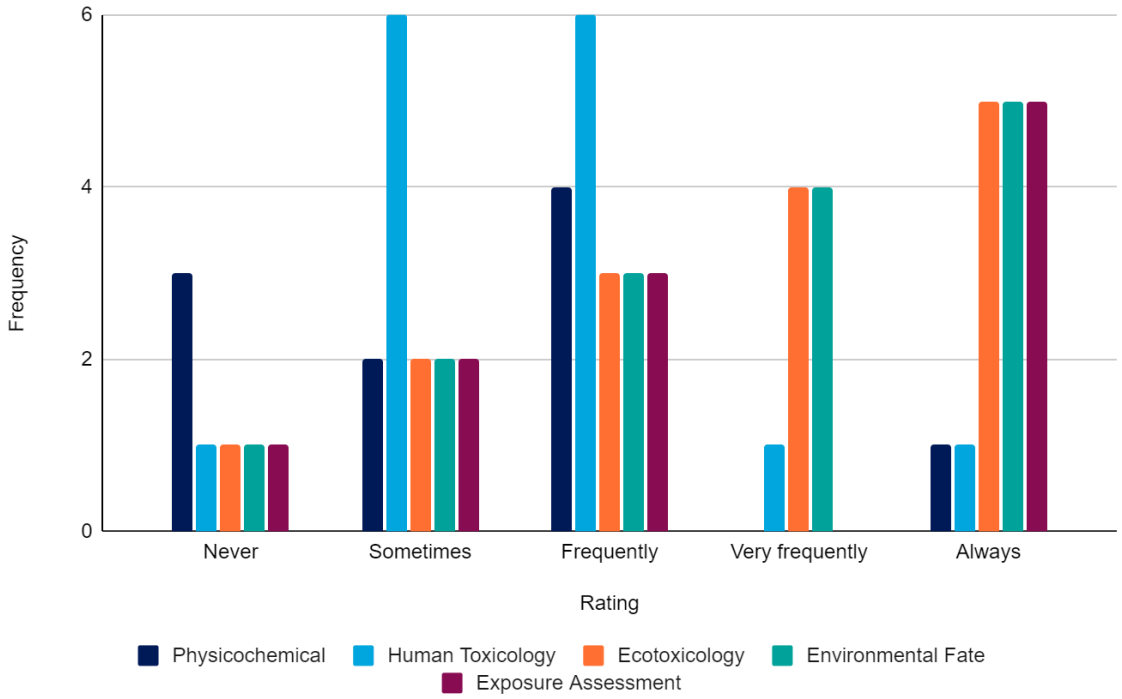

Figure 3.26 Frequency of endpoints that require researchers, NGOs and other RSS users (n=23) to reference to full study report because of incomplete RSS when evaluating the hazard endpoint (response to survey questions QC12 for other users)

Test Guideline

More than 50 percent of evaluators reported that there is sufficient information requested in the method section of the RSS to describe the test guideline used along with any deviation.

However, for the evaluators who reported that there could be more information included in the RSS, they suggested the following information be added by authors when preparing the RSS:

- Test guideline version number or year of publication
- Publishing organisation of test guidelines
- GLP checkbox
- Method used to investigate endpoint should be identified when more than one alternative option is possible, and the rationale why this method was selected
- More information should be provided on methods to support results interpretation, such as species and strain, dose selection, number of animals, treatment period

Evaluators pointed out that they do not always have access to ISO test methods, so it can be difficult to determine if a similar OECD/EU method is acceptable.

Confidence

The survey asked evaluators which elements increase their confidence in the RSS. Of all the options included in the responses to QC 12, 15 and 18, the following are the ones that were rated the highest:

- Toxicology endpoints
    - Test material information
    - Repeated dose studies: frequency of dosing
    - Dose applied, vehicle information, maximum volume of dose
    - Inhalation endpoints: form of test material e.g., gas, vapour, aerosol, dust, mist etc and diameter
- Ecotoxicology endpoints
    - Exposure duration
    - Basis of effects
    - Nominal and measured concentrations
    - Test material information
- Environmental fate endpoints
    - Biodegradation endpoint
    - Complete results for the observations / examinations

In addition, some evaluators indicated that the inclusion of tabulated data would help increase the overall confidence of the RSS. Evaluators specified that the absence of tabulated data can make it difficult to independently assess the results provided in the RSS. For example, some evaluators specifically indicated that including tabulated data on organ weights or histopathology findings is essential to assess (non-significant) dose-response. Furthermore, evaluators mentioned that, for repeated dose toxicity, reproductive toxicity, and developmental toxicity RSS, authors rarely include tabulated data about the frequency of findings in different dose groups and their severity. In addition, it was highlighted that genotoxicity in vitro study RSSs usually do not include the relevant tabulated data supporting the dose selection and interpretation of the results. All these tabulated results would be helpful to conduct the regulatory review of the RSS.

Author

Evaluators identified several areas of the RSS that are not typically well completed by authors. Those most frequently identified were:

- Toxicology elements
    - Test material information (source, purity, stability, prior treatment/formulation, physical state applied, particle size, size distribution, etc.)
    - Repeat dose studies: dose selection rationale
    - Complete results for the observations / examinations
    - Information on analytical monitoring of samples and methods
- Ecotoxicology elements
    - Complete results for the observations / examinations
    - Information on analytical monitoring of samples and methods
    - Raw data
    - Test material information
- Environmental fate elements
    - Adsorption/desorption endpoint: matrix properties, details on HPLC method and temperature, duration of adsorption/desorption equilibrium
    - Hydrolysis endpoint: results and information on transformation products
    - Biodegradation endpoint: parameter followed for estimation
    - Test material information

One of the key reasons specified for the poor reporting of data in the RSS has been that tabulated data is often missing. Other reasons include that there are often missing essential elements, such as lack of test material information, dose selection rationale, incomplete results for the observations, which could be due to a lack of understanding of analytical chemistry and study monitoring by the authors. These reasons tally with what respondents identified in whether RSS were fit-for-purpose.

Report type

78 percent of researchers, NGOs and other RSS users stated that in their experience, RSS quality is dependent on the type of report from which the RSS was created, as we have discussed above. In general, study reports following OECD guidelines or that are GLP compliant result in higher quality RSS with peer reviewed academic publications resulting in a lower quality RSS as they do not generally follow test guidelines, sometimes explore new test methods, and often do not include all the method details and results in the publication.

However, some respondents suggested that the Klimisch score may be given too much importance in REACH as it does not relate to the relevance of the findings, and therefore academic publications generally get a lower score of K2 or K3. Peer reviewed academic publications, old reports that predate OECD and GLP guidelines and studies conducted by government authorities and independent research institutes were identified as being more commonly associated with a disputed reliability score by other RSS users.

RSS Template and Guidance

In the OECD Harmonised Templates (hence in IUCLID), there is a field in the results section, titled 'Any other information on results incl. tables'. Nearly all evaluators mentioned that the type of information that could be provided to make toxicology and ecotoxicology RSS more useful includes tables with quantitative results and raw data. Some of the data highlighted in the responses to this question indicated the following elements:

- Toxicology elements
    - Group and individual data
    - Treatment
    - Organ weights
    - Histopathology findings
- Ecotoxicology elements
    - Sublethal effects in a lethality study
    - Number of mortalities per test concentration
    - Sampling time
    - Effects at each time point
- Environmental fate elements
    - Degradation products
    - Table with complete results (e.g., bioaccumulation study should include substance concentration in fish per test concentration and sampling time)
    - Results on the distribution of radioactivity
    - Data to assess the validity criteria

However, as we have shown above, authors found it challenging to include tables in RSS.

The usefulness of RSS guidance to author reports is debated. While some authors say that there is plenty of guidance on the ECHA website for example, others say that they do not use the guidance as it is difficult to find the relevant information needed, and easier to learn from colleagues and through comparing similar existing RSS. Some authors even reported preparing short guidance for their organisation's internal purposes to help with consistency in RSS structure, format, and information to be included.

Approximately half of authors reported that the RSS guidance is generally sufficient for all substance types. Challenges authors faced in using the various guidance documents often centred around the balance between the guidance being too generic and having sufficient detail. There was generally considered to be a lack of guidance on:

- Pesticides
- Nanomaterials
- How to deal with different physicochemical results for multi-constituents or UVCB
- Inorganic substances, such as metals

It was also pointed out that data in RSS do not vary extensively for different types of substances.

Further, it was noted that guidance:

- Is often out of date and criteria change often. For example, concerns were raised about the usefulness of the IUCLID manual, which when updated from IUCLID 5 to IUCLID 6, only included the information relevant to the use of the software, and therefore lost all the information relevant for new users on how to fill-in RSS.
- That harmonisation of guidance is important as there are different guidance and information requirements for REACH and biocides for example.
- Existing guidance does not cover unusual cases (e.g., testing of substances that are only available in solutions or mixtures).

Some suggestions made by authors for improvement include the provision of examples of filled out RSS that fulfil the requirements for various endpoints. These could be used to supplement the guidance by providing authors with best practice examples. Specifically, authors indicated that being able to refer to examples for non-standard situations would be beneficial. Other respondents mentioned that guidance cannot replace training and experience.

Communication

In the interviews, some authors revealed that they have received feedback from ECHA on RSS through compliance checks. However, in most instances, ECHA requested the full study report instead of asking for specific questions in the RSS, so it is difficult for authors to know if their RSS are satisfactory in terms of quality and content. However, in some cases, accessing the full study reports can be a way for evaluators to confirm the existence and the validity of the data included in the RSS. Thus, a request for the full study is not necessarily linked to a low-quality RSS.

Most evaluators confirmed having contacted RSS authors in a few instances to gather missing information. They reported that in most cases, it was communicated to registrants through draft decisions and notification letters, and that it generally resulted in the publication of an improved RSS. Some evaluators also used informal communication channels to gather additional information from the RSS author. In most cases, it was concluded that the information requested was not available in the full study report, which resulted in the rejection of studies. Other evaluators preferred to ask directly for the full study report as they say an improved RSS does not necessarily provide all the information required.

3.4.2 Information Availability

As mentioned above, most evaluators confirmed having contacted RSS authors to gather missing information, while other evaluators preferred to ask directly for the full study report. In the survey, evaluators identified some of the most common reasons why they request access to the full study report (Figure 3.27). These include a lack of information or detail on the following aspects of the study:

- Nature and severity of effect, dose descriptor, basis of effect, and conclusions
- Observations and examination performed in the study
- Test materials
- Dose, exposure, route of administration, frequency, etc.

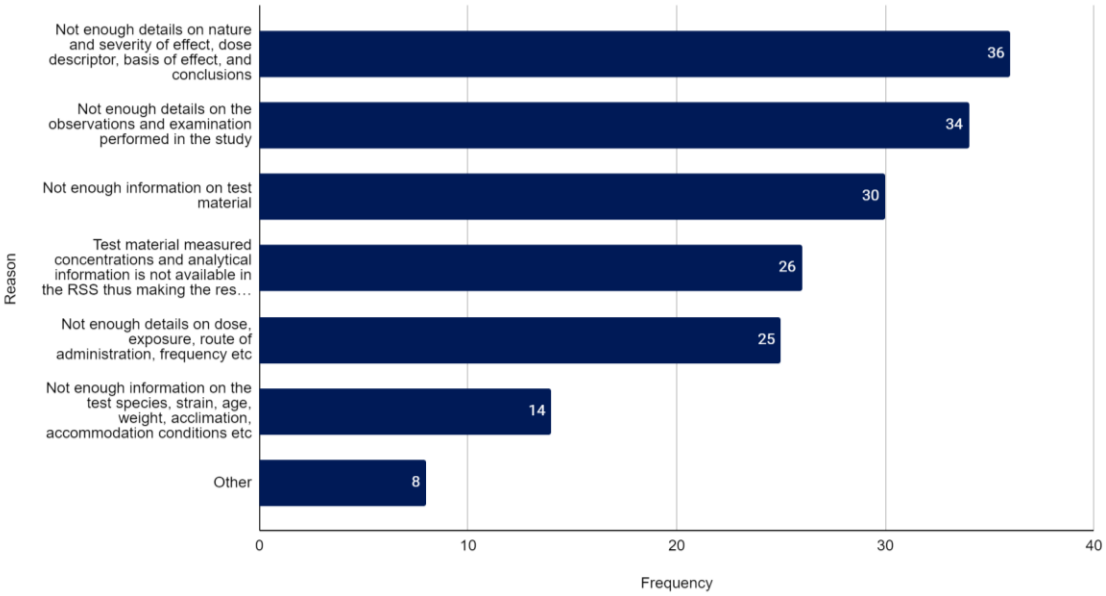

Figure 3.27 Commons reasons to seek a full study report identified by evaluators (n=56) (survey question QC1)

Examples of other reasons that were identified by evaluators include a lack of tabulated data and control data, and a lack of quality control from independent evaluators.

Similarly, researchers, NGOs and other users identified the main reasons for seeking a full study report to support the RSS is when there are not enough details on dose, exposure, route of administration, frequency, etc., or when there is not enough information on test material.

Substance

Evaluators were divided on whether the nature of the substance affects the information available in the RSS, with 52 percent stating that it does, and 48 percent stating that it does not affect the RSS. The evaluators who stated that the nature of the substance could affect the information available in the RSS mentioned that for some UVCBs, nanomaterials and novel materials such as biologically active substances (e.g., pheromones), there is often a lack of information in the RSS. In contrast, evaluators who said that the substance does not affect RSS referenced that all substances should be well described in the RSS, independent

of their nature. In addition, they mentioned that the RSS author has a much greater impact on the RSS than the nature of the substance.

The opinion of RSS authors was similar to those of evaluators, with 56 percent of authors also saying that the nature of the substance can affect the information that is provided in the RSS. Most researchers, NGOs and other users (67 percent) also stated that the nature of the substance can affect the information available in the RSS. Although some highlighted that the RSS should provide sufficient information regardless of the test compound, some respondents highlighted that, for some complex substances as listed above, there is often a lack of information in the RSS.

Technical Detail

63 percent of RSS authors stated that the endpoint influences the technical detail required to create an acceptable RSS. It was emphasised that more complex, higher tier studies require more details as those studies have a greater number of parameters, and a therefore greater degree of technical detail required. Respondents pointed out that some of the information should be the same across all studies, such as reliability or substance identity, but that the detail provided for the test methods and results may vary depending on the study tier. It is also expected that there will be more discussion and interpretation provided for the more complex endpoints. On the other hand, some of the respondents stated that all RSS must contain the required level of detail, no matter the endpoint or length of the study.

Furthermore, 74 percent of authors said that the difficulty and level of detail required varies depending on the subject area for RSS. A few respondents mentioned that the level of detail should be sufficient for a third party to understand the test method applied and to judge whether the results obtained are acceptable, irrespective of the endpoint. However, physicochemical endpoints were identified by several respondents as being simpler to summarise and requiring less technical detail than more complex endpoints. It was also suggested that toxicologists may not understand all the terminology used in ecotoxicology, so the expertise to prepare the RSS may not be transferable. The complexity and subject-specific knowledge of ecotoxicology were particularly highlighted as problematic for RSS, such as long-term fish study, chronic toxicity, and environmental fate.

Data Extraction

Through the survey, authors have reported that data extraction for RSS authoring is easiest from study reports generated by CROs that are compliant with OECD guidelines and GLP (Figure 3.27). The most challenging report types from which to extract data were identified as abstracts, summaries, and peer reviewed academic publications. This was also supported by participants interviewed, who confirmed that study reports were preferred to peer reviewed academic publications when extracting data for inclusion in the RSS.

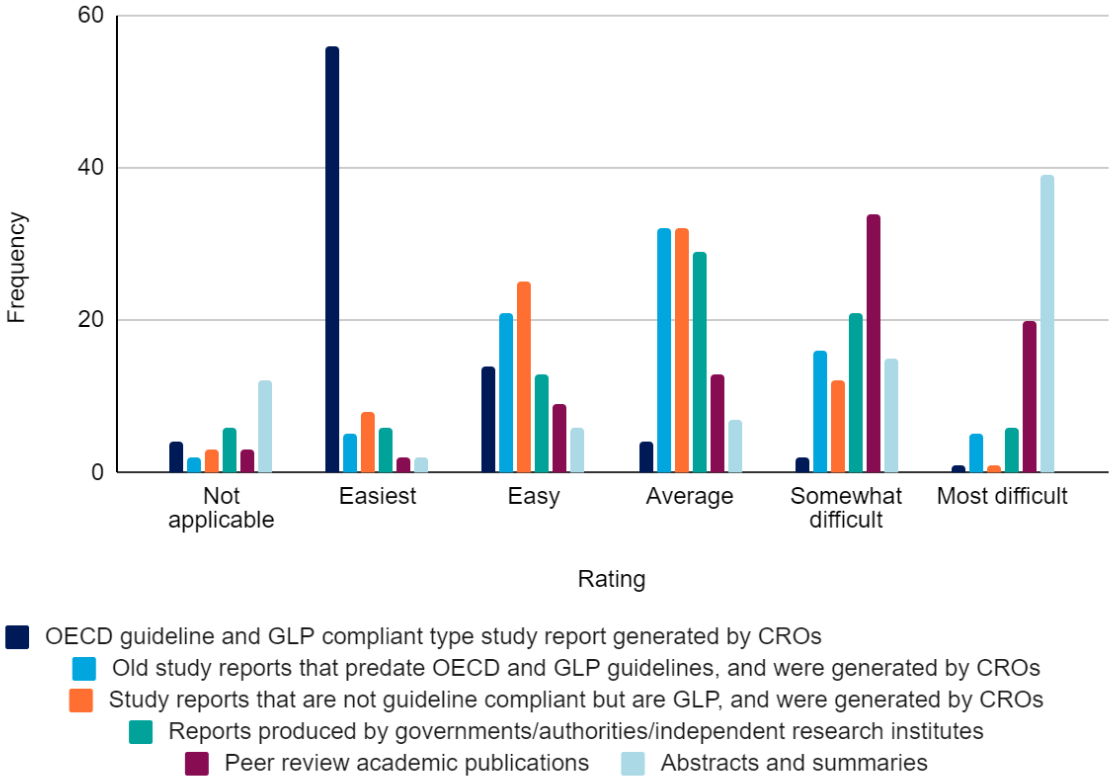

Figure 3.28 Level of difficulty of various document types for authors (n=81) to extract the information needed to write an RSS (survey question QC6 authors)

More than 50 percent of researchers, NGOs and other RSS users indicated that RSS is suitable to summarise results from a peer reviewed article. Although respondents from that group acknowledge that a peer reviewed article is already a form of summary and is more heterogeneous than results generated through OECD test methods, a survey respondent mentioned that *"systematic review criteria not only can handle this variation, but they are more objective, better able to reveal the accuracy ('reliability') of a finding*" and is therefore suitable for RSS purposes.

3.4.3 RSS Authoring

Information specific to RSS authoring is summarised below.

Time

In the interview, authors reported the time required to prepare RSS. Although they emphasised that the time requirement is dependent on the endpoint and the author's experience, there were similarities in the responses (Table 3.2).

Table 3.2 Time required to author RSS as reported in the interviews

Time	Endpoints
1 hour or less	● Physicochemical ● Short-term study, e.g., acute oral toxicity ● OECD 471 (bacterial reverse mutation test)
Up to 10 hours	● Extended one-generation or one-generation studies ● OECD 443 (extended one-generation reproductive toxicity study) ● OECD 408 (repeated dose 90-day oral toxicity) ● Acute study ● Carcinogenicity
More than 10 hours	● Repeated dose study

Data Transfer

RSS authors stressed that the process of transferring the results of a full study report to the RSS can be a challenge when summarising the hazard database and that authors need to avoid advocacy and biased interpretation when doing the hazard description.

Authors also confirmed that when the study report was done according to guidelines, it is very simple to transfer the data into the RSS template in IUCLID for example. Some authors mentioned that it is useful to refer to an RSS of a study completed using the same guidelines as an example when filling in the IUCLID fields.

Authors also emphasised that RSS data transfer depends on the endpoint and that it generally needs to be done by an experienced expert or scientist. That is, authors need to understand the study and its parameters. A few respondents suggested that it might be more consistent if the lab conducting the study filled out the RSS.

Tables

In the OECD Harmonised Templates, there is a field in the results section, titled '*Any other information on results incl. tables'.* As part of the survey, authors were asked how often they use this section. Most authors reported that they use this section to include raw data in the form of tables that are important to explain the conclusions. Others use it to add information when the RSS fields are not relevant for newer test guidelines. This field was reported to be mostly used in higher tier studies when additional data is more likely to be needed. As it is challenging to include tabulated data in IUCLID, some respondents reported that the original layout of a table included in this section is sometimes modified when copied, which can make the table difficult to read.

Templates

In the survey, authors were asked which RSS template fields they use the least. Table 3.3 highlights the key fields identified by authors as not being frequently used.

Table 3.3 Overview of some of the IUCLID fields that are the least commonly used by RSS authors (survey question QC10)

Field	Summary of comments
Attached documents	● It is rare to attach full study reports as they do not form part of the RSS (except for biocides) ● Attachments are usually subject to copyright
Overall remarks	● Most data are provided in other sections, so this section was identified as not being used frequently
Other information*	● Redundant
Executive summary	● Redundant ● Information provided in Endpoint Summary, especially if more than one endpoint in study ● Duplication of Conclusions section
Conclusions	● Redundant, duplicate of Executive Summary, Interpretation of Results and Endpoint Summary
Test substance	● Typically use confidential field for these
Tables	● Table function is not user friendly and is difficult to populate

*There are two other information fields: "Any other information on materials and methods incl. tables", and "Any other information on results incl. tables"

We feel that these are interesting findings and point to areas of the template which could be revised: either by removing the field and thus potentially allowing some space for further elaboration elsewhere (for e.g., complex endpoints), or, by improving the field implementation in existing software applications (i.e., for tables).

Endpoints

In the interview, authors confirmed that the most challenging endpoints to complete when authoring RSS are toxicology endpoints and higher tier studies, such as mammalian toxicology, mutagenicity, reproductive toxicity, and developmental toxicity. On the other hand, acute studies with only a few observations, in vitro studies and ecotoxicology endpoints were reported as being easier to report accurately. One of the reasons highlighted for the difficulty in reporting results such as genotoxicity and endocrine disruption is that the emotions and bias of authors might get in the way of accurate reporting.

In the survey, authors were asked to specify the elements of the RSS that are most challenging to complete for each type of endpoint. Table 3.4 provides a summary of the more frequent elements identified.

Table 3.4 Most challenging elements to complete when authoring an RSS (summary of responses to survey questions QC11, 12 and 13 for authors)

Endpoint	Element
Toxicology	Information on analytical monitoring of samples and methods
	Test material information
	Complete results for the observations / examinations
Ecotoxicology	Information on analytical monitoring of samples and details on analytical methods
	Statistical methods and assumptions
	Sampling methodology
	Raw data
Environmental fate	Test material information
	Repeat dose studies: dose selection rationale
	Complete results for the observations / examinations

When asked to clarify the responses provided, once again, authors specified that the ease of completing the RSS is highly dependent on the quality of the original study being used and that it is particularly challenging to include tabulated data in an RSS.

We feel it is important to highlight how frequently the complexity of certain human toxicology, ecotoxicology and environmental fate endpoints comes up in both the survey and interview and how often it was these challenging elements that were highlighted as affecting the quality of RSS.

Substances

In the interviews, authors were asked if the substance type influenced the approach used to author RSS. Most of the authors confirmed that there were differences and that UVCB and multi-constituents were more challenging to summarise because of the nature and variability of the substance, and the large quantity of data available. On the other hand, studies for mono-constituents were reported as very straightforward to summarise.

Quality Control

The main quality control measure identified by RSS authors during the interviews was peer review. Authors reported collaborating, discussing and sharing their RSS with peers to validate and check their report. Other authors said that they rely on the technical completeness check

in IUCLID. Some authors stated that they can consult other RSS if they are unsure how to complete a section for a given study.

Tools

The only tool used by authors to compile RSS was IUCLID, as reported by interview participants. Some respondents highlighted that the IUCLID interface is not optimal due to the length of sections on the screen which makes it challenging to quickly access relevant sections. Authors need to scroll up and down the page a lot, which has been identified as a major inconvenience. Two authors also referenced transferring data from IUCLID to Chesar or the QSAR toolbox to do the chemical safety assessment.

Training on RSS

Interview participants were asked to describe the approach they recommend when introducing someone new to RSS. Overall, the key highlight is that authors need to practice. Here are the key methods suggested to gain that practice and become a more experienced author:

- Read ECHA and internal guidance
- Ensure familiarity with test guidelines, as well as reading and understanding study reports
- Review completed RSS and compare it to the full study report to understand how information is summarised
- Understand the IUCLID tool (administrative processes in IUCLID, study records and flexible records)
- Practice with simple studies (e.g., acute study, skin irritation) and work up to more complex studies

3.4.4 Regulatory Context

As shown in Figure 3.29, nearly 60 percent of RSS authors work within one regulatory context. However, those who work across multiple regulations observed some major and minor differences. That said, one participant highlighted that RSS are very comparable across legislation, even if each legislation has its own requirements, making it easier for an experienced RSS author to prepare RSS for any legislation. It may be, then, that it is simply a matter of gaining experience to be able to work across regulations.

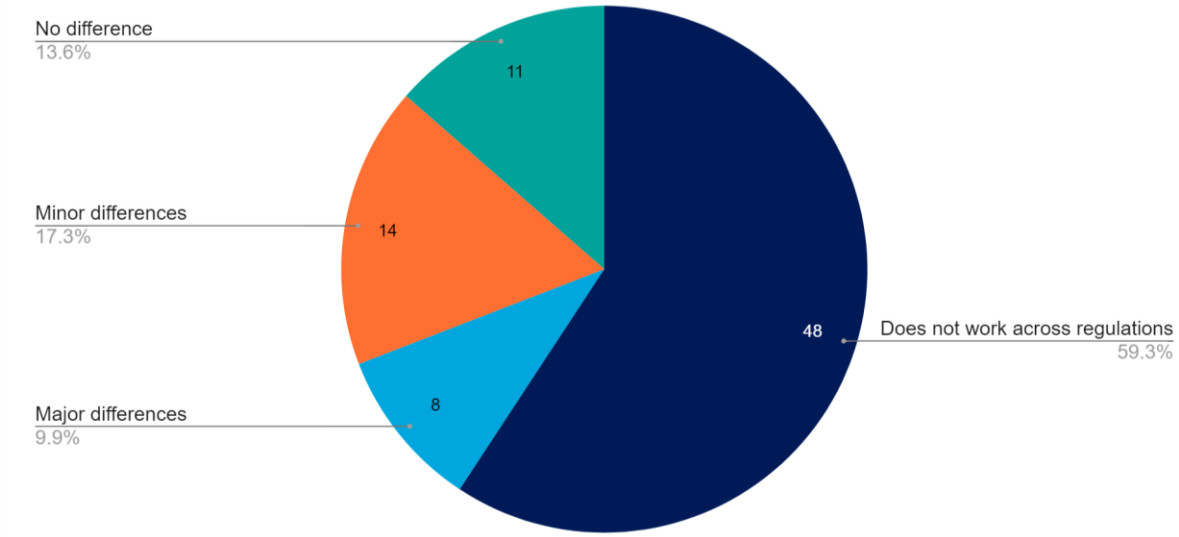

Figure 3.29 Author's (n=81) experience of differences when writing RSS for different regulations and geographies (survey question QC5 authors)

Some of the key differences highlighted in the survey responses include:

- **RSS language:** Some countries (e.g., Turkey, Korea, Taiwan) require RSS to be submitted in the local language, and respondents reported that accuracy of translation is critical. However, there is little support in IUCLID for translation and validation of the translation, which can lead to inconsistencies and errors in the reported information (e.g., of technical information), especially as RSS authors lose control over translated content.
- **RSS format:** Several tools can be used for RSS preparation, including IUCLID, online submission portal, or Word documents. If an RSS has been prepared initially in IUCLID, it will likely require additional editing and formatting to submit in another regulatory context.
- **EU REACH vs EU PPP**: EU PPP requires more information to be included (e.g., references and attachments) and is thus more comprehensive than the REACH RSS. This may create a disadvantage for some clients as other companies might use the REACH RSS information after it has been published. Some respondents suggested that the fact that EU PPP requires the attachment of the full study report in addition to the RSS suggests that the RSS does not meet the purpose of being a standalone summary[24].
- **EU REACH vs Australia**: The only difference highlighted for Australia is around the human health CLP versus GHS conclusions.
- **EU REACH vs US TSCA and FIFRA:** The cut-off values, data requirements and data presentation are slightly different in the regulatory contexts.

[24] Note from ECHA: The difference between the EU REACH and EU PPP requirements comes from where the responsibility of the assessment lies. For REACH, industry is responsible for the assessment while for PPP it is with the authorities. Therefore authorities need to access the full study report for PPP as, in the current state of the legislation, they are required to write or validate the summaries provided.

Most of the researchers, NGOs and other RSS users specified that they do not work across multiple regulations in the context of RSS. For those who are familiar with multiple contexts, the key difference identified in the approach taken was between the US and EU risk assessment approaches. One respondent indicated that they find the US EPA risk assessments and RSS weaker than those prepared under EU regulations.

3.4.5 Summary and Analysis

Overall, respondents shared that RSS quality can vary based on several factors, including the author, endpoint complexity, substance, and study type. One of the key reasons specified for the poor RSS quality is the lack of data, specifically tabulated data. Despite their limitations, most respondents indicated that RSS are at least *'somewhat reliable'* for conducting hazard assessment.

We feel it is important to highlight how frequently the complexity of certain human toxicology, ecotoxicology and environmental fate endpoints comes up in both the survey and interview and how often it was these challenging elements that were highlighted as affecting the quality of RSS.

To address one of the questions raised in section 3.1.5 regarding whether there are issues related to quality and reliability associated with certain subject areas being outside the expertise of respondents, it seems that, based on the responses provided, most authors, regardless of their scientific background, can prepare a quality RSS for physicochemical endpoints. However, for those with a toxicology background, the expertise is more challenging to transfer to ecotoxicology or environmental fate endpoints, and therefore result in quality issues for the RSS, if not verified by an expert in ecotoxicology.

The use of RSS guidance by authors to prepare RSS is debated. While some authors say that there is plenty of guidance on the ECHA website for example, others say that they do not use the guidance as it is difficult to find the relevant information needed.

Some of the key recommendations to improve RSS quality include:

- Use RSS examples instead of guidance
- Improve the templates so that tabulated data can be added more easily
- Assess scientific competence of RSS authors

3.5 Areas of Improvement

Throughout the surveys and interviews, respondents shared their ideas about areas for improvement in relation to RSS. The suggested improvements were grouped into themes, as highlighted in Figure 3.30.

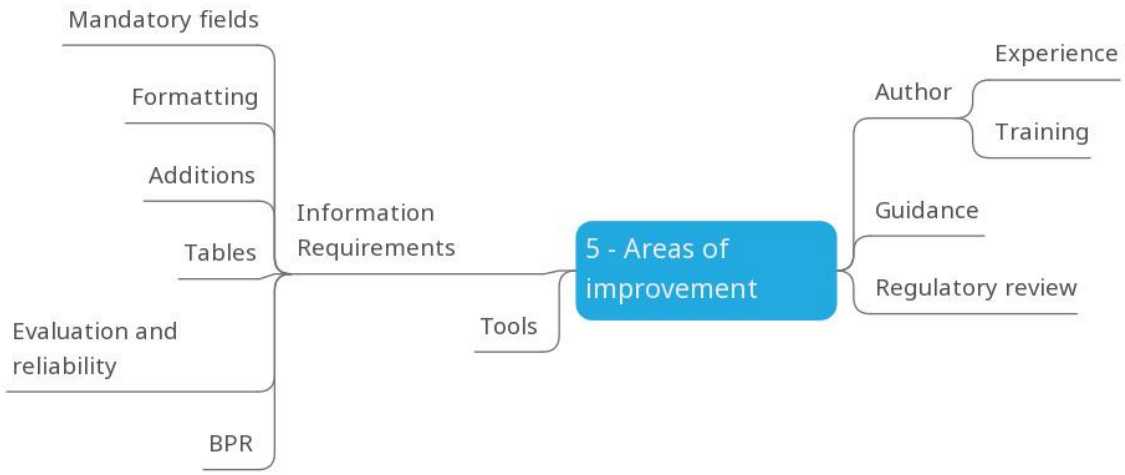

Figure 3.30 Thematic categories in Topic 5 - Areas of Improvement

3.5.1 Information Requirements

While suggestions for improvement were made, respondents emphasised that RSS is meant to be a *summary* of study objectives, methods, results, and conclusions and that including too much detail in the RSS would be counterproductive. Similarly, several respondents felt that the information requirements for RSS are sufficient so changing those requirements would not result in improvements.

We have organised suggested improvements to the data requirements into themes:

Mandatory Fields

- Essential data should be mandatory so RSS cannot be submitted with missing mandatory fields
- Identify mandatory fields (e.g., with an asterisk), as well as those that are not mandatory
- Make copying/pasting discussions, conclusions, and summaries from GLP reports mandatory to reduce author bias and censorship

Formatting

- Update the format to follow OECD test guidelines more closely

Additions

- Include additional fields to cover individual test data, i.e., where adverse effects are observed
- Add justification fields for effects that are considered secondary, or not treatment related
- Include an RSS form for systematic review results
- Expand pre-selection options in the picklists, e.g., to choose characteristics of the substance (inorganic vs UVCB), to describe toxicological effects, avoid the use of "other" in picklists
- To assess that all the data is included in the RSS, implement the OECD test validity criteria checklist into the RSS

Tables

- Improvements are needed in the way to present tabular data, especially to reduce human error
- The current process to recreate or copy tables in the IUCLID fields can lead to errors. The template should be more flexible to fit data in multiple formats
- Presenting data tables should be mandatory in the RSS, even if no effects are seen

Evaluation and Reliability

- Consider some criteria to evaluate the reporting of the study, as opposed to only evaluating the reliability of the study design. This would help identify whether there are issues with the study design, or the study report, or both
- Consider using a different method than Klimisch to assign reliability of studies, as this scoring method gives more weight to GLP and OECD test guidelines studies, which could result in disregarding other important studies.
- Assess both the reliability and relevance of the study. This would help understand how the authors concluded whether this is a supporting or key study

BPR

- One respondent suggested reorganising IUCLID section 7 (Intended uses and exposure) under the BPR working context
- Include more options to provide alternative units of measurements, specifically in the context of EU BPR

Some participants suggested attaching systematically the full study report to the RSS, however, other respondents do not agree with this approach as this takes away the benefit of the RSS as a summary. It was also pointed out that there may be associated confidentiality and data breach issues.

Finally, it was suggested that redundant fields, such as "additional information" and potentially the executive summary, should be removed from the RSS template.

3.5.2 Tools

With regards to RSS tools, as previously confirmed, the key tool identified to publish RSS is IUCLID. The most frequent recommendation to improve IUCLID as regards its functionality,

specifically in relation to the inclusion of tabulated data, as we have noted. Some respondents also highlighted that the overall interface is challenging to use, with small boxes that do not expand until after the data is added, the juxtaposition of the layers instead of having a full-page view, the order of the fields in the IUCLID template, and the general flexibility of the tool. The key recommendations for improvements of IUCLID include:

- More free text fields that can be enlarged
- Free text cells that align better with the formatting in MS Word
- Opportunity to include images and screenshots of the results table that can be combined with explanatory text in free text fields
- Improve formatting options for text and tables
- A data uploader for tables and graphs in various formats
- Interface between IUCLID and SAP to map data
- Add search, comparison and change history functions
- Indicate required (mandatory) fields to avoid submission of incomplete RSS

Some respondents also suggested that it would be useful to have a set of specific templates for different study types, such as conditional formatting, to increase the mandatory fields to fill in and reduce errors.

Automation was suggested by several respondents to automatically upload and retrieve data from existing databases, scan PDF study reports or facilitate copying information from a study report to the RSS to reduce the potential for human error. Some mentioned that data should be imported directly from the testing facility through the Laboratory Information System (LIS). Some respondents also suggested that testing laboratories should directly enter the information into the RSS, or that IUCLID just be more integrated with the LIS. As highlighted in previous sections, integration of tabulated data into RSS is a key issue for most authors, and this should be addressed through an improvement to the IUCLID platform.

Respondents also recommended improving the automated tools for checking the RSS, such as the Validation Assistant in IUCLID. The validation assistant should check that all hazard assessment fields are filled in to indicate any data gaps to the author. Another comment was to improve the visualisation of results to highlight the key results in a more distinct manner.

With regards to the template itself, respondents mentioned that more details should be included in the template through pop-up windows with explanations and examples of information expected in the fields, to help authors fill out the RSS adequately.

In terms of regulatory comments, a respondent highlighted that the comments and annotations by authorities should be visible on the RSS and easily transferable and printable.

Another improvement that was suggested by an interview respondent is to develop an automated module that would assess the fitness of the information included in the RSS based on the requirements of the OECD test guidelines. The results could be a score that indicates how the information matches the guidelines, and how much overlap there is with the provided information. The example given that “the provided data has an 85 percent match with test guidelines 421 and 422 reproductive developmental toxicity screening test, 45 percent overlap

with an extended one generation reprotoxicity study". The respondent mentioned that this score would allow evaluators to see how well certain elements of the test guidelines are covered.

3.5.3 Author

Recommendations were made by respondents with regards to author experience and training. Furthermore, some survey and interview respondents mentioned that testing laboratories could complete the RSS as they conduct the studies, which would remove opportunities for errors in the RSS. More automation of data import into IUCLID would also likely reduce the human error associated with the transfer of data by authors.

Experience

Some survey respondents indicated that it would be useful for RSS authors to meet a minimum threshold or qualifications, however, it was acknowledged that those could be difficult to establish and challenging to implement and monitor. Nevertheless, the following criteria were suggested:

- Educational background
- Years of experience in a technical field
- Years of experience as RSS author
- Years of experience using IUCLID

Some respondents mentioned that peer review of RSS by more experienced authors is an efficient process, however, they recognise that it is challenging to verify peer review.

Others indicated that RSS author training would address this issue better, as every author would receive consistent training that is specific to the topic. Proof of training or a certain RSS authoring accreditation could even be adopted to allow RSS submission to the authorities. Some respondents thought that training should be offered but should not be mandatory. One of the potential issues highlighted is that it might cause institutional group thinking. A few respondents also stated that since they felt that the current RSS guidance is sufficient, additional training for authors is not needed.

Training

70 percent of survey respondents who commented about RSS training were favourable to having formal training in place for RSS authors. The key training recommendation was that ECHA evaluators should deliver the training, if possible. It was also agreed that the training should be available online, and that training videos and webinars would be preferable, so they can be referenced and reviewed as needed. Some respondents indicated that training should be free.

Some of the elements that survey, and interview respondents suggested being included in training are:

- Technical requirements of an RSS
- How to prepare a compliant RSS
- Context of regulatory review of hazard assessment (to help authors understand how the information is used by regulators, and why certain data is requested)
- Understand how risk assessors make conclusions
- How to evaluate reliability of a study
- Endpoint specific training
- Review content of OECD guidance documents

In general, we suggest that the thoughts on training are an important finding and training videos produced by evaluators would be a low-cost and straightforward way to help improve the consistency, quality, and reliability of RSS.

3.5.4 Guidance

Given the important level of responses on the current guidance documents, it is unsurprising that several respondents suggested improvements. The most frequent recommendation is to include a practical guide and worked examples of completed RSS for various endpoints and study types, including non-standard studies (e.g., old literature reviews). More details could be provided for more complex studies and different types of substances.

Respondents highlighted the importance of keeping the guidance simple, as they felt that it is currently quite complicated. They suggested that guidance should be peer reviewed by expert users. A few respondents also suggested that a way to make the guidance more accessible would be to develop it in the form of an interactive guide, with different areas for different endpoints. Respondents made the following suggestions to improve existing guidance:

- Guidance by type of endpoint
- Provide clear guidance as to what is meant in each data field
- Improve the layout of the guidance so it is more user friendly
- Clearly indicate minimal data requirements for each endpoint, potentially in a summary table
- Clearly indicate which parameters are mandatory
- Address EFSA and PPP requirements in guidance

Several respondents suggested linking the guidance directly to IUCLID, so it is accessible from the tool. For example, some suggested including context dependent help directly in the relevant IUCLID fields, including minimum data requirements and mandatory fields directly in the tool to avoid having to refer to separate guidance. The Help function in IUCLID could also be enhanced with more guidance to avoid people having to search for responses outside of IUCLID when writing RSS.

While several suggestions were made for improvements to the guidance, some respondents highlighted that author training and author experience should be prioritised over changes in

guidance, as most authors ignore the guidance. However, for those who said they ignore the guidance, the main reason stated is because it is too long, complex, poorly formatted, and difficult to navigate. Therefore, some of the suggestions above could improve guidance use.

Given the recommendations above regarding using videos for training and bearing in mind the ones here about where guidance would be helpful, it may be possible to develop a series of guidance videos, perhaps embedded in IUCLID in the Help function.

3.5.5 Regulatory Review

Survey respondents indicated that regular regulatory review of RSS requirements would be useful, while others stated that it would be challenging as it would create more work for authors, who would need to constantly refer to new guidance. Although those that suggested they be reviewed on a regular basis hoped those revisions would integrate stakeholder feedback, others suggested it only be reviewed when there is a change in the test guidelines or for new endpoints. However, we point out that respondents also noted frustration with the guidance when it becomes out of date due to regulatory change, so regular review and update of RSS requirements would likely be helpful.

Several survey respondents indicated that it would be helpful to provide more feedback on the OECD Harmonised Templates. Some respondents suggested that an effective way to provide feedback is when asked directly for their opinion, such as in a survey. For example, several of the OHTs are not adapted for certain regulations (e.g., PPP), so it is difficult to provide all relevant information. This feedback could then be provided to ECHA or OECD so that improvements can be made.

Some interview respondents mentioned that evaluators have a limited view on RSS and there appears to be an inconsistency in how the data is used by evaluators. For example, it was reported that the UK requested the full study report while ECHA did not require the full study report for a risk assessment using the same RSS. Another challenge identified by an interview respondent was that some attachments (e.g., full study reports) were made available publicly by regulators who published the full dossier by mistake. Concerns about confidentiality are a serious issue that needs to be avoided.

Respondents were clear that the usage of RSS is very EU-centric, and that it is important to move to a global scale soon.

3.5.6 Summary and Analysis

While suggestions for improvement were made, respondents emphasised that RSS is meant to be a *summary* of study objectives, methods, results, and conclusions and that including too much detail in the RSS would be counterproductive. Similarly, several respondents felt that the information requirements for RSS are sufficient so changing those requirements would not result in improvements.

However, there were several recommendations made to improve various aspects of RSS, specifically around the functionality of the RSS template and the methods to evaluate its

reliability. Automation of data transfer from study reports to IUCLID was a key recommendation to reduce the potential for errors.

Recommendations were made by respondents with regards to author experience and training. Some survey respondents indicated that it would be useful for RSS authors to meet a minimum threshold or qualifications, however, it was acknowledged that those could be difficult to establish and challenging to implement and monitor. Respondents were also favourable to having formal training in place for RSS authors, which would be accessible online.

Improvements to the guidance were also suggested, in the form of a practical guide with worked examples of completed RSS for various endpoints and study types. While several suggestions were made for improvements to the guidance, some respondents highlighted that author training and author experience should be prioritised over changes in guidance. Given the recommendations above regarding using videos for training, it could be useful to develop a series of guidance videos, perhaps embedded in the IUCLID Help function.

4. Conclusion

Over the course of this study, we observed a good interest from stakeholders and received relevant feedback from the different RSS user types. We are confident that the survey captures the major users of RSS. However, we are aware that there may be further sub-groups like 'traders' and 'researchers' who have either not been captured or sufficiently explored. Other areas of future research with regards to the RSS users would be to look at consultancies and service providers as a user group since they represented 20 percent of the respondents and were embedded within the RSS author user group in this study. This large representation indicates a depth of specialist expertise amongst consultants and other service providers and therefore they could be an important stakeholder category to consider in future research.

A key driver of this study was to obtain views from stakeholders regarding the reliability of RSS. First, stakeholders confirmed the purpose of the RSS, which is to summarise study reports for hazard and risk assessment. In that context, the results indicate that both authors and evaluators found RSS suitable for hazard assessment purposes. Furthermore, when they are completed correctly, there is a satisfactory level of confidence that they are fit-for-purpose. However, RSS limitations are a key indicator of its reliability. Some of the limitations of RSS lie in the quality and type of information that it contains, the nature of the study it summarises, the author and the endpoint.

Some of the strengths of RSS are the consistency of the format, as well as the time and resources savings that result from using the summarised data. RSS is identified as an important source of information. Although many of the strengths are associated with the fact that RSS are summaries, many weaknesses are also related to this. For instance, evaluators identified that insufficient explanation of the study methods and results is the most frequent weakness when evaluating the RSS.

The results gathered from respondents will be used to inform the study selection and RSS writing in Work Package 2 of the ongoing study, which aims at analysing the accuracy of RSS and comparing the content of the RSS with the content of the full study report. Integrating stakeholders input into study selection and RSS writing will help select a range of studies that will be used to verify assertions made by stakeholders. Furthermore, the results of the stakeholder's engagement activities will be carefully integrated into Work Package 3 of this study, to identify approaches that can be used to improve the usefulness of RSS for all stakeholders and address potential shortcomings identified.

Future work that could be done to improve the reliability and quality of RSS would be to improve the RSS guidance by adapting it to a more user-friendly and interactive format. A suggestion made by respondents is to integrate the guidance into the IUCLID template and Help section. Furthermore, the development of completed RSS templates, to be used for reference purposes, was frequently identified as something that would be useful for authors. Author training is another area identified to improve the quality of RSS. The delivery of online training videos by the regulatory authorities was identified as useful to place all the authors on a similar plain field.

Disclaimer

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