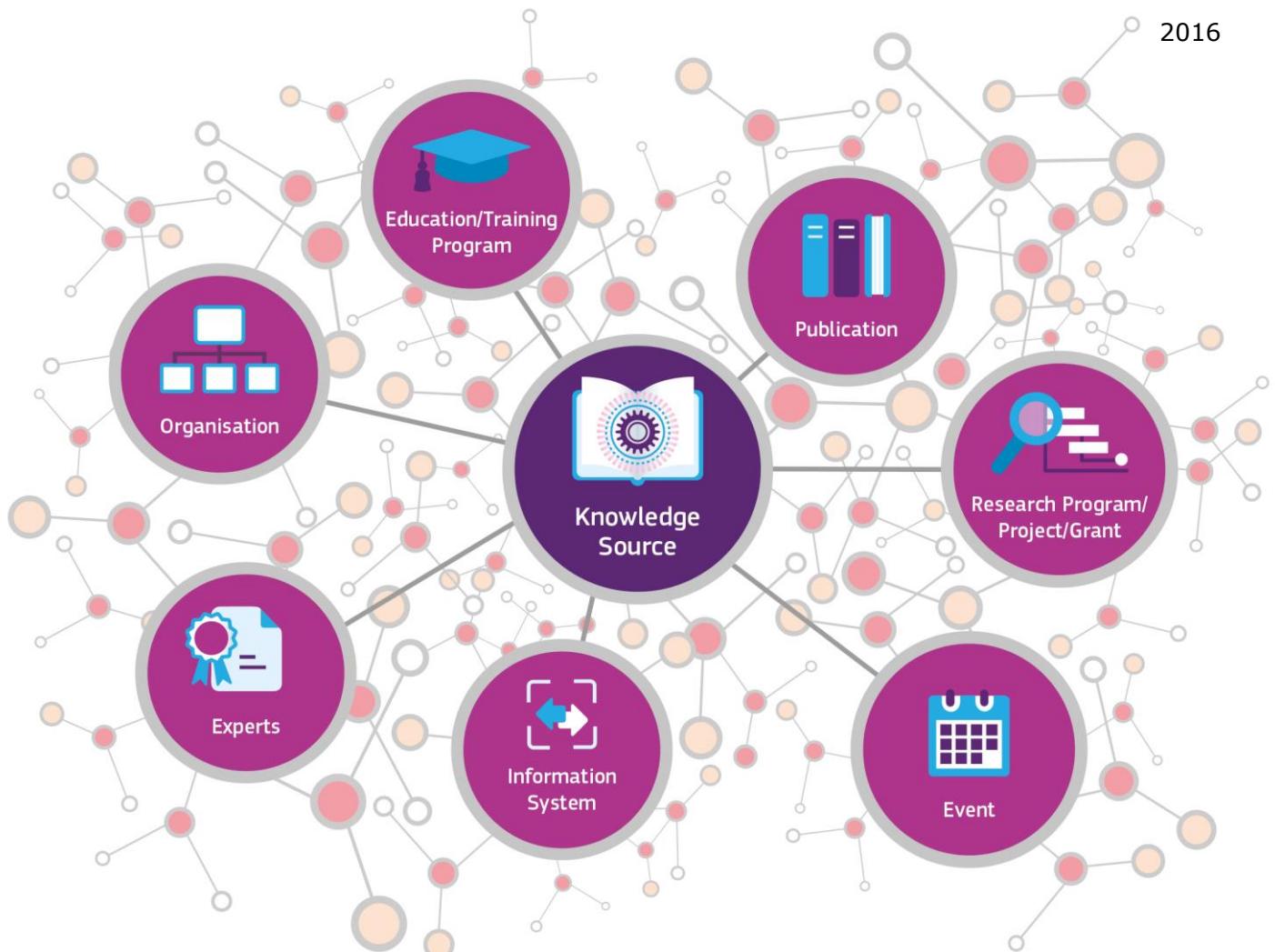


## JRC SCIENCE FOR POLICY REPORT

# Accelerating progress in the Replacement, Reduction and Refinement of animal testing through better knowledge sharing

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**Accelerating progress in the Replacement, Reduction and Refinement (the Three Rs) of animal testing through better knowledge sharing**

Abstract

The replacement, reduction and refinement of the use of animals in science are legal requirements under EU legislation. The sharing of knowledge in this area is crucial not only towards the goal of full replacement but also to advance the scientific tools. This report assesses how this knowledge is currently shared and proposes options towards enhancing knowledge sharing.

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We also express our sincere gratitude to our many stakeholders, peers, colleagues and collaborators who assisted in the dissemination of the survey and, of course, to the survey respondents who dedicated their time and effort to complete the questions which have informed the outcome of this report. Your contributions are much appreciated, thank you.



## Executive summary

### Policy context

The European Citizens' Initiative (ECI) "Stop Vivisection" was signed by 1.17 million citizens and submitted to the European Commission in March 2015. It called for a new regulatory framework to replace Directive 2010/63/EU and to phase out all use of animal experiments. The initiative also proposed that alternative methods with more relevance to the human species should replace the animal model and be a legal requirement. In its response to "Stop Vivisection", the European Commission emphasised that it shares the ultimate goal of complete replacement of the animal model, but explained that Directive 2010/63/EU is still needed. In order to accelerate the development and uptake of non-animal approaches in research and testing the Commission identified four actions, one of which (Action 1) sets out to assess the current situation regarding the sharing of knowledge which is relevant to the 3Rs (see the Quick guide below).

This report and the underpinning research were carried out to complete Action 1. The evidence-based assessment presented here considers how to systematically accelerate knowledge exchange through communication, dissemination, and education and training for the replacement, reduction and refinement of animal testing.

### Main findings

The European Commission's Joint Research Centre (JRC) has created a detailed inventory of **800 knowledge sources** (KS) relevant to the 3Rs. These knowledge sources have been described in a way which facilitates their curation and the subsequent analysis of potential knowledge gaps and means of sharing. The inventory covers different types of knowledge sources (e.g. organisations, events, expert groups, etc.) and identifies the ways in which these share information.

In parallel to the creation of the inventory, a public survey (of people working in the 3Rs area) was carried out which aimed to elicit individual input on what knowledge sources exist, how they are linked, and how they are currently being used to further the 3Rs. The wealth of information provided by the **351 survey respondents** has been invaluable to identify further opportunities for knowledge sharing. A third of these respondents replied on behalf of their organisations. Notably, many of the survey respondents stated that the available means of knowledge exchange are adequate, whilst two thirds also state that knowledge sources are lacking in their area.

The report has found that whilst there are many 3Rs relevant knowledge sources available, there is room for improvement, particularly regarding the communication and outreach of knowledge. The need for better coordination of how knowledge is gathered and managed and how it can be delivered to the recipient in a more efficient way was highlighted and the means through which this can be achieved are considered in this report.

### Key conclusions

The analysis of the knowledge sources, combined with input from knowledge users, confirm that a more concerted effort is required to effectively manage existing knowledge so that it can impact positively on the advancement of the 3Rs.

The options proposed herein are:

- i) The existing knowledge sources need to be better **coordinated**. There is a vast amount of relevant information, but it needs to be better structured. This could be achieved using the current networks of leading knowledge providers.
- ii) The existing knowledge sources need to have a greater **outreach**, to increase the beneficiaries of the knowledge and to bring about more dialogue across sectors and between different groups.

- iii) **Education and training** opportunities relating to the 3Rs need to be increased and improved, extending across 3 levels of learning: professional, undergraduate and school-goers. There need to be more resources for educators and these should be freely available.
- iv) How this knowledge is **communicated** needs to be better considered. Although there are many examples of good practice of knowledge exchange, in general people require more guidance and trust in the KS which are available.

The report indicates that the current provision of knowledge sharing opportunities and existing networks provides a good basis for the establishment of a stronger and better connected structure to facilitate the management of this knowledge.

### **Quick guide**

*The Three Rs concept* is the requirement to **Replace**, **Reduce** and **Refine** the use of animals wherever possible (Russell and Burch 1959). The Three Rs are firmly anchored in all EU legislations.

*A European Citizens' Initiative* is a mechanism which enables European citizens to call on the European Commission to propose legislation in areas where the EU has the competence to legislate<sup>1</sup>. *The European Citizens' Initiative (ECI) "Stop Vivisection"* proposes a European legislative framework aimed at phasing out animal experiments.

*As part of the European Commission's reply to the ECI*, this report assesses the current situation regarding the availability and sharing of knowledge which is relevant to the 3Rs. This assessment considers how to systematically accelerate knowledge exchange through communication, dissemination, education and training.

*By mapping knowledge sources relevant to the Three Rs*, examining how knowledge is being shared, and identifying possible gaps and opportunities, this study has contributed to this exercise and concludes with a set of options to further enable progress.

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<sup>1</sup> <http://ec.europa.eu/citizens-initiative/public/basic-facts>

## 1 Introduction

The use of animal experiments to advance science and medicine and for human safety assessment has been a contentious subject for many years. Although they have informed numerous scientific achievements, the objections to such studies on both ethical and scientific grounds have found strength with the increase in new alternative approaches which do not use animals. In addition to the **replacement** of the animal model, alternative approaches also include methods of **refining** and **reducing** the use of animals for scientific purposes (the Three Rs, as described by Russell and Burch 1959). These new approaches and methods in turn generate new sources of knowledge and, as technologies have advanced, so have the means of sharing such knowledge. The internet has presented an extremely rich and versatile medium for the storage and dissemination of information. Thus the volume of information has expanded vastly and access to specific information can be extremely fast, provided that specific information is sought and the user knows how to look for it effectively. To ensure that all involved in areas where animals have traditionally been used for scientific purposes can work together towards the ultimate goal of full-replacement, the management of this knowledge requires attention.

The European Commission has taken the first step in this process of knowledge management by assessing the current state of knowledge in the area of the 3Rs by looking at what knowledge sources exist and how that knowledge is being shared. In response to the European Citizens' Initiative "Stop Vivisection"<sup>2</sup>, in May 2015 a Commission Communication proposed a number of actions<sup>3</sup> to accelerate the development and uptake of non-animal approaches in research and testing, reflecting the provisions of Directive 2010/63/EU on the protection of animals used for scientific purposes. The first of the four actions refers to:

"Building on existing activities of the Commission, relevant EU agencies and OECD, the Commission will analyse technologies, information sources and networks from all relevant sectors with potential impact on the advancement of the Three Rs, and will present by end 2016 an assessment of options to enhance knowledge sharing among all relevant parties. The assessment will consider how to systematically accelerate knowledge exchange through communication, dissemination, education and training".

The EU Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM), of the European Commission Joint Research Centre, is working closely with Directorate General (DG) for the Environment, the responsible Commission service for Directive 2010/63/EU, to identify opportunities to encourage knowledge sharing across disciplines and sectors aimed at more efficient development and use of alternative approaches. By mapping knowledge sources relevant to the 3Rs, examining how knowledge is being shared, and identifying possible gaps and opportunities, this study contributes to this exercise and concludes with a set of options to further enable progress.

This report is a comprehensive but non-exhaustive review of the supply and demand status of 3Rs knowledge. The objectives of the study which forms the basis of this report were (i) to identify 3Rs knowledge sources (the supply) which are available to everyone who works in areas where animals have traditionally been used for scientific purposes; (ii) to create an inventory of these knowledge sources; (iii) to assess and characterise the KS in the inventory; (iv) to analyse the adequacy of the knowledge sources and (v) to identify potential gaps. In addition, another aim was to identify knowledge sharing across disciplines and sectors that could lead to a more efficient development and use of alternative approaches.

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<sup>2</sup> For the full text of the initiative please see: [http://ec.europa.eu/citizens-initiative/public/initiatives/\\_successful/details/2012/000007](http://ec.europa.eu/citizens-initiative/public/initiatives/_successful/details/2012/000007)

<sup>3</sup> [http://europa.eu/rapid/press-release\\_IP-15-5094\\_en.htm](http://europa.eu/rapid/press-release_IP-15-5094_en.htm)

To establish the inventory, a **systematic** search for existing knowledge sources was carried out and collected data were analysed. All the data included in the inventory and used to characterise the knowledge sources were collected exclusively from public information provided by the knowledge source owner on their websites, publications or other dissemination materials. For practical reasons, only sources presented in English language were considered. The inventory collects the most visible sources and details them in an easy to use and searchable format. Whilst an attempt has been made to cover as many knowledge sources as possible, this inventory is not exhaustive. However, the intention of the study was not to identify all existing knowledge sources but to collect and analyse the most prominent knowledge sources relevant to the area of the 3Rs, and to perform an evaluation on how the knowledge is disseminated, looking into the ways in which knowledge resource developers prefer to share their knowledge and to identify potential gaps.

In parallel to the inventory, the JRC (on behalf of the European Commission) also carried out a survey of people with experience in the 3Rs to solicit **individual** input on what knowledge sources exist, how they are linked, and how they are currently being used to further the 3Rs. In addition, the survey aimed to identify additional knowledge sources which could be beneficial to include in the inventory. By drawing on the "real-life" experiences of individuals and organisations working in relevant areas, the survey also aimed to establish where effective knowledge exchange is having a positive impact, as well as gathering suggestions about how this could be enhanced.

The report begins with an overview of the knowledge sources which have been identified and included in the inventory. This includes a description of how these were curated and how the functionalities of the inventory can facilitate searches and detailed analysis of the knowledge sources. The survey responses have been summarised and presented with statistics which have informed the findings of the report. The discussion considers what knowledge exists, who is benefiting from it and how it is shared, based on both the inventory and the survey, and leads to the proposal of four opportunities for the enhancement of knowledge sharing.

## 2 Methodology

### 2.1 Inventory of Knowledge Sources

The knowledge sources (KS) considered for this inventory refer to any **entity, tool or event that creates, collects, holds or disseminates knowledge with potential 3Rs relevance** for the knowledge source types. The information captured in the inventory cover different KS with 3Rs relevance, e.g. information systems, experts and organisations, specialised websites, communities, associations and professional networks, social media, conferences and workshops, industry initiatives and research programs, etc. In the context of the European Citizens' Initiative "Stop Vivisection", a particular emphasis was given to KS that relate to the development and use of new and emerging non-animal technologies in biomedical sciences (e.g. 3D printing, human relevant cell models, engineered tissues, high throughput *in vitro* testing methods, etc.). On top of more typical, or explicit knowledge sources (e.g. publications, educational materials and events), other media used for knowledge dissemination and sharing, such as social media and scientific communities or 3Rs relevant research initiatives which may contain more tacit knowledge, were also included.

#### 2.1.1 Selection criteria

The selection of the knowledge sources in the inventory was based on the following:

- The knowledge source is represented by an entity, tool or event that creates, collects, holds or disseminates knowledge with 3Rs relevance for the knowledge source category. The owner/developer should be easily identified.
- The knowledge refers to at least one of the 3Rs principles: replacement, reduction or refinement.
- The knowledge is disseminated through one or more channels.
- The information is provided in English.

#### 2.1.2 Identification of Knowledge Sources

In order to characterise the KS, to structure the inventory and to facilitate the knowledge curation, four main groups of data concerning the KS were defined and included in the inventory:

- KS identification - name, abbreviation, owner/developer, country, language, URL, contact details, brief description and logo (where applicable)
- KS category - Educational/Training Programs, Organisations, Experts, Information Systems, Publications, Research Program/Project/Grant and Events
- Knowledge dissemination and sharing - dissemination channel(s), the audience, user access, updating frequency (where applicable)
- Knowledge characterisation - 3Rs relevance, purpose (of activities, e.g. regulatory testing, education and training, validation, etc.), relevant legislative framework and technology

#### 2.1.3 Collecting the information

Based on predefined KS categories and the **selection criteria** (see above), the methodology for data curation to be captured in the electronic inventory followed these steps:

- 1) Identification of 3Rs relevant KS, mainly by using:

- The EURL ECVAM Search Guide<sup>4</sup>, which includes an inventory of various types of 3Rs information sources, was one of the background documents considered as a starting point for this study.
  - Information available on 3Rs specialised websites;
  - Specialised 3Rs search engines<sup>5</sup>;
  - Information provided by different organisations as 3Rs useful links;
  - Information collected in a public survey (see 2.2);
- 2)** Collection of the information into the inventory according to the predefined groups of information (as described in 2.1.2).
- 3)** Categorisation of KS (categories and subcategories in 2.1.4 and Annex I respectively).

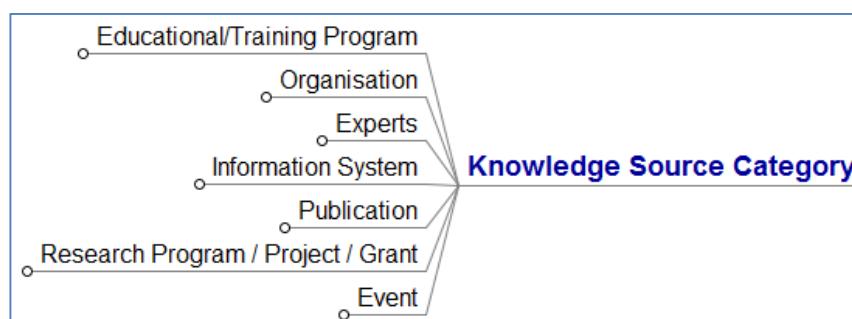
All the data included in the inventory and used to characterise the KS were collected exclusively from public information provided by the KS owner on their websites, publications or other dissemination materials.

*Limitations to the methodology* - It is possible that some modes of communication were not captured by this study as the primary sources of information were websites. Therefore, for example, if an **organisation**, **event** or **expert group** offers printed material for disseminating information then this may not have been registered.

#### 2.1.4 Categories

The KS were grouped in seven categories (Figure 1). Each KS was assigned to one category only. Therefore in the case of multiple KS belonging to the same developer/owner (e.g. a knowledge base and a webinar developed by the same organisation), each single KS was added separately to the inventory.

To each category, various subcategories were identified (see Annex 1) in order to create a more structured inventory and differentiate the sources more specifically. The inventory features give the possibility to filter the entries based on individual subcategory, which was useful for the KS analysis.



**Figure 1** Predefined categories for knowledge sources in the inventory

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<sup>4</sup> Roi A, Richmond J, Grune B. The EURL ECVAM search guide - good search practice on animal alternatives. <http://bookshop.europa.eu/en/the-eurl-ecvam-search-guide-pblbn124391/>

<sup>5</sup> Go3R Web <https://cse.google.com/cse/home?cx=012355066084994158061%3Arihd-ud3nie&hl=en>; GoPubMed <http://www.gopubmed.org/web/gopubmed/>; Norecpa <https://norecpa.no/search>

## 2.1.5 Dissemination and Sharing

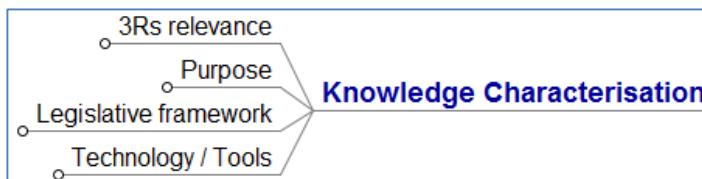
In order to identify what is the strategy of each entity to disseminate and share its knowledge, one aim of the study was to capture information on the main dissemination channel(s), the targeted audience (as specified by the KS owner), potential target audience (according to an analysis of the content available)<sup>6</sup>, on how the knowledge is accessed and, if available, how frequently the information is updated (Figure 2).



**Figure 2** Descriptors for knowledge dissemination and sharing

## 2.1.6 Characterisation

The KS are described in a structured manner providing the key information related to their 3Rs relevance, purpose(s), relevant regulatory framework or technology corresponding to each entry (Figure 3). For the characterisation of each of the KS, a set of uniform descriptors for each knowledge source was used.



**Figure 3** Descriptors for the characterisation of knowledge sources

For associating a KS to its purpose, i.e. the expected context in which the information provided through the KS would be used, a number of descriptors were defined which are shown in Annex 1. It was not obligatory to assign these descriptors for each KS, but where the information was available, (for example, based on the information provided by the KS developers or owners on their websites under 'home' or 'about us' or based on visible products and services), one or more of the descriptors was attributed.

### 3Rs Relevance

Relevance to at least one of the Rs: replacement, reduction or refinement was the main selection criteria for KS to be included in the inventory. There is an emphasis on knowledge sources that relate to the development and use of new and emerging non-animal technologies, which was decided in the context of the European Citizens' Initiative "Stop Vivisection". The 3Rs relevance of a KS was assessed based either on the explicit information provided by the KS developer or it was deduced from the KS description (activities, impact, mission statement, etc.). However, a clear distinction between replacement and reduction relevance was sometimes difficult, as in most of the cases this is not indicated by the KS. Therefore, in some cases where this information was not explicitly given, the assignment to one or more of the 3Rs was based on an

<sup>6</sup> The audience targeted by the KS mentioned in (or deduced from) the information found on the KS dissemination materials was captured in order to measure the targeted users. An analysis was then performed on the KS to establish the potential target audience by considering who could also benefit from access to the information.

interpretation of the available information on the knowledge source in question. In other cases, the link to one or more of the 3Rs is clearly specified within the name of the organisations or program (e.g. The 1R Institute, The 3Rs-Centre, The Platform for replacement, reduction and refinement, etc.).

## 2.2 Survey

In order to solicit input from individuals, a public survey of relevant interested parties was carried out. This was accessible via the EU Survey website<sup>7</sup> between 1<sup>st</sup> February 2016 and 11<sup>th</sup> March 2016. An invitation to participate was disseminated via EURL ECVAM's consultation and advisory bodies and contact persons in key stakeholder organisations and other interested parties. The addressees were contacted in their roles as representatives of their organisations and requested to distribute the survey further amongst their networks.

### 2.2.1 Survey design

The survey questions (see Annex 2) were designed with the aim of eliciting the following information:

- User profile
- Types of KS that the user considers relevant
- Current modes of sharing the user thinks are effective
- Opportunities to improve the current means of 3Rs knowledge sharing

The survey respondents were also asked to share their views (open-text answer) on promising new non-animal technologies or approaches that they consider have the potential to shape the future of areas where animals are still used today.

## 2.3 Analysis

### 2.3.1 Knowledge sources captures in the inventory

The process of analysis of the KS included in the inventory followed these steps:

- 1) Description and assessment of the knowledge by assigning predefined descriptors related to dissemination and sharing, 3Rs relevance, potential legislative framework, and related technology or tools.
- 2) Analysis using the functionalities of the inventory (searching, filtering and exporting of the data).

The KS were assessed in terms of their relevance and potential impact for the area of 3Rs. The **purpose** of the information and networks from different sectors of activity was analysed (e.g. fundamental studies, testing, documentation, etc.) as well as the relevant **technology** applied (e.g. *in vitro*, *in silico* or *in vivo* methods, tissue engineering, omics, etc.) across each category (and subcategory). The analysis of **knowledge dissemination and sharing** forms an important part of this study: different methods of information sharing used by KS developers, the **target audiences** and how accessible is the information to users were looked at in detail. The interconnectivity between different KS, cross-sector knowledge sharing and potential gaps were also analysed.

The **targeted audience** mentioned in (or deduced from) the information found on the KS dissemination materials (an objective analysis) was captured in order to measure the targeted users. A subjective analysis was then performed on the KS to establish the **potential target audience** by considering who could also benefit from access to the information. For about 13% of the KS, the targeted audience was not specified or was

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<sup>7</sup> <https://ec.europa.eu/eusurvey/home/publicsurveys>

not evident, but based on the information provided it was possible to assign those to one or more audience categories. Generally, all KS could be targeted more specifically to one of the audience profiles. The determination of the potential target audience is, as mentioned, subjective, and so the resulting figures are to be used as an estimate of where there are opportunities for KS to reach out to a wider audience.

Tools used for data analysis:

- Venny 2.1.0<sup>8</sup> - an interactive tool for comparing lists using Venn diagrams
- KnowledgeBase Builder 4.9<sup>9</sup> - to create mind maps and flowcharts to organise ideas
- Text 2 Mind Map<sup>10</sup> - free mind-mapping tool

### **2.3.2 Replies to the survey**

The replies to the survey were processed to generate the statistical evidence presented in this report. For the single or multiple choice questions, the processing was simple. However, eight of the questions presented a free-text field which required careful processing. The following steps were followed to process the free-text answers:

1. All survey replies were downloaded into an Excel spreadsheet.
2. Initial processing (filtering, sorting and counting) of the replies was performed using Excel functions.
3. Open text answers were first studied in their entirety in order to define categories (also relating to the question) for capturing the provided information. Subsequently, each reply was examined individually and assigned to one of the categories. In order to reduce the chance of subjectivity, each answer was assessed in this way by three independent analysts. To further reduce subjectivity and to increase the confidence in the categories used, colleagues of the European Commission were consulted to give their opinions on the answers and to try to categorise them. The results from this exercise were combined with the separate results from the three analysts to give an overall estimate of confidence in the awarded categories.
4. Subsequent statistical analyses of these categorised open-text answers were performed using Excel functions.

In order to represent people's views as fairly as possible, several iterations of the categorisation process were performed. However, where there was ambiguity in some of the answers (i.e. if they did not specifically address the question), these were excluded from the statistics.

### **2.3.3 Comparing the inventory and the survey**

The findings of both the inventory and the survey were included in an overall analysis with the aim to compare and contrast the supply of and demand for KS and to assess whether 3Rs KS are reaching those who could benefit from them. The aim was to provide answers to the following questions:

1. What KS exist and are easily visible and accessible?
2. Who is benefiting from these KS (and who could also benefit who may not be directly targeted)?

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<sup>8</sup> Oliveros, J.C. (2007-2015) Venny. An interactive tool for comparing lists with Venn's diagrams <http://bioinfogp.cnb.csic.es/tools/venny/index.html>

<sup>9</sup> <http://www.buildyourmap.com/>

<sup>10</sup> <https://www.text2mindmap.com/#>

3. How is the knowledge shared? (i.e. which channels are used for dissemination)
4. What can be improved?

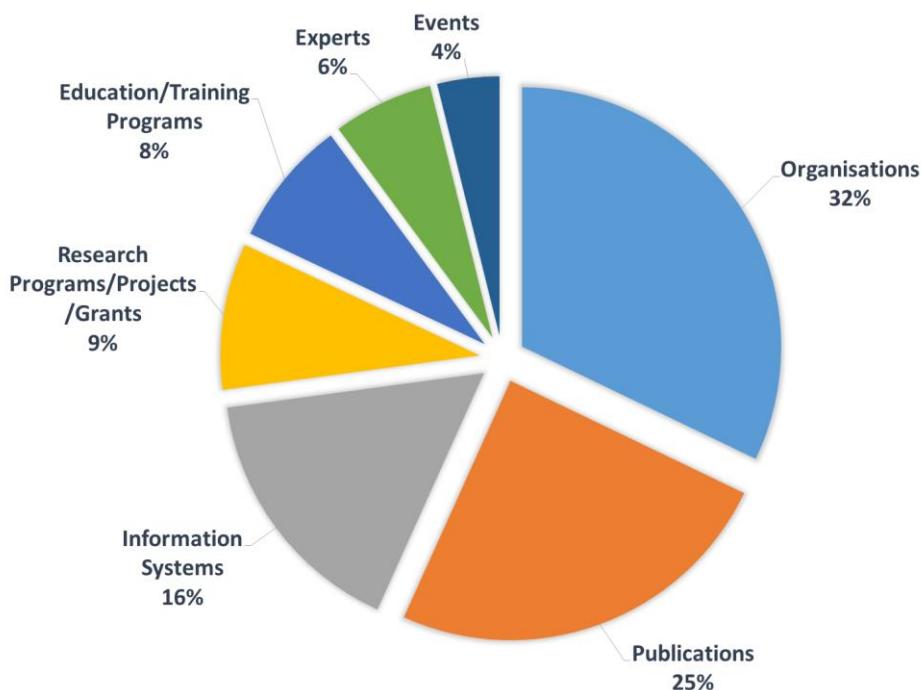
The discussion generated by these questions leads to the conclusions and proposed opportunities presented at the end of the report.

### 3 Summary of Findings

#### 3.1 Inventory

##### 3.1.1 Knowledge sources contained in the inventory

The inventory contains 800 KS, which are easily identifiable, accessible and relevant KS. The distribution of KS over the various predefined categories (see section 2.1.4) is shown in Figure 4.

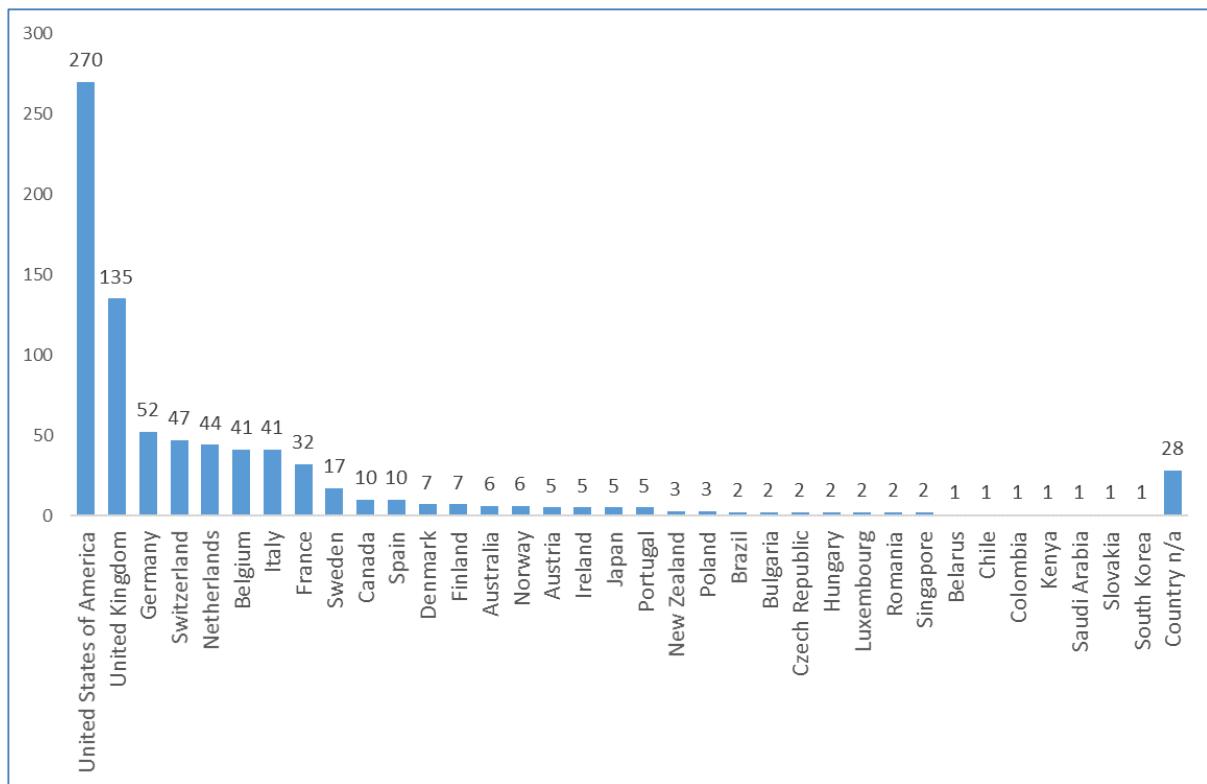


**Figure 4** Knowledge sources included in the inventory per category

Organisations, publications and information systems make up almost two thirds of the KS in the inventory, with organisations being the most abundant type of KS (257 entries).

Geographical distribution of the KS included in the inventory:

- KS located in 35 countries are captured in the inventory (Figure 5).
- For 28 KS, the country was not specified.
- For international organisations or programs, the country in which that particular organisation or the owner of the program resides was included in the inventory.



**Figure 5** Geographical distribution of the KS included in the inventory

### 3.1.2 Knowledge Source holders

A rough estimation results in about 500 unique holders of the KS that were listed in the inventory, and about 200 unique holders if the KS that have been categorised as organisations or publications are excluded. However, it seems impossible to determine more precisely the number of holders, as some KS belong to more than one holder and in some cases these are not easily identifiable. An example of a KS holder which holds several KS can be seen in Figure 6.

## Knowledge source holder



## Knowledge sources

ECVAM Scientific Advisory Committee (ESAC)

EURL ECVAM's Network for Preliminary Assessment of Regulatory Relevance (PARERE)

ECVAM Stakeholder Forum (ESTAF)

Chemical Lists Information System (CheLIST)

ChemAgora Portal

EURL ECVAM Database Service on Alternative Methods to Animal Experimentation (DB-ALM)

QSAR Model Database and QSAR Model Reporting Formats

Tracking System for Alternative test methods Review, Validation and Approval in the Context of EU Regulations on Chemicals (TSAR)

European Union Network of Laboratories for the Validation of Alternative Methods (EU-NETVAL)

European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM)

Alternative methods for regulatory toxicology – a state-of-the-art review

EURL ECVAM Recommendations

EURL ECVAM status report on the development, validation and regulatory acceptance of alternative methods and approaches

EURL ECVAM strategy for achieving 3Rs impact in the assessment of toxicokinetics and systemic toxicity

The ECVAM search guide - Good search practice on animal alternatives

- Experts
- Information system
- Organisation
- Publication

**Figure 6** An example of a knowledge source holder (the European Commission's Joint Research Centre) which holds several knowledge sources across a range of categories.

From this list of unique holders, the top holders (with at least three KS listed in the inventory), were the following:

- European Commission, including Joint Research Centre (EC-JRC)
- US Environmental Protection Agency (US EPA)
- Society of Toxicology (SOT)
- Johns Hopkins University, Center for Alternatives to Animal Testing (CAAT)
- National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs)

- U.S. Department of Health and Human Services, National Toxicology Program (NTP)
- Cosmetics Europe
- Innovative Medicines Initiative (IMI)
- The Jackson Laboratory (JAX)
- Newcastle University
- European Society for Alternatives to Animal Testing (EUSAAT)
- People for the Ethical Treatment of Animals (PETA)
- The Organisation for Economic Co-operation and Development (OECD)
- Utrecht University

There are another 24 holders with at least two KS listed in the inventory.

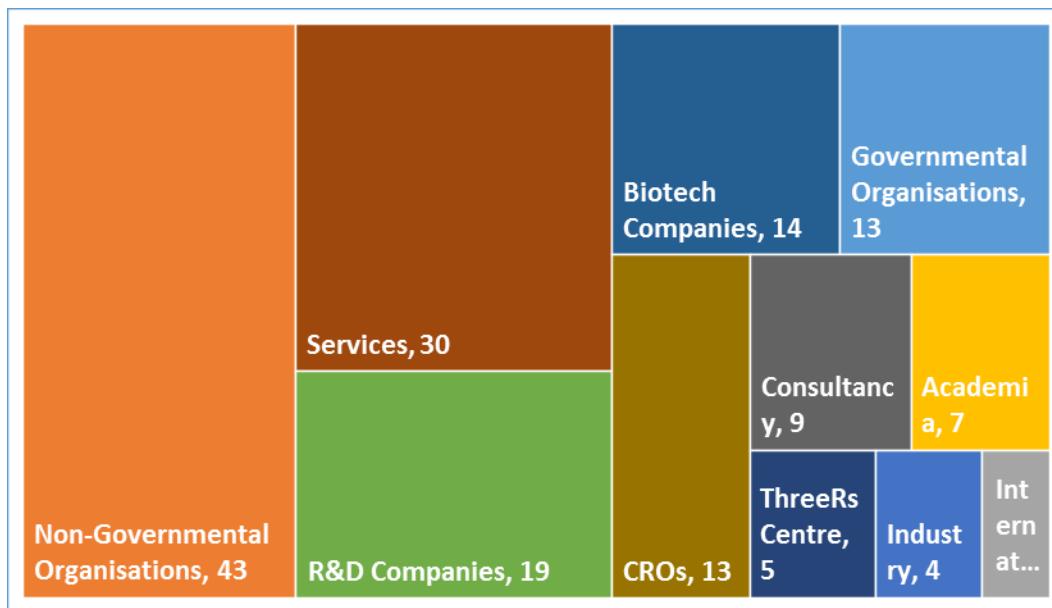
The **publications** were excluded from the analysis presented above, as the holder/developer was considered to be the journal for the review articles in which they were published, the publisher for the books, etc. so it was difficult to define the owners of the publications. In any case, the estimations show about 130 unique holders for the total of 197 Publications included in the inventory, therefore a quite diverse source of information was used for this category of KS. The holders with at least four KS included in the inventory are listed below:

- Alternatives to Animal Experimentation (Journal)
- Toxicology in Vitro (Journal)
- Alternatives to Laboratory Animals (Journal)
- Regulatory Toxicology and Pharmacology (Journal)
- John Wiley & Sons, Inc. (Publisher)
- Mary Ann Liebert, Inc. publishers (Publisher)
- Elsevier Inc. (Publisher)
- Taylor & Francis Group (Publisher)
- Springer International Publishing (Publisher)
- European Commission, Joint Research Centre (Organisation)

For about 22 KS, the holder was not identified or registered in the inventory (especially for the Online Communities on LinkedIn and specialised websites).

Most of the groups of **experts** included in the inventory (34 KS) are related to one or more organisations, while for the other KS (16), the holders were not identified. The latter KS are represented mainly by the online communities (e.g. on LinkedIn), for which the holder is not always easily identifiable. The organisations related to the experts are represented mainly by NGOs, governmental organisations and academia.

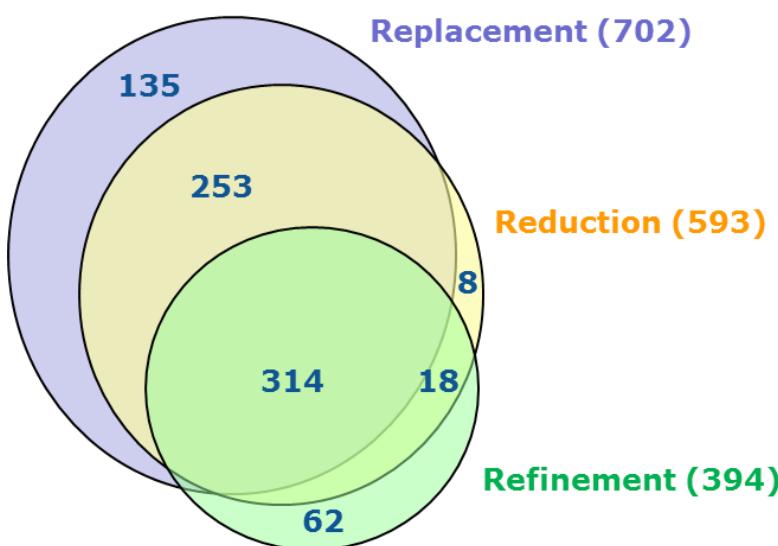
Among the **organisations** included as KS in the inventory (257) different types can be identified as depicted in Figure 7. Whilst NGOs account for the highest proportion of such KS, private businesses (including services, companies, industry, consultancies and Contract Research Organisations (CROs)) are also well represented. International organisations, such as the European Partnership for Alternative Approaches to Animal Testing (EPAA), account for 3% of the identified KS, but it must be noted that such organisations bring together a vast number of experts, which are themselves KS.



**Figure 7** The proportion of different types of organisations contained in the inventory (as a percentage of the total number of organisations). A knowledge source could be assigned more than one subcategory where necessary.

### 3.1.3 3Rs relevance of identified knowledge sources

Seven hundred and two KS have relevance to replacement while 135 (17%) KS are relevant to replacement only. Three hundred and fourteen (40%) of the identified KS have relevance to all 3Rs, while 253 (32%) are linked to replacement and reduction and 18 (2%) to reduction and refinement. Eight (1%) KS are relevant for reduction only and for refinement only, 62 (8%) of the total (Figure 8<sup>11</sup>). Overall, the majority of KS identified for this study are related to all 3Rs. As a result of placing emphasis on identifying KS related to non-animal technologies (see 2.1.6), the inventory has a higher representation of KS with relevance to replacement and reduction than those with relevance to refinement.

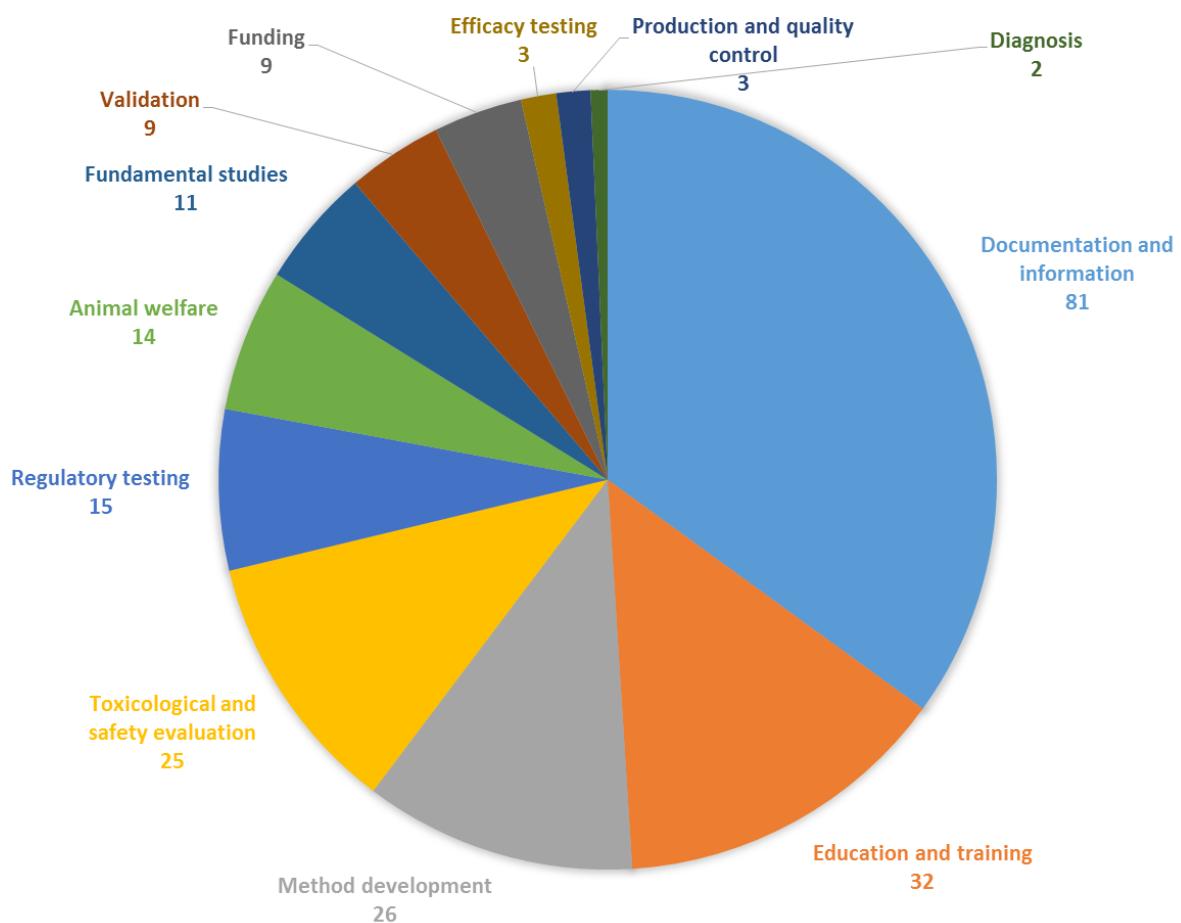


**Figure 8** Number of knowledge sources captured in the inventory that are relevant to one or more of the 3Rs

<sup>11</sup> Analysis was performed with Oliveros, J.C. (2007-2015) Venny. An interactive tool for comparing lists with Venn's diagrams. <http://bioinfogp.cnb.csic.es/tools/venny/index.html>

### 3.1.4 Purpose of the identified Knowledge Source

The distribution of the different purposes (as listed in Annex I) of the KS in the inventory is displayed in Figure 9. Each KS could be assigned one or more of the defined purposes.



**Figure 9** Percentages of knowledge sources included in the inventory linked to a specific purpose (one or more was possible for each knowledge source)

About 81% of the KS are linked to documentation and information purposes. This purpose indicates a more explicit form of knowledge (as opposed to more implicit forms of knowledge which are perhaps not documented but held by individuals or groups) and therefore it is comprehensible that it applies to most of the KS. The next abundant purpose of the identified KS is education and training (32%) followed by method development (26%) and toxicological and safety evaluation (25%).

The distribution of the 3Rs relevance relative to the different purposes of KS in the inventory was analysed (see Table 1).

**Table 1** Portion of knowledge sources included in the inventory linked to a specific purpose (multiple attribution of a KS to more than one purpose descriptor was possible) and their relevance to replacement, reduction and/or refinement.

Purpose	% of KS for each purpose		
	Replacement	Reduction	Refinement
Fundamental studies	93	76	39
Toxicological and safety evaluation	96	77	30

Production and quality control	100	85	42
Efficacy testing	100	81	41
Diagnosis	92	85	62
Education and training	81	71	66
Documentation and information	88	76	55
Regulatory testing	94	75	44
Animal welfare	74	69	83
Validation	100	84	47
Method development	93	74	32
Funding	94	77	65

The numbers indicate the percentages of the total KS associated with a specific purpose which are relevant to each individual R (i.e. all of the KS for the purpose of production quality and control are relevant to replacement, whereas 85% are relevant to reduction and 42% to refinement). For each purpose, the majority of the KS are relevant to replacement and/or reduction. There is a high representation of KS relevant to replacement for most purposes, with the exception of animal welfare, where there is a higher percentage of KS relevant to refinement. The purposes of animal welfare and education and training have a lower variance in the distribution of the KS across the 3Rs compared to the purposes of toxicological and safety evaluation, method development and efficacy testing (it must again be noted that emphasis was placed on identifying KS associated with non-animal technologies).

### 3.1.5 Audience targeted by the knowledge sources

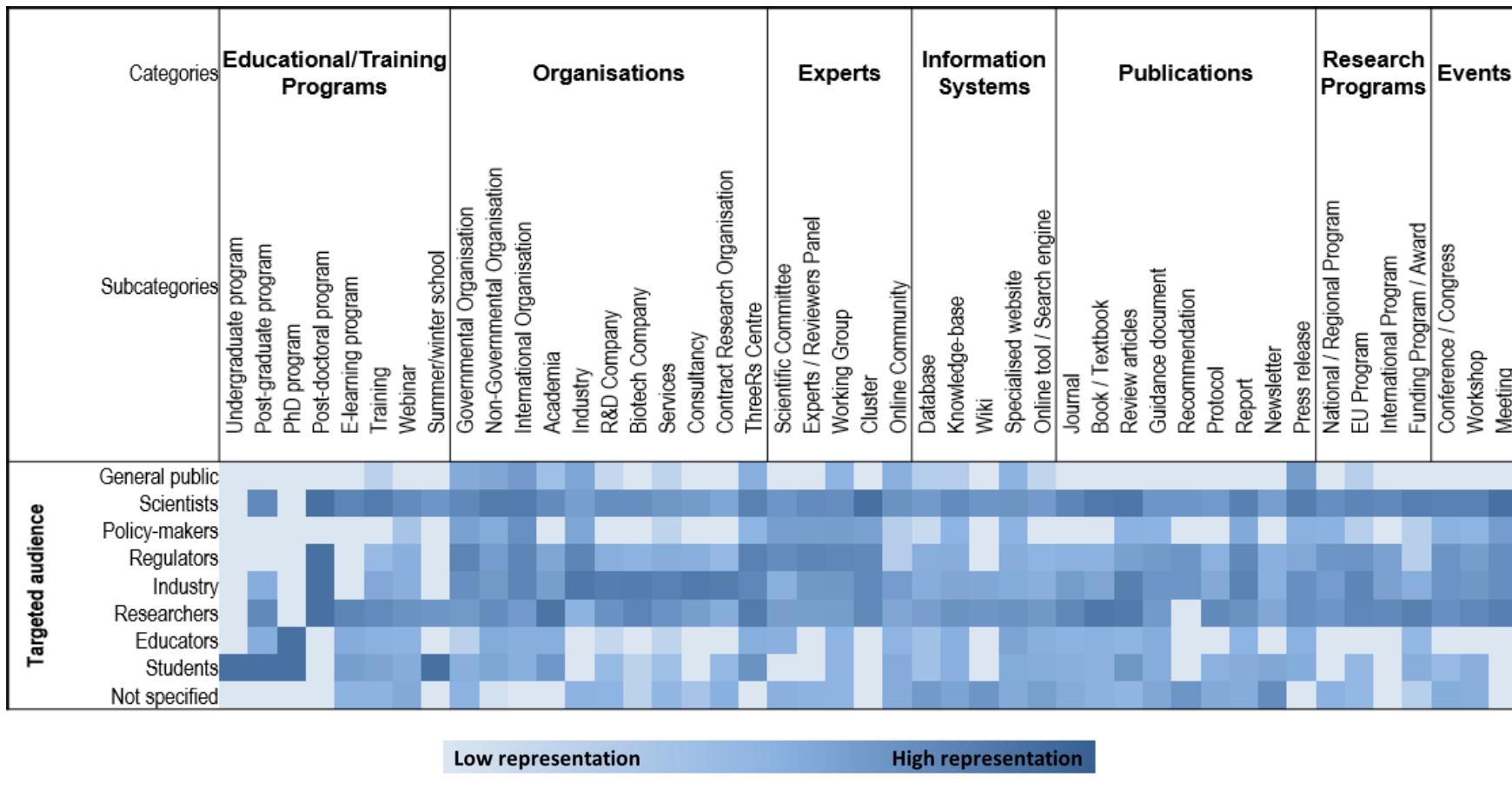
The spread of different target audiences depending on the categories and subcategories of KS (where it was specifically mentioned) is shown in Figure 10 (depicted in the format of a so called heat map<sup>12</sup>). From this chart the following observations can be made:

- The main target audiences of the identified KS are scientists and researchers<sup>13</sup>, followed by regulators and industry.
- Industry is targeted by most of the KS. However, among the identified KS, there are only few training and educational programs specifically targeting industry; generally, this type of KS is mainly addressed to researchers and scientists from academia and research organisations.
- Not many KS target the general public, educators or policy makers. Most of those KS that do target the public come from governmental or international entities and NGOs (especially those which are active in the area of animal welfare).
- Regulators and policy makers tend to be targeted by the KS represented by or coming from governmental and international organisations, NGOs, industry and expert groups.
- KS explicitly dedicated to educators (teachers) were generally difficult to identify.

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<sup>12</sup> A heat map is a graphical representation of data where the individual values contained in a matrix are represented as colours or as dots/squares of different density of a colour.

<sup>13</sup> The tag 'researchers' was used to indicate that the KS contains information dedicated to individuals involved and performing research activities or knowledge which can be used for research purposes, while the tag 'scientists' had a broader meaning, covering different categories of professionals (e.g. biologists, veterinarians, medical doctors, etc.) or different scientific purposes.



**Figure 10** Targeted audience depending on the subcategory of KS listed in the inventory

### **3.1.6 Dissemination tools and sharing of knowledge**

Most of the KS use websites for dissemination of information (Table 2). There is a small number of KS, such as online communities, which do not share information via a website, but use social media or online networks.

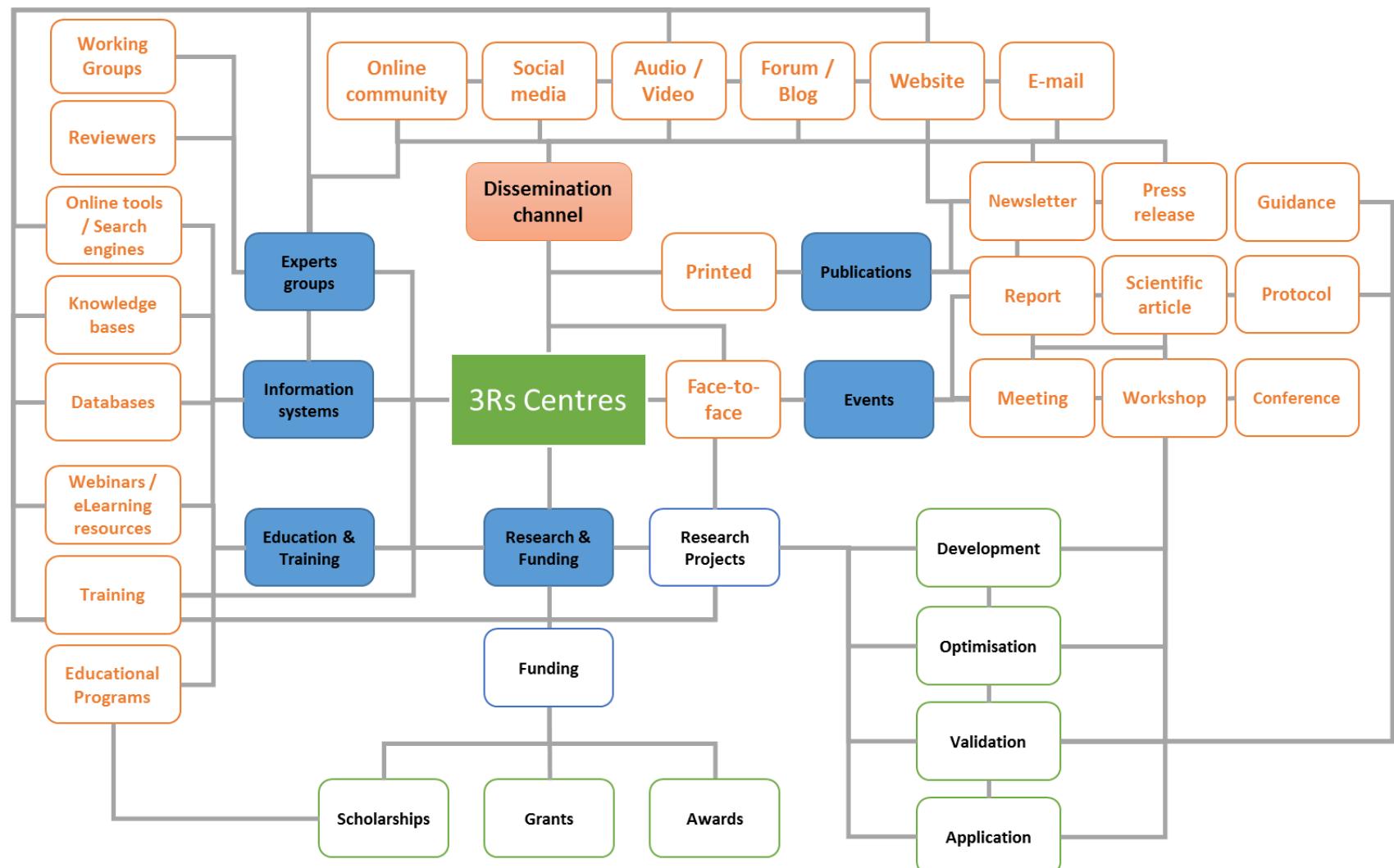
**Table 2** Percentage of KS using the different channels for dissemination and sharing of information

<b>Dissemination channel</b>	<b>KS (%)</b>
<b>Website</b>	98
<b>Social media</b>	31
<b>Audio / Video</b>	22
<b>Professional online network</b>	18
<b>Face to face</b>	14
<b>Printed</b>	14
<b>E-mail</b>	13
<b>Forum / Blog</b>	7

Besides using websites, a significant number of KS disseminate information through:

- **social media** (e.g. Facebook, Twitter, Google+);
- **video material**, placed either in specialised channels (e.g. YouTube) or directly on the website run by the KS or by the KS owner;
- Scientific **online networks** (e.g. LinkedIn).

Taking an organisation such as a 3Rs centre as an example, a schematic (Figure 11) demonstrates the wide variety of means by which this type of organisation can disseminate knowledge. This is a general schematic for a 3Rs centre, as each centre has a unique profile. Typically, these centres support the development and dissemination of 3Rs activities as well as interconnecting different groups or sectors and 13 such centres have been identified in this study. Therefore, the ways in which they collect, coordinate and disseminate information can be viewed as an example of good practice in knowledge sharing as they exploit many channels to reach a variety of target audiences.



**Figure 11** General profile to show the knowledge sharing strategies for a 3Rs centre (blue box=main category; orange box=descriptor; orange outline box=subcategory; other boxes=subcategories not featured in the inventory).

### **3.1.7 Interconnected knowledge sources**

The inclusion of the 800 KS in the inventory means that they have good visibility and therefore this should facilitate to some extent the sharing of knowledge. There are examples of KS which are highly collaborative across all of the KS categories in the inventory and these by their nature may be considered to be well-interconnected. The 3Rs Centres, acting as independent institutions or affiliated with different governmental, NGO or academic bodies, are visibly well connected: they connect different groups or sectors working towards the same goal of developing and implementing new alternatives to animal testing. Research programs/projects/grants are usually built upon the initiative of organisations or experts and are funded by various public or private resources and so by their nature, they create connections between a variety of organisations and experts. These comprise over 10% of the KS in the inventory and provide many tools and opportunities for connecting people and knowledge sharing.

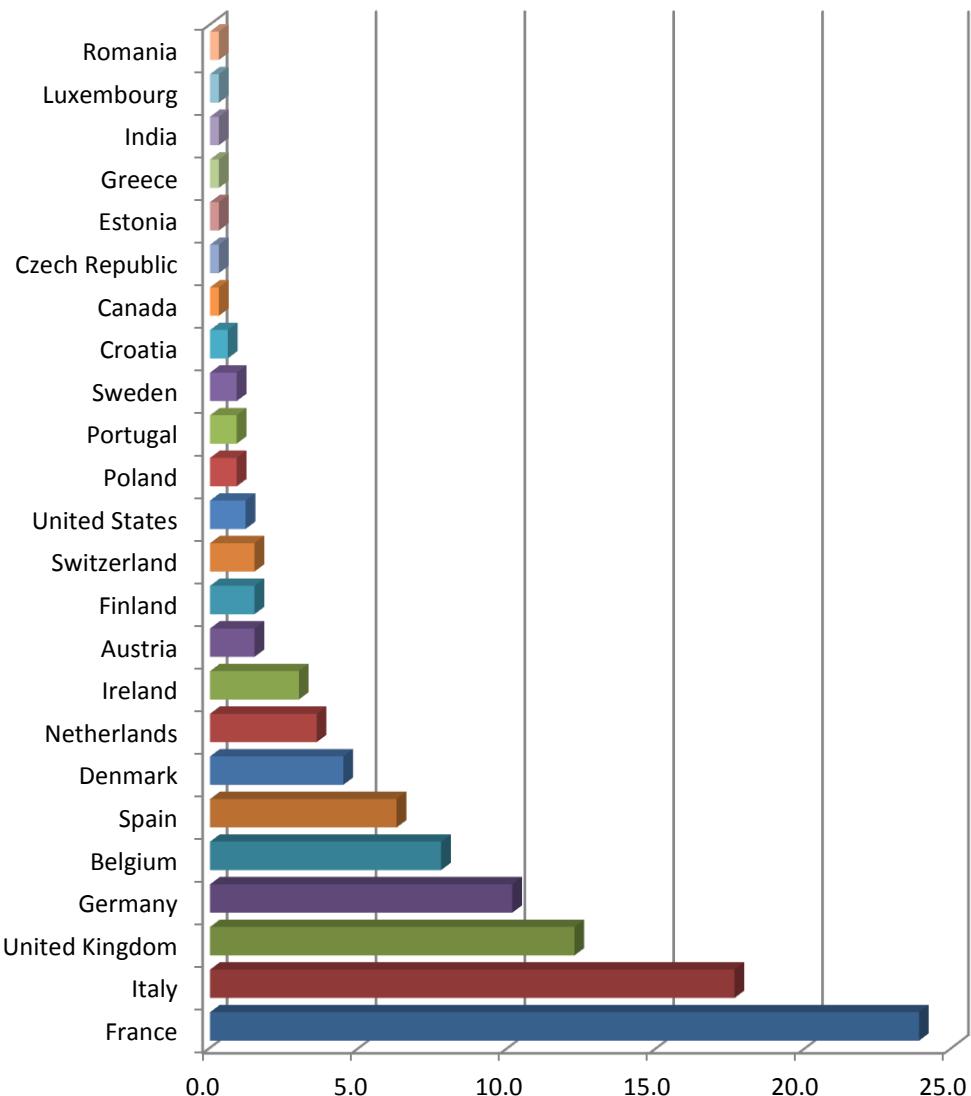
## **3.2 Survey**

In the following the profiles of the 351 survey respondents are described; subsequently the answers are summarised and illustrated by some statistics and figures, where appropriate. The method of analysis for the free text answers is described in section 2.3.2.

### **3.2.1 Profile of respondents**

#### ***Country***

Respondents were asked to provide their country of professional activities. This was a free text answer and some of the replies stated more than one country, cities or regions (including responses such as worldwide or Europe and Asia). In general the replies consisting of cities or regions were updated to their parent country, while replies stating multiple countries or more global answers were excluded. If a reply stated their primary country, then their primary country was included in the statistics. Individuals from 24 countries replied to the survey (see Figure 12) with 98% of replies originating in Europe.

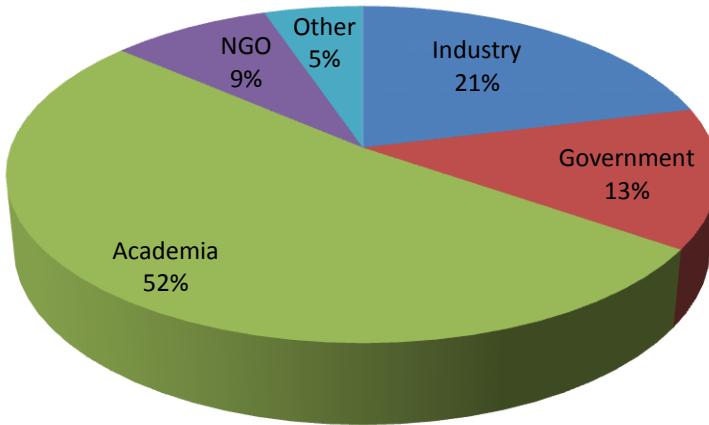


**Figure 12** Percentage of respondents from each country

### Sectors

The respondents were asked to indicate the sector in which they are active and it was possible to indicate more than one sector. The sectors provided in the multiple choice options were: academia; government; industry; non-governmental organisation; other. For the purpose of statistical analysis including associating the sector with the replies to other questions, only those who clearly indicated one sector were included in the summary.

The sector representation in the survey is given in (Figure 13) (considering only replies mentioning a single sector). The majority (over half) of the respondents come from the academic sector. The "other" category includes consultancy services, public research organisations, trade associations and scientific consortia.



**Figure 13** Sector representation in the survey

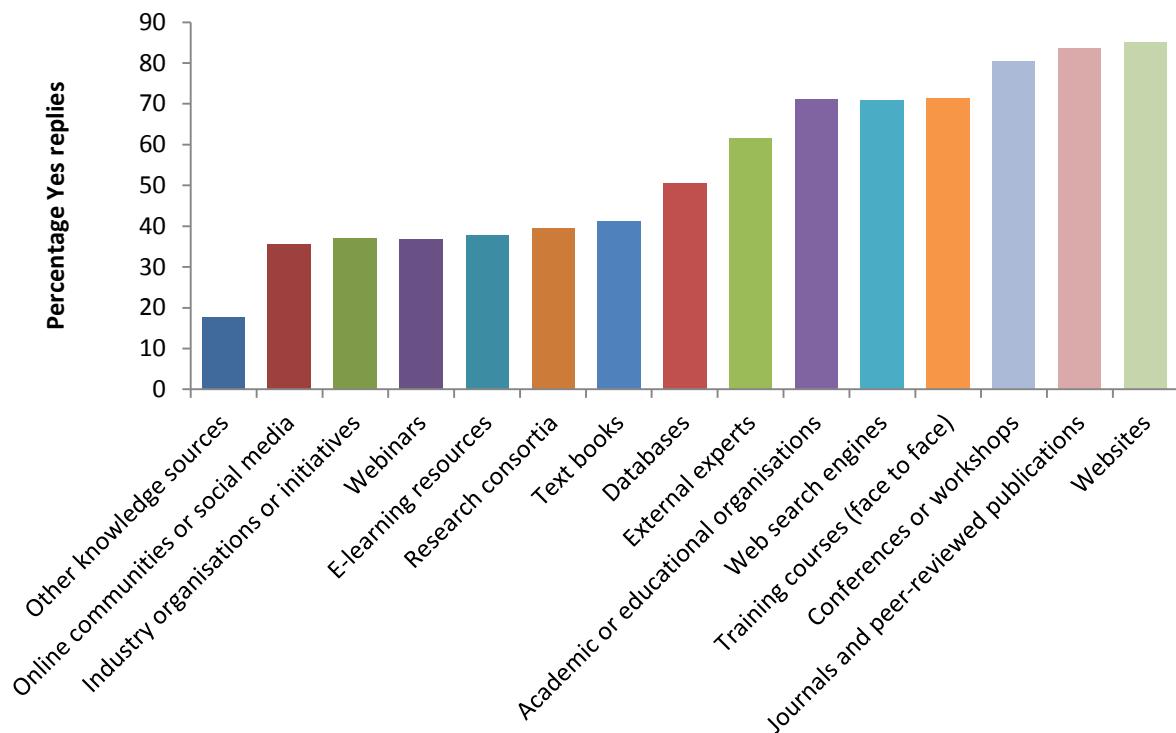
Approximately **one third of respondents replied on behalf of their organisations**, whilst 2% replied both as an individual and on behalf of their organisation. Roughly 40% of the respondents responding on behalf of an organisation belong to very large organisations (>1000 employees) whilst 14% belong to small organisations (2-20 people). Therefore, considering that at least one or more colleagues will have contributed to the answers, the number of respondents represented in this survey is likely to be appreciable.

### 3.2.2 Answers to survey questions

#### ***Which type of knowledge sources are important to people?***

Multiple choice and free text answers - 348 replied to this question, 3 did not reply.

## Knowledge Sources



**Figure 14** Knowledge sources used by the survey respondents (as a percentage of the replies)

The results are displayed as the percentage of respondents to this question who answered yes to using the KS listed in question 1 (Which KS are important to people?).

The most used types of KS are **websites** 85% and **journals or peer reviewed publications** (84%), followed by **conferences or workshops** (81%).

Among the **web search engines**, which are used by 71% of the respondents, 38% use Google and a small percentage specified Go3R<sup>14</sup>. The Norecopia search engine<sup>15</sup> is used by 6%, most of whom come from the industrial sector.

Webinars are used by just over a third of respondents, with the general consensus that these are cost effective opportunities to share knowledge very effectively. LabRoots<sup>16</sup> is used by around 20% of these respondents.

**E-learning** resources are also used by just over a third of respondents whilst more traditional **face to face training courses** are used by 71%. Approximately a third of respondents use **online communities** or **social media**. Half of these are from academia; 40% from industry; 12% government; 18% NGO and 12% other. Thirty five percent of those who use these channels specified using LinkedIn; 20% Facebook and Twitter; 10% use ResearchGate<sup>17</sup>. Half of the respondents use **databases**, a third of which are from industry.

**Research consortia** are used by 39%: half of these come from academia and a third from industry.

<sup>14</sup> Go3R - semantic internet search engine for alternative methods to animal testing

<sup>15</sup> <https://norecopia.no/>

<sup>16</sup> <http://www.labroots.com/>

<sup>17</sup> <https://www.researchgate.net/>

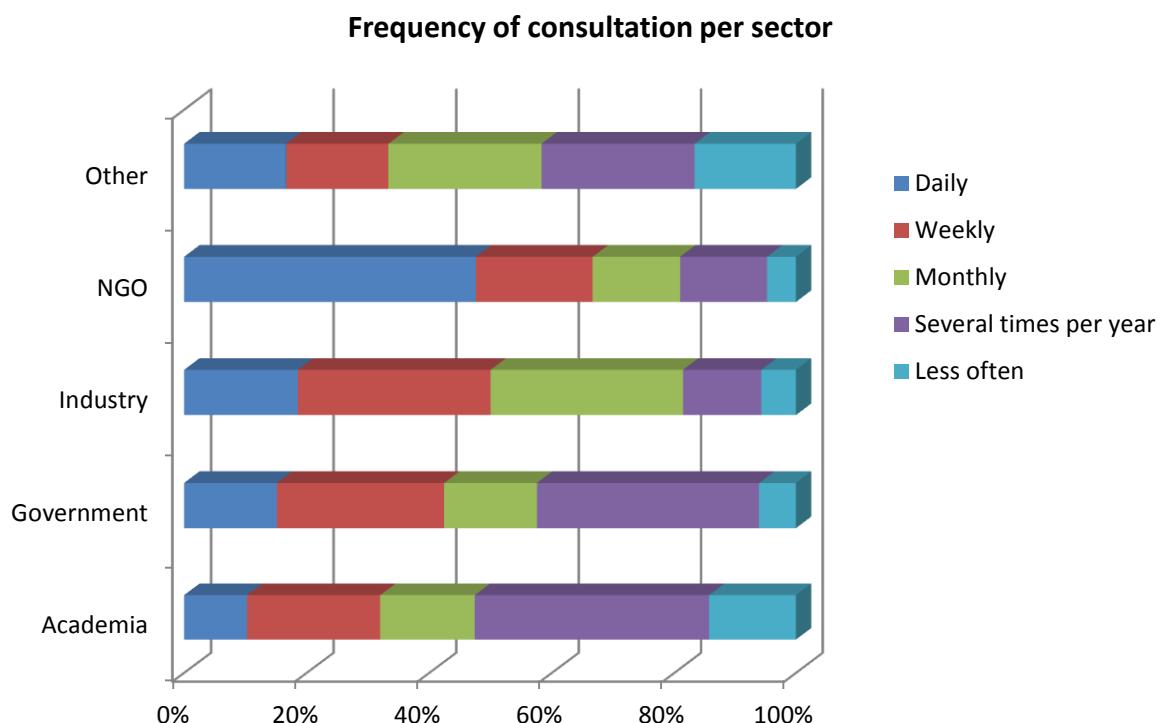
37% use **industry organisations or initiatives**, with the majority of these users coming from industry.

18% opted for the "**other**" category, and this includes: newsletters and email notifications; informal discussions with internal experts/colleagues; networking and information from Directive 2010/63/EU or from the European Commission.

### **How often do people consult 3Rs knowledge sources?**

Single choice answer - 351 replied to this question, 0 did not reply.

40% of the respondents consult 3Rs KS weekly or more often (16% consult them daily), whilst 20% consult them monthly, 29% several times per year and 11% very infrequently. Looking across the sectors<sup>18</sup> in Figure 15, it is apparent that NGOs consult these KS more frequently than the other sectors followed by industry.



**Figure 15** The frequency of consultation of 3Rs KS by respondents from each sector

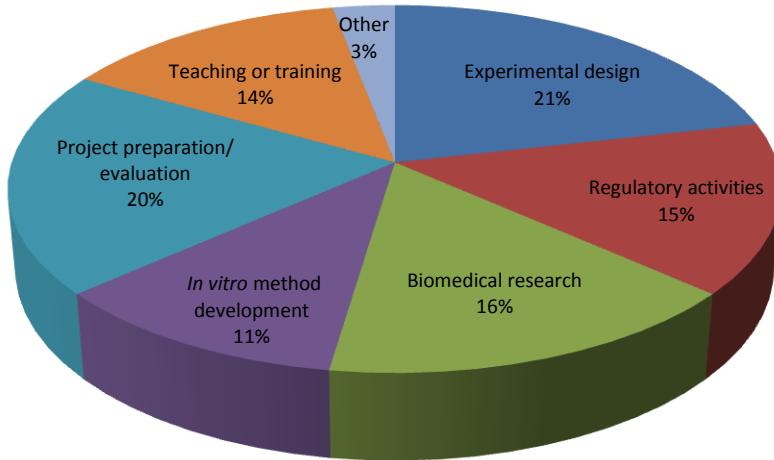
### **For which purpose do people consult 3Rs knowledge sources?**

Multiple choice answer - 351 replied to this question, 0 did not reply.

Respondents were asked the purpose for which they consult 3Rs KS. A list of pre-selected categories was provided from which one or more categories could be chosen. In the cases where the category "other" was selected, no further information was provided by the respondents. The breakdown of replies (Figure 16) ranges from *in vitro* method development (11%) to experimental design (21%).

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<sup>18</sup> Only where one sector was specified by a respondent.



**Figure 16** Purposes for consulting 3Rs knowledge sources as specified by the survey respondents.

**What benefits has the use of 3Rs knowledge brought to people/organisations?**

Free text answer - 291 replied to this question, 60 did not reply.

- A considerable proportion of the respondents stated that they have benefited through improvements in **reduction** (23%) and **refinement** (30%). **Replacement** benefits account for 8%.
- A quarter of respondents reported that the 3Rs KS have resulted in **scientific benefits**, such as more reliable results and aiding the design of more effective experiments.
- Improved **communication** with others working in the field as well as access to relevant information is claimed as a benefit by many people. Enhanced communications also enable the promotion of advances in science and animal welfare by increasing opportunities for collaborations and interdisciplinary exchanges.
- **Financial** benefits have also been mentioned by some people as they can perform more efficient experiments, can access information about research funding and in some cases, have had commercial benefits through product development.

**How would you describe yourself or your organisation as a 3Rs knowledge source? In other words, what knowledge have you gained through your work and interests?**

Free text answer - 294 replied to this question, 57 did not reply.

A quarter of the respondents to this question have knowledge in the area of refinement; 14% in reduction and 9% in replacement. Those who have expertise in education and training account for 17% whilst 27% state that they are involved in the communication of 3Rs knowledge in some way (such as through networks, social media, meetings and seminars).

### **Do you proactively share your knowledge?**

Multiple choice and free text answers - 338 replied to this question, 13 did not reply.

The answers to this question indicate that people share their knowledge using similar means to how they obtain their knowledge. However, there are sometimes marked differences between access and sharing channels, particularly regarding the use of web-based tools for dissemination.

Figure 17 illustrates that a large proportion of people use face to face opportunities, such as **face to face training courses** (53%), **conferences** and **workshops** (48%), as the key mode of knowledge transfer. **Journal publications** are also a key mode of sharing (46%) and **organisational initiatives** feature highly in the methods of sharing (43%). These are closely followed by **academic or educational courses** (39%) and **websites** (36%). **Online communities or social media** are used by 22% of the respondents.

- For the KS captured in the inventory, **websites** are the main channel (98%) used for communication, dissemination and sharing of information with potential users. This is well in line with the habits of the survey respondents, of which 85% use websites to obtain knowledge (input) and 36% to share information (output).
- **Databases** are also not highly represented as a means of sharing (15%) by the survey respondents.
- Notably, there are relatively few respondents who report that they use **e-learning resources** (11%) or **webinars** (7%) as a mode of sharing compared to the number who use **face to face training** as a means of obtaining knowledge.



**Figure 17** How people/organisations share their 3Rs knowledge (percentage of respondents to this question).

The category "other" was selected by almost a quarter of respondents (not shown in figure) and includes: giving talks at schools, newsletters, communication of results to animal welfare officers, teaching students, expert working groups, internal seminars,

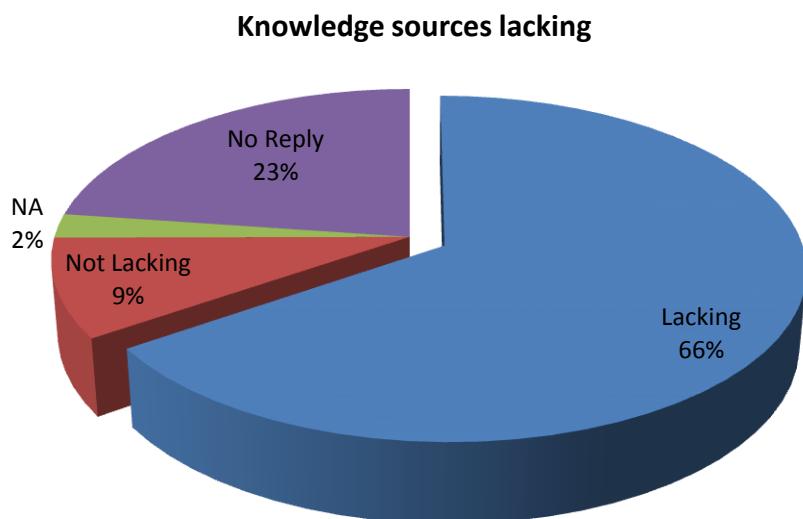
blog articles in online publications, dropbox (or other drives) and informal face to face discussions.

**What knowledge sources are lacking that you feel would be relevant to your activities?**

Free text answer - 272 replied to this question, 79 did not reply.

As shown in Figure 18, nine percent of the respondents stated specifically that they feel there is nothing lacking in terms of KS relevant to their activities, whilst 23% gave no reply to this question. Amongst the comments from the 66% who felt that there is a lack of KS, the following areas for improvement were identified:

- Better coordination of the KS
- Communication
- Improvements in education and training (including access to this)



**Figure 18** Breakdown of answers to the question about lack of KS

More general suggestions included increasing the KS available for regulatory purposes. Regarding the three issues mentioned above the respondents commented in more detail as follows:

- **Coordination** - There is a widely held opinion amongst the respondents that the KS are not so well coordinated and that navigating through the volume of information takes a lot of time.
- **Communication** - A quarter of the respondents to this question mentioned that communication of information in some areas is lacking. Specifically, a lack of sharing of information on new methods and/or novel techniques was highlighted by a small number of respondents. A suggestion in the survey was that such gaps could be addressed by funding more research initiatives which facilitate the sharing of this type of information, particularly between academia and industry.
  - Amongst other suggestions it was requested that the **language** used could be better adjusted to the audience. On the one hand, there could be more KS available in languages other than English in order to reach audiences that do not feel comfortable with this language. On the other

hand, more information in lay (less technical) language would be useful to better inform users without a technical background (e.g. general public, policy makers).

- **Databases** are also reported to be lacking, particularly open access to data which have been collected in a harmonised way. A couple of suggestions included the availability of a database to compare animal, human and *in vitro* results for the testing of reference substances.
- **Education and training** is an area in which gaps exist for 10% of the respondents to this question. According to the survey replies the following are lacking:
  - standardised/harmonised teaching material (and a specification of a certain number of hours for study);
  - education about 3Rs in high schools;
  - access to e-learning courses (deemed especially useful for professionals with limited time for training courses);
  - cost-effective training courses;
  - specific courses to educate project evaluators about legislation concerning the 3Rs;
  - training materials/courses in languages other than English.

A small number of respondents to this question (3%) mentioned a lack of information on negative study results, which could be of benefit to avoid the duplication of similar experiments and so in this way reduce the number of animals used.

### ***Do you think you have reasonable access to 3Rs knowledge sources that are relevant to your activities?***

Free text and check box answer - 338 replied to this question, of which 294 answered *yes*, 44 answered *no* and 13 did not reply.

The vast majority of respondents to this question believe that they have reasonable access to 3Rs KS which are relevant to their activities. Of the respondents who stated that they do not have reasonable access, 34% indicated that the information which exists is not always well communicated. Comments relating to **communication** include:

- lack of exchange between groups;
- unstructured resources which can be difficult to navigate;
- not knowing about the existence of some resources.

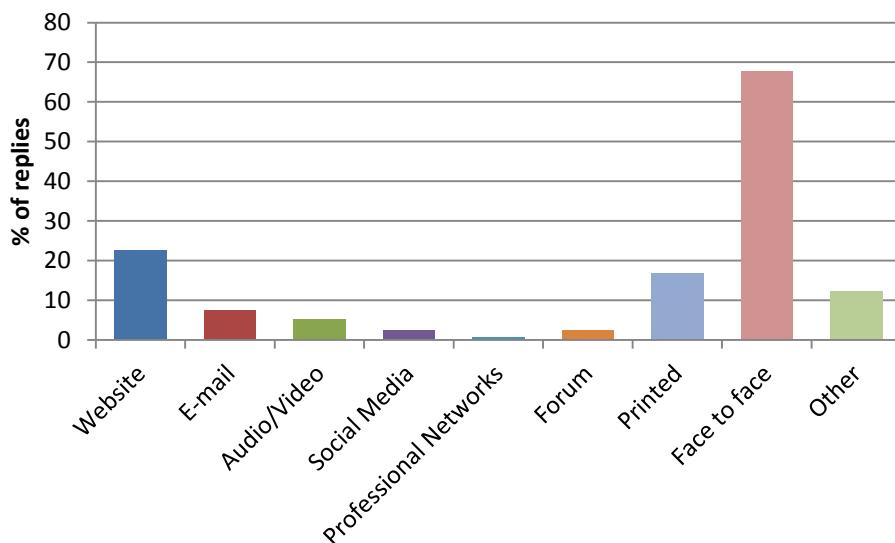
Other responses to this question include financial restrictions on information (16%) and a further 16% stated that information relating to alternative methods is insufficient.

### ***What means do you find most effective for exchanging knowledge with others?***

Free text answer - 292 replied to this question, 59 did not reply.

To understand what means are currently working well, the respondents were asked to identify the means which they find most effective. **Communication**, in general, was reported to be the most important means of exchanging knowledge (67% of all respondents). **Education and training** was specified by 14% of respondents, which may include face to face as well as non-face to face opportunities (such as e-learning). Thirteen percent of respondents consider **centralised resources** to be effective whilst a very small number of people (1%) stated that they found **data-sharing** to be the most effective.

As **communication** is a very broad category, the answers in this category were further analysed (Figure 19). The majority of the respondents (68%) stated that communicating **face to face** was the most effective means of exchanging knowledge. Such opportunities included meetings and conferences; direct discussions; seminars and workshops. The value of personal interaction with other people was emphasised by many respondents. A further 22% felt that **websites** were the most effective means whilst 17% feel that **printed** material is valuable.

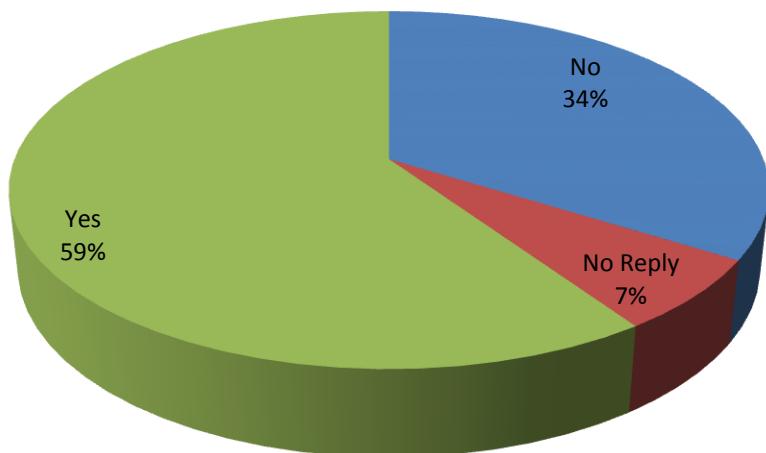


**Figure 19** Means of communication which are effective for knowledge sharing according to the survey

### ***Do you think current means of sharing knowledge are adequate?***

Free text and check box answer - 328 replied to this question, of which 209 answered *yes*, 119 answered *no* and 23 did not reply.

This question complements the previous question and intended to identify further opportunities to improve in the means of sharing 3Rs knowledge.



**Figure 20** Breakdown of how many think current means of knowledge sharing are adequate or not

The majority (59%) felt that current means of knowledge sharing are adequate (Figure 20). Of the 34% who think that inadequacies exist, the following issues were raised:

- More opportunities for **face to face** discussions and meetings are needed.
- KS could be **better coordinated** to facilitate retrieval of information.
- **Networks** could be better exploited to disseminate the knowledge.

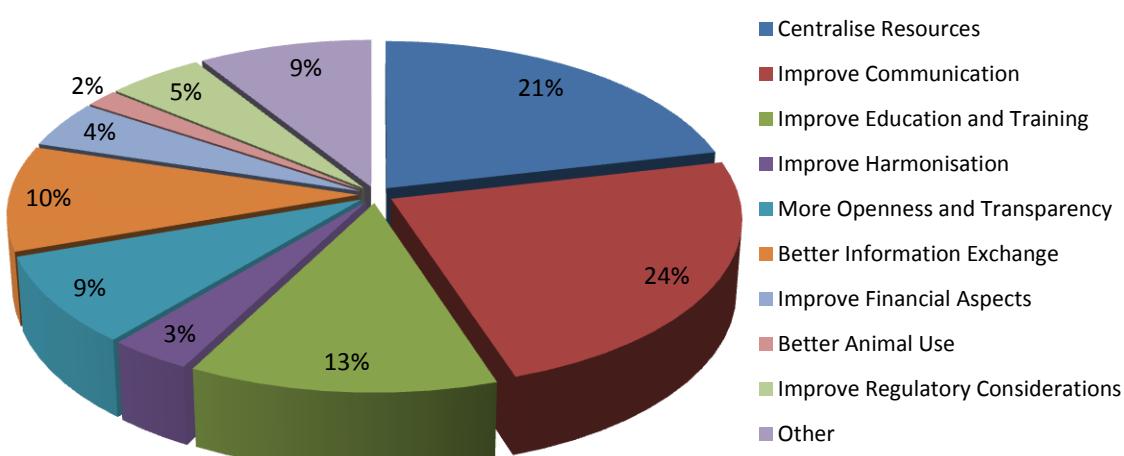
Other comments include:

- There needs to be a **better global cooperation**.
- The status of methods in the validation workflow lacks **transparency**.
- More opportunities for **cross-sector collaboration** are needed.
- Some individuals are not made aware of the need or means of knowledge sharing.
- Access to **negative results** would be beneficial.

### **What ideas do you have for better sharing of knowledge that would benefit the 3Rs?**

Free text answer - 246 replied to this question, 105 did not reply.

The respondents were invited to suggest their ideas for better knowledge sharing. Although the majority feel that current means of knowledge sharing are adequate and that they have reasonable access to knowledge sources relevant to their activities, two thirds stated that they felt that there are KS lacking (see above). In answer to this question, most of the 70% who replied had very detailed suggestions for improvement (Figure 21).



**Figure 21** Breakdown of ideas for improvement of 3Rs knowledge sharing

**Improved channels of communication** are needed, according to 24% of respondents, especially with a view to ensuring that individuals engage regularly with information

sources which are relevant to their activities. Communication channels can take the form of conferences, workshops, one-to-one interactions, social media, public engagement activities, discussion fora, newsletters and email updates from websites.

The idea of **centralised resources** was suggested by 21% of the respondents, with the widely held belief that there are many resources available and this can be overwhelming. A centralised resource is also understood to mean a coordinated network of resources, not necessarily one dedicated website which is curated by a single competent authority which would therefore be ultimately responsible for the management of all 3Rs KS. This echoes the comments in previous questions where the problem of the disperse nature of the KS was mentioned.

Other suggestions focused on **standardisation and harmonisation** of the available information. It was also pointed out that the legislations and regulatory requirements are often different between countries, making collaborations quite difficult. Improving **regulatory considerations** also include providing specific information and expertise for regulators to consult when reviewing studies. It was proposed that regulators and funding bodies need to work with animal researchers to help them find alternatives, perhaps on an individual basis. Regulatory agencies could explain clearly on their websites, what are the options to avoid animal testing for their sector.

Improving **education and training** was suggested by 13% of the replies to this question. These suggestions ranged from practical training for laboratory scientists for staying up to date on new methods and techniques, to university and primary school level education. Education and training may cover practical training, seminars and workshops, e-learning, university education, primary and secondary school education and mentoring.

The use of animals in **university** life science courses for teaching purposes requires more attention in order to focus on improving *in vivo* experimental design. Additionally, several respondents suggested addressing **primary and secondary education** as a way of changing the culture of thinking about animal experimentation in both the scientific and public spheres.

Better **information exchange**, including data and knowledge sharing, was proposed by 10% of the respondents to this question. The answers contained within this category highlight the use of repositories and networks to enhance the exchange of knowledge. It was also suggested to aim for a greater collective effort in this area: individuals need to make an effort to access existing information, whilst some organisations could push their knowledge forward enough to reach those who would benefit.

**Openness and Transparency:** the comments received in this category focused on the sharing of data and also requested the publication of negative results so as to avoid unnecessary duplication of animal studies and thus reduce the number of animals used. Other issues raised include:

- Clearer description of the methods used (e.g. through the establishment of guidelines on publishing 3Rs methods in journals);
- Fair and balanced reporting on tests using animals (i.e. what are the benefits as well as the assessment of the suffering);
- Open scientific debates and more interaction between different groups (e.g. academia, industry, regulators, etc.).

This category also includes comments on the need for more open dialogue between *in vitro* and *in vivo* research communities to promote the 3Rs principles. Respondents indicated that there needs to be a transparent and fair comparison between *in vitro* and *in vivo* methods performances and a "bidirectional, open, not self-defensive, communication attitude".

**Improving financial aspects** could enhance knowledge sharing according to 5% of respondents. Suggestions included ensuring that all work which has been financed by public funds is freely available.

The category **better animal use** includes several aspects of animal use, ranging from good experimental design for *in vivo* studies, improving animal welfare assessment and sharing of animals between groups.

Further suggestions were provided which were categorised as "**other**". Such suggestions include:

- Promoting the use of Spanish;
- Establishment of a dedicated 3Rs journal;
- Speeding up the validation process;
- Developing online knowledge communities/social networks;
- Integrating 3Rs into mainstream scientific meetings.

**What are the most promising new non-animal technologies or approaches that you think have the potential to shape the future of areas where animals are used today, including biomedical research, chemical hazard assessment, efficacy testing, and education and training?**

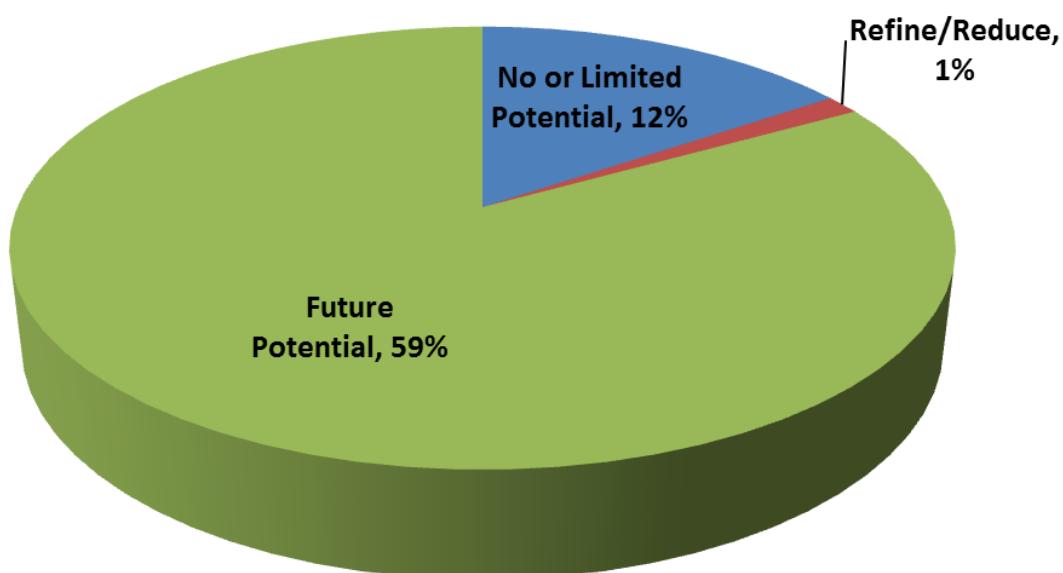
Free text answer – 295 replied, 56 did not reply.

In order to process the answers to this question, categories were defined to capture the ideas which were put forward (Figure 22). These were:

**Future Potential:** those who identified new promising technologies and/or approaches

**No or Limited Potential:** do not believe animal experiments can be replaced in the foreseeable future, limited replacement/reduction may be possible

**Refine/Reduce:** replies based on refinement or reduction without considering non-animal technologies or approaches



**Figure 22** The number of respondents for each category related to ideas concerning promising new technologies or approaches (16% did not reply and 12% did not specifically address the question).

Overall, 59% of the total survey respondents identified promising new non-animal technologies or approaches, 12% of respondents do not believe that the animal model can be replaced in the foreseeable future, whilst 16% did not reply and 12% of replies did not specifically address the question. The remaining 1% gave answers based on refinement or reduction without considering non-animal technologies or approaches.

The main ideas which were put forward as promising new non-animal alternatives are described in more detail below.

**Computational approaches** were seen as promising or very promising by approximately 30% of respondents. These approaches include, for example, the use of *in silico* models for predicting organ toxicity, quantitative structure activity relationship (QSAR) models, and machine learning applications.

**Advanced cell systems** such as stem cells or engineered cell lines were considered as promising by around 25% of answers. Roughly 40% of respondents also identified a strong potential in the application of **technologies** such as **organ-on-a-chip** and **3D cell culture models**.

A multitude of techniques, including **omics**, non-invasive **imaging** strategies, as well as new technologies such as **3D printing**, **next generation sequencing** and **high-throughput screening** were mentioned in around 20% of replies.

**Approaches** such as **Adverse Outcome Pathways (AOPs)**, **Integrated Approaches to Testing and Assessment (IATA)**, **read-across** and the **consistency approach** for quality control of established vaccines, together with the need for more standardisation and harmonisation are seen as having a potentially valuable contribution to regulatory framework(s). **Education and training** is also seen as having a vital role in shaping the future of where animals are used today. Many of respondents suggested investing in new educational tools such as virtual reality, virtual mannequins, e-learning and video training.

## 4 Discussion

The inventory has provided a snapshot of the current, most visible and available KS which are relevant to the 3Rs, whilst the survey has collected the views of the KS users regarding what they think is important, useful or lacking, and what can be done to enhance knowledge exchange in their areas. There is a vast amount of information captured in this study which will merit further analysis if we are to better understand what makes a KS useful and how do people share and access knowledge effectively. For the purpose of this report, we have drawn comparisons between the survey outcome and the inventory in order to understand the current status of 3Rs knowledge sharing, and to provide a starting point for further analysis.

### 4.1 The availability of knowledge sources

This study has collected 800 KS with a potential impact and relevance to the 3Rs, with the majority of the sources having relevance to all 3 of the Rs. These KS serve a wide variety of purposes and audiences, yet the analysis has indicated that there are potentially some areas which could benefit from further development. For example, **education and training** knowledge sources could be more widely disseminated and publicised, and this was also mentioned by the survey respondents as an area which was lacking.

The vast majority of these KS use websites and so they should have good visibility to everyone. Of course, **access** to some KS may not always be free or open, and this is certainly a consideration for the sharing of knowledge. Two thirds of the respondents to the survey consider that there is a **lack of knowledge sources** which are relevant to their activities, and some of these cite a lack of open and free access as a barrier to accessing knowledge. While the majority of the KS in the inventory are open or free access, a number of the KS have restricted access or a fee-based access and this affects how this knowledge can be shared. Although the majority of survey respondents also stated that they consider that they have reasonable access to knowledge sources relevant to their activities, the term "reasonable" suggests that there is room for improvement. Even if there is a good representation of open access 3Rs information in the inventory, the creation of more open access services and coordinated platforms can improve the knowledge sharing process and lead to further developments. Access to information systems represents a solution to enhance knowledge sharing among stakeholders through online systems (e.g. centralised platforms where existing information in a sector or domain is gathered and shared). Data-sharing and increased openness and transparency have been suggested by several respondents to the survey, and would certainly be useful. However, it may not always be feasible when interests of industry (financial, competitive) or issues of propriety rights are touched. These online tools can benefit not only individuals, but also organisations and groups of experts by facilitating their access to information, and further support the exchange of information within research and educational programs.

The inventory also considered the frequency of updating the KS (where this information was available) and it was found that just over half of the KS in the inventory are updated frequently, or have been updated since 2010. Of course, some KS may not need to be updated so frequently, but the lack of updating could be considered by users as an indicator of lack of **reliability** of the information.

Many of the survey respondents also indicated that they consider that there is a vast amount of information available, but that it is not so well **coordinated** or structured. This means that it can be difficult to assess which KS are reliable, hence the preference for face to face opportunities indicated by the survey respondents (see 3.2.2). There is a lot of information available which is relevant to the 3Rs, but how this is coordinated and organised needs to be addressed in order to increase user confidence in the knowledge. Thus, knowledge sharing could not only benefit from curation of the **content**, but also from widening the accessibility of the KS by developing more open access services and

platforms. There are many examples of KS in the inventory which could be considered as leading **providers** of knowledge as they are very well interconnected, use a variety of dissemination channels to good effect and reach a wide audience. How to better coordinate the KS (organisations, platforms, networks, etc.) to reduce the redundancy of the content, identify gaps and to use the current **resources** more efficiently is a question which could potentially be tackled by developing a network between these current leading KS providers. Such a strategy could also address the issues of trust in and reliability of the KS.

## 4.2 Target audiences

For about 13% of the KS the targeted audience was not specified or was not evident, but based on the information provided it was possible to assign those to one or more audience groups. The analysis of the potential audience is, as mentioned, subjective, and so the following observations are to be used only as an estimate of where there are opportunities for KS to reach out to a wider audience.

As expected, the main target audience are the scientists and researchers<sup>19</sup>, followed by regulators and industry. On the other hand, much of this knowledge could serve as a good information source equally for students, educators or other groups of professionals interested or working in areas related to 3Rs (associations, animal welfare, etc.). Similarly, the information explicitly addressed to the general public is much less than that addressed to professionals. However, some of these appear to have a good KS potential for a broader audience, implicitly for the general public (e.g. LabRoots, CCAC Three Rs Microsite, European Parliamentary Research Service Blog, PETA International Science Consortium, etc.) their dissemination materials could be easily understood by non-scientists, and could facilitate a bridge between various public groups with the scientific community. Generally, the global animal welfare NGOs have a good potential to reach out to the general public and disseminate scientific information in a more understandable way for a broader audience. The differences between the potential target audience and the actual target audience are summarised below, showing possible gaps and eventual opportunities.

### *Students*

There is a good representation of activities targeted towards students from academia (as expected) and NGOs, but less visibility of such activities from private companies. Facilitating the access of students (school and university levels) to resources, services and development of new technologies in the area of 3Rs could reduce this gap. There is also an opportunity for private companies to offer training directly on their own products to university students. In summary, there is a high potential for much of the knowledge to also be used by students.

### *Educators*

KS explicitly dedicated to educators (teachers) were generally difficult to identify, yet much of the existing information could potentially be used by educators. For example, books in the area of 3Rs are generally addressed to researchers and scientists, but their potential to be used towards teaching materials is quite high.

### *General public*

Generally, 3Rs KS for the public are not uniformly represented, but this is to be expected as much of the knowledge is intended for specialist purposes. The governmental

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<sup>19</sup> The tag '[researchers](#)' was used to indicate that the KS contains information dedicated to individuals involved and performing research activities or knowledge which can be used for research purposes, while the tag '[scientists](#)' had a broader meaning, covering different categories of professionals (e.g. biologists, veterinarians, medical doctors, etc.) or different scientific purposes.

institutions and NGOs (especially those being active in the area of animal welfare) dedicate sections of their websites or prepare material for the general public. However, considering that social media are used widely by all organisations, it could be that information on 3Rs coming from other sources (industry, biotech, academia) could be useful to the general public interested in this specific domain. Another opportunity is related to publications, which do not target the public (except press releases), thus sections in journals, newsletters or reports could be dedicated to a broader audience, explaining the opportunities, but also the limitations in applying the alternative methods for assessing the safety of drugs, chemicals or other consumer products.

Interestingly, many of the comments from the survey echo what was deduced from the inventory: that is, specific groups are not being targeted by the KS, including students, educators, the public, and according to some respondents, the regulators. Clearly, there is a need to push the knowledge further than it is currently reaching and to increase the beneficiaries of the knowledge. Some of the existing knowledge could be repurposed accordingly as a way of reaching these other groups.

#### *Facilitating knowledge exchange between different groups*

**Non-governmental organisations** are well represented in the inventory, covering broad areas from fundamental studies to animal welfare, educational programs or research funding and professional associations. The interdisciplinary nature of NGOs creates good opportunities for dialogue and knowledge exchange and brings perspectives from different geographic and scientific backgrounds (life scientists together with sociologists, politicians, and technology scientists). The structure and profile of NGOs facilitates the dialogue and the dissemination of ideas and they can also support other organisations by forming groups of experts. The non-profit organisations usually have a broad coverage of activities addressing scientific issues, but also looking at the **public agenda**, and they usually facilitate and provide conferences and workshops, educational programs and publications.

Similarly, the **3Rs Centres**, acting as independent institutions or affiliated to different governmental, NGO or academic bodies, have an important role in supporting and disseminating 3Rs approaches, as well as interconnecting different groups, stakeholders and sectors working towards the same goal of developing and implementing new alternatives to animal testing. These centres have different approaches and strengths, providing some excellent examples of how knowledge from a wide variety of sources can be collected, organised and shared effectively.

Scientists collaborate and share their expertise in events, research programs and publications, as well as within **groups of experts**. The experts organised in various forms (online community, working groups, scientific committees, reviewers, clusters, etc.) are usually brought together by **organisations or research projects**, with the aim of gathering experts (and their knowledge) within a specific area. Thus, the groups of experts facilitate the collaboration between scientists from different sectors (e.g. industry, academia and the public sector) to finally provide a reasoned and evidence-based scientific solution to a specific issue.

In addition, there appears to be an opportunity for **education and training** to facilitate more cross-sector knowledge sharing. E-learning programs could bring scientific and educational materials, events and webinars closer to the users. These online systems facilitate the sharing of information and communication between different stakeholders, enabling global networking. Interdisciplinary workshops focusing on 3Rs could bridge some of the gaps, by using interactive sharing methods which combine knowledge from different sciences, like engineering, life sciences, arts, social sciences or business, to fully exploit the innovative potential of multi-disciplinary teams (e.g. ReThink3R program<sup>20</sup>). These interactive learning methods could also bring together students or

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<sup>20</sup> <https://www.animatch.eu/rethink3R>

educators with industry professionals, therefore facilitating the knowledge exchange from business to academia, and vice versa.

**Research initiatives** present valuable opportunities for knowledge sharing between various groups, and are usually built upon the initiative of organisations or experts and are funded from various public or private resources. The programs could be initiated at national, regional or international level and have a determined duration. Research projects are encouraged (e.g. within EU framework programs) to create partnerships and to include organisations from different sectors such as academia, industry, NGOs, SMEs, etc. Thus, the experts from these organisations can share their experience within joint actions.

There are evidently many opportunities represented in the inventory to facilitate the exchange of information between different groups, yet there are areas which would benefit from further development to also push the knowledge in other directions. It could be considered to repurpose, or adapt, some of the existing knowledge so that it could be used to benefit other groups. Examples of this kind of repurposing include adapting knowledge intended for professional scientists so that it could be used to inform students, or restructuring a report to inform policy-makers.

It is highly important to initiate more strategies to bring people together to facilitate the exchange of information. Some of the survey respondents reported that there is a low exchange of information between different groups and that there needs to be a more unified approach in order to speed up progress.

### 4.3 Education and training

Amongst the many suggestions for improvements in knowledge sharing, the survey respondents also indicated that there could be better provision of education and training opportunities. These suggestions range across **three levels**: *professional, university and school*.

*Professionals* often have limited time for learning and would therefore like better access to e-learning courses. Free, or at least more cost-effective, training courses are also requested by this group. Indeed, around half of the KS categorised as Education and Training in the inventory are fee-based and so increasing the availability of free courses would have a positive impact on knowledge sharing.

At *university* level, there are very few courses which could be identified in the inventory which are specifically teaching the 3Rs (or have a formal component of their courses which addresses the 3Rs). This issue was also raised by the survey respondents as needing attention: there needs to be better provision of 3Rs courses and the teaching materials could also be harmonised to ensure a standard approach across Europe. A further suggestion from the survey was that a mentoring network could be established with established researchers to support early-career scientists.

A few respondents also specified that *school-age* students could also be taught about the 3Rs, and this complements the previous comments about public outreach. Educating students who are making choices about following a scientific career could also raise awareness of the tools available and promote the pursuit of alternative methods within the next generation of innovators, scientists and regulators.

As observed in the inventory (see 3.1.5), KS explicitly dedicated to **educators** were generally difficult to identify. This represents a gap which could be filled by developing more **resources** for teaching and learning across the 3 levels. This could be achieved by establishing, or exploiting existing, partnerships with educators to develop these resources with a view to making them freely available. This would have the added benefit of promoting standardisation of the resources. It is also necessary to consider how to educate the educators, and to communicate the existence of the resources as well as how to use them.

## 4.4 Communicating the knowledge

A KS has to communicate not only its content, but also its existence to its target users. In this respect, a KS possibly invests as much in promoting its existence as it does in communicating its content. Thus the frequency and means of communication become highly important as the preferences and needs of the user ought to be taken into account. The majority of the respondents to the survey stated that their preferred means of knowledge sharing is face to face, whilst only 14% of KS in the inventory were identified as using face to face means for dissemination. Of course, face to face is not always practical or cost-effective, but perhaps this desire for more interpersonal communication comes back to the wish for better coordination of KS: how do people know which ones to trust? The psychology and sociology of how people share knowledge and why certain means of knowledge sharing are preferred is beyond the scope of this study, but these results present a wealth of information regarding the personal experiences of knowledge sharing which could merit further analysis.

The issue of trust could be particularly relevant considering that Directive 2010/63/EU is still relatively young, and so at a national level, ensuring the promotion of alternative approaches may require more confidence in terms of knowing what information is accurate and relevant. There are National Committees in place to ensure that information is distributed effectively, but it is clear from the survey responses that information on new developments needs to be communicated to the right people at the right time. This can be achieved using the effective networks which are currently in place to disseminate information quickly and to the right people.

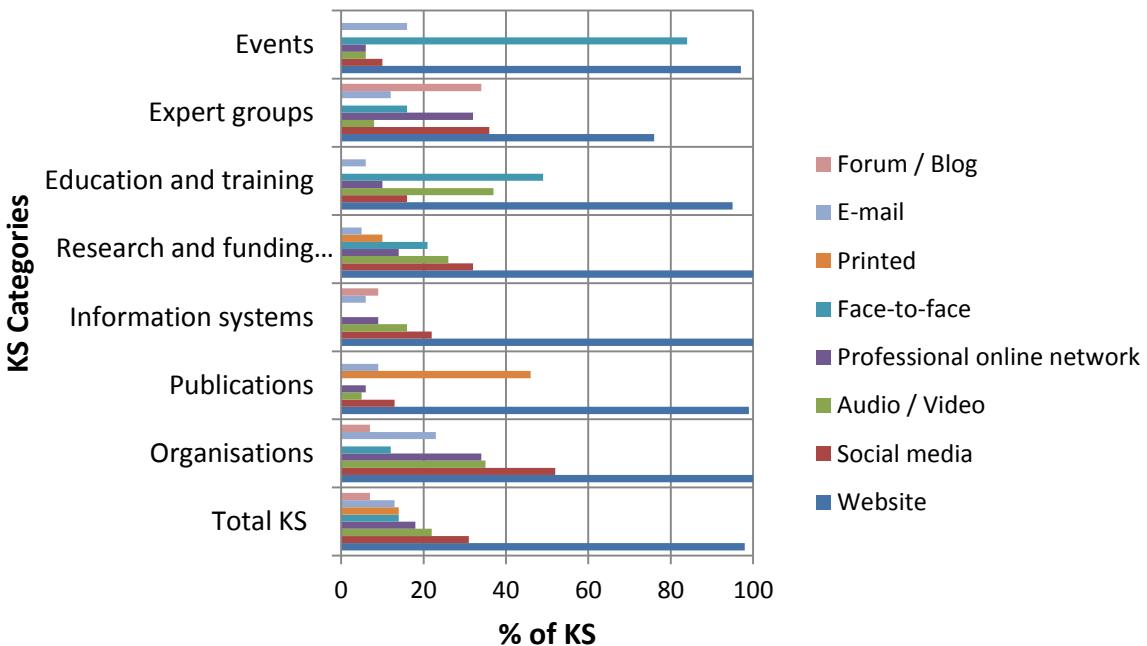
### *Dissemination channels and categories in the inventory<sup>21</sup>*

The fact that KS utilise **websites** the most for disseminating their information (Figure 23) is not surprising as this form of communicating knowledge is highly popular according to the survey respondents. It facilitates a fast, easy to use, easily updatable and, when managed effectively, easily searchable information tool. Other electronic dissemination channels (fora/blogs, e-mail updates/newsletters, social media) are also widely used, for similar reasons.

There are some expected differences between channels used by different KS, such as **publications** use **printed material** more than **events**, which use more **face to face** communications, etc.

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<sup>21</sup> It must be noted that these types of analyses should be taken as "light" observations, as they are based only on what was immediately visible in the inventory.



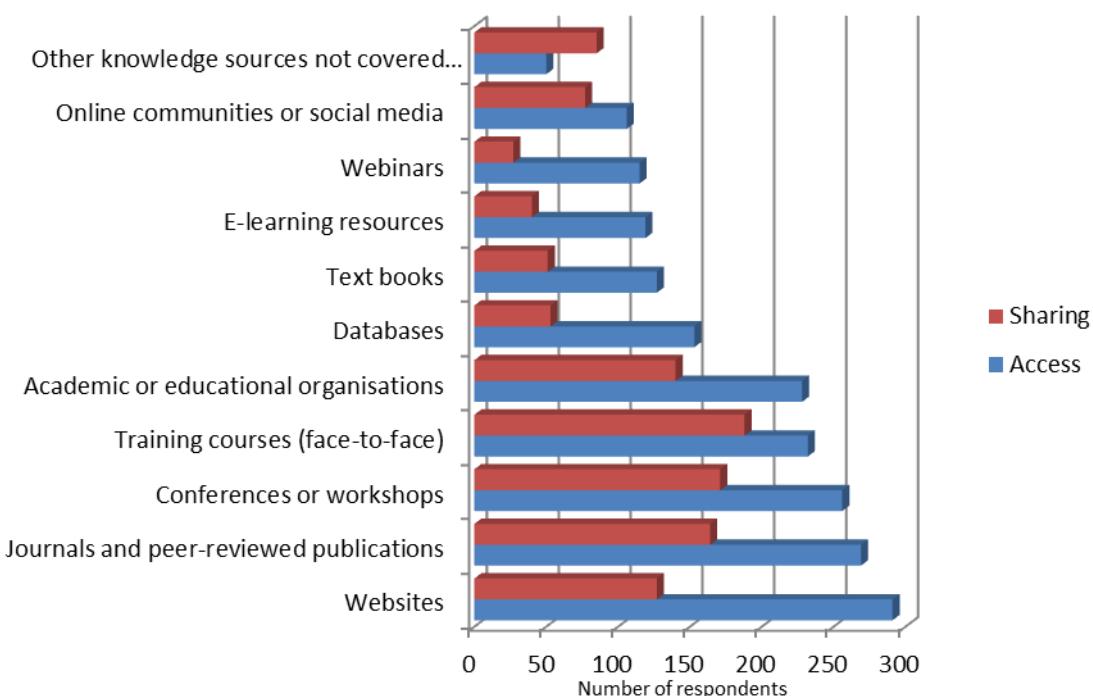
**Figure 23** Different channels used for the dissemination and sharing of knowledge (of KS in the inventory)

There are interesting differences in the use of **social media** across the KS categories. **Organisations** appear to rely on this mode the most, followed by **expert groups**. On the other hand, periodic **newsletters** or updates by **email** are quite popular means of communication amongst the survey respondents. According to some of the answers, this method works well as the audience receives updates without the need to actively look for the new information. It enables people to have the information delivered straight to them and to stay updated with minimal effort or time. The frequency of this kind of communication is also important as sometimes people need to be reminded of the existence of a KS. **Social media** allow for instant alerts to news items in a bite-sized format and it is in fact the second most popular dissemination channel for 4 out of the 7 KS categories in the inventory. Considering the advantages of social media, these may become even more popular in future for more KS, as they represent an "on-the-move" method of communication.

The use of **fora/blogs** is mostly identifiable with the **expert groups**, who seem to use these modes of communication more than **face to face** channels. These groups, along with **organisations**, are also the highest users of **professional online networks**. Furthermore, these tools are also relatively new and thus their use will probably be further exploited in future. Another aspect could be that these channels are more useful to certain target groups, whose members seek immediate answers to very specific problems/questions.

#### *Dissemination channels in the survey*

The survey results show (see Figure 24) the extent by which the various channels used for knowledge access and sharing differ. Apart from the "other" category, it is notable that people tend to use these KS types more for obtaining knowledge than for sharing. This is significant particularly with web-based resources (**webinars**, **e-learning resources** and **websites**). **Text books** are also used significantly less for sharing, whilst journals and **publications** show a smaller difference and an overall greater popularity. As the survey was intended to gain a more personal input on modes of sharing, it is perhaps not so surprising that individuals do not report using **web based tools** for disseminating as extensively as organisations, training programs, information systems, etc. (the KS categories within the inventory).



**Figure 24** Comparison of channels used for access to 3Rs knowledge (blue) versus KS used for sharing of knowledge (red)

**Databases** are well-used by almost half the respondents yet less than one fifth indicated that they use them for sharing. This is mirrored in the survey results where the (open) access to databases was deemed to be lacking (see 3.2.2).

Users obviously have a preference for **face to face training courses** for both obtaining and sharing information as the difference here is not so pronounced. The face to face element features again in the high number of people who reported using conferences to gain knowledge, as well as for sharing their knowledge. In fact, the popularity of **conferences and workshops** is quite similar to **publications**, which is not a face to face interaction, but it could be that this is a trusted resource as it is a peer-review process.

Regarding **online communities** and **social media**, a different picture to the inventory is obtained from the survey, according to which these tools are not highly used for sharing knowledge (Figure 24), the reason for which could be the fact that these tools are relatively new forms of knowledge exchange and so their popularity is still growing. Another explanation could be that information distributed through social media is not curated and therefore deemed less reliable as other sources, as well as often being very fragmented. However, social media certainly has a role to play in publicising 3Rs KS news and events as it is a direct and immediate means of communication.

The "other" KS category, which includes KS such as newsletters, expert working groups, direct requests to other companies for test data, participation in national committees, personal communications, legislation and local surveys (see 3.2.2), is used, according to the survey, slightly more for sharing than for use. The other means of sharing include: giving talks at schools, newsletters, communication of results to animal welfare officers, informal discussions with colleagues and peers, teaching students, expert working groups, internal seminars, blog articles in online publications, dropbox (or other drives). Many of these means of sharing include informal face to face information exchanges, which again suggest that people need to be able to trust the KS.

The discussion points presented in this section and the main clear messages that have emerged from this study can be summarised briefly:

- There are many KS which are relevant to the 3Rs.
- The fragmentation of the knowledge is an issue for many users and it requires better coordination.
- The presentation of some KS could be standardised.
- People need to trust the KS.
- There need to be more opportunities for knowledge exchange between different groups.
- Access to education and training courses is highly valued and there needs to be more free resources for this.
- The knowledge sources need to be better publicised and communicated with the users.

## 5 Conclusions

This study has provided an overview of existing 3Rs knowledge sources which people tend to use. It has also indicated where there are opportunities for improvements to enhance 3Rs knowledge sharing to achieve a greater impact in this area. The inventory (which will shortly be made publically available) will provide a useful basis for future work, as well as a practical tool for others to use as a quick guide to existing KS. The study also shows that in order to accelerate 3Rs knowledge exchange, improvements are desirable which should specifically concern coordination, outreach, education and communication. How this can be done is outlined below.

### Coordinate

According to many of the survey respondents, the high volume of knowledge can be too time-consuming to search, and often there is the question about which KS are valuable, useful or even trustworthy. A one-stop-shop, or centralised portal, may not necessarily be the answer, as there is a multitude of different disciplines and expertise contained within the KS. However, there is certainly a benefit in bringing some of them under an umbrella to be better coordinated. Within the inventory, there are well-connected organisations which are also well-known centres of knowledge. The establishment of a coordinated network of such expert centres, or leading 3Rs knowledge providers, which could work together to guide and facilitate knowledge exchange could also be considered as a strategy to manage 3Rs KS.

Improved coordination of the knowledge could be achieved by exploiting the existing networks and resources as follows:

**Providers** – these are the people behind the knowledge. Developing a more formalised and **unified network** between the **current leading knowledge providers** to manage and curate the knowledge base according to their individual strengths and competencies could facilitate better coordination. These key providers, or centres of 3Rs expertise, need to work together to guide knowledge exchange through coordination of the *content* and *resources*.

**Content** – the knowledge itself. There is a large amount of 3Rs relevant content and so by careful curation of this, gaps and redundancies in the content may be identified more easily. This would not only make the navigation of the content more manageable and less-time consuming, but could also prevent the unnecessary duplication of knowledge. Taking this inventory as a starting point, it is possible to see how the KS can be described and defined in a more uniform way which could facilitate interoperability and the curation of the content.

**Resources** – better use of the existing resources. The use of existing well-curated knowledge bases, search engines and platforms could be **shared** between groups to provide more centralised knowledge sources, saving time and money.

### Outreach

The potential for extending the target audience of many of the KS, particularly to students, educators and the general public, is significant enough to merit further attention. Therefore, a key opportunity which presents itself here is that KS could make themselves more available and accessible to these groups in order to broaden their outreach. A well-informed public generates a stronger incentive for the development, uptake and use of alternatives across all areas where animals are currently used.

**Beneficiaries** – increasing the beneficiaries of the knowledge is recommended to bring about more dialogue and opportunities for knowledge exchange. The establishment of a core knowledge management network can assist with identifying other directions in which knowledge could be directed and the best means of doing so.

**Repurpose** – some of the knowledge which has been developed for specific purposes or groups can be redesigned to inform others and so there needs to be more consideration of how knowledge can be repurposed where possible to address certain gaps.

**Cross-sector** – the need for cross-sectorial exchanges and cooperation is clearly beneficial to progress and there needs to be more opportunities for these types of knowledge exchanges. A closer analysis and identification of what achievements have arisen from these exchanges and initiatives could be undertaken to provide further incentives for funding similar activities to build collaborations.

## **Educate**

Clearly, education and training is a key feature for progress in any area and there are many opportunities to increase and enhance these.

**Three levels** – the approach for education and training should cover three levels: professional, undergraduate and secondary school levels. Firstly, there needs to be more opportunities for **ongoing learning activities for people working in the 3Rs area**. These can include e-learning as well as more practical face to face activities. Secondly, the inclusion of **3Rs-focused modules in university life science courses** is also fundamental to achieving the goal of ultimate replacement of the animal model. The 3Rs could therefore be included as a compulsory and credited component of any life science course to increase the awareness of the alternative approaches as well as the ethical and legislative considerations. This could require harmonisation of what is being taught which could be facilitated by the development of universal *resources*. Finally, bringing the 3Rs into **secondary school education**, to students who are embarking on scientific careers, could also raise awareness of the tools available and promote the pursuit of alternative methods within the next generation of innovators, scientists and regulators.

**Educators** – there need to be more *resources* available for educators across all levels. Enabling educators to incorporate the 3Rs into their activities without increasing their workload is important. **Resources** which can be easily used by the educators as well as trainees should be freely available. Educational materials could be developed in partnerships with educators, and these partnerships could be initiated and coordinated by expert networks. Such resources do exist, but certainly more could be achieved by a better coordinated response from key players.

## **Communicate**

Delivering the existing wealth of knowledge in an effective and timely way to raise awareness where it is needed is crucial and how this is achieved needs to be addressed. The means of communication which are currently being used have been assessed in this study to see what is working and what can be improved. The analysis performed here has indicated that the following actions could be taken:

**Existence** – knowledge sources can do more to make people more aware of their existence. A knowledge source cannot be considered very useful if nobody knows about it, and so publicity can be as important as content. By coordinating and sharing platforms/resources between knowledge providers, the communication of the existence of a source can be amplified.

**Face to face** – one of the main messages which has been delivered by the survey respondents is that face to face communication is highly valued. As a means of dissemination, face to face sharing represents 14% of the KS in the inventory and so this could be considered as an opportunity for the KS providers to increase this mode of communication.

**Frequency** – people appreciate regular updates, such as newsletters by email containing highlights and links to items and other sources. Some organisations are already using this strategy and this seems to be welcomed by users. A coordinated network could collaborate to provide such updates via a shared newsletter to ensure that

busy professionals can access relevant information easily and through a more centralised tool.

Whilst it is true that technology has enhanced the communication potential, the human aspect must still be considered. How people prefer to communicate is a central aspect of knowledge sharing and with this in mind, knowledge should be packaged, structured and shared in a more considered way to have stronger impact.

The findings presented in this report provide a strong evidence base for developing strategies to improve access to knowledge and the sharing of this knowledge to achieve a positive impact on the advancement of the 3Rs. EURL ECVAM has identified the four main areas to be addressed and, with the investment of other key players, will explore the ways in which these opportunities can be realised. However, efficient and effective progress can only be made possible through the collaborative and proactive engagement of a variety of stakeholders and actors.

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## List of abbreviations and definitions

3Rs	Replacement, reduction and refinement of testing on animals
AOP	Adverse outcome pathway
CRO	Contract research organisation
DB-ALM	EURL ECVAM's DataBase on ALternative Methods
DG	Directorate General
Directive 2010/63/EU	European Union legislation on the protection of animals used for scientific purposes
EC	European Commission
ECI	European Citizens' Initiative
EPAA	European Partnership for Alternative Approaches to Animal Testing
ESTAF	EURL ECVAM Stakeholder Forum
EU	European Union
EURL ECVAM	European Union Reference Laboratory for alternatives to animal testing
GmbH	Gesellschaft mit beschränkter Haftung (German) - Limited Liability Company
JRC	Joint Research Centre
KS	Knowledge source(s) - any entity, tool or event that creates, collects, holds or disseminates knowledge with potential 3Rs relevance for the knowledge source types
NC3Rs	National Centre for Replacement, Refinement and Reduction of Animals in Research
NGO	Non-governmental organisation
OECD	Organisation for Economic Cooperation and Development
PARERE	EURL ECVAM's Network for Preliminary Assessment of Regulatory Relevance
SME	Small and medium-sized enterprises
SRL	Societate cu Răspundere Limitată (Romanian) - Limited Liability Company
TSAR	Tracking System on Alternative Methods

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## Annexes

### Annex 1. Identification, categorisation and description of knowledge sources

Knowledge Source Identification	
<b>Knowledge source name</b>	[text box]
<b>Abbreviation</b>	[text box]
<b>Owner/Developer</b>	[text box]
<b>Abbreviation</b>	[text box]
<b>Country</b>	[list of all countries]
<b>Language</b>	multiple selection
<b>URL</b>	[text box]
<b>Contact</b>	[text box]
<b>Contact email</b>	[text box]
<b>Description</b>	[text box]
<b>Photo</b>	[upload photo]

Knowledge Source Category	
<b>Educational/Training Program</b>	Undergraduate program
	Post-graduate program
	PhD program
	Post-doctoral program
	E-learning program
	Training
	Webinar
	Summer / Winter School
<b>Organisation</b>	Governmental Organisation
	Non-Governmental Organisation
	International Organisation
	Academia
	Industry
	R&D Company
	Biotech Company
	Services

	Consultancy
	3Rs Centre
<b>Experts</b>	Scientific Committee
	Experts / Reviewers Panel
	Working Group
	Cluster
	Online Community
<b>Information System</b>	Database
	Knowledge-base
	Wiki
	Specialised website
	Online tool / Search engine
<b>Publication</b>	Journal
	Book / Textbook
	Review article
	Guidance document
	Recommendation
	Protocol
	Report
	Newsletter
	Press release
<b>Research Program/Project/Grant</b>	National / Regional Program
	EU Program
	International Program
<b>Event</b>	Conference
	Workshop
	Seminar / Lecture
	Meeting

Knowledge Dissemination and Sharing	
<b>Dissemination channel</b>	Website
	E-mail
	Audio / Video
	Social media
	Professional online network

	Forum
	Printed
	Face to face
<b>Targeted audience (specified/objective analysis)</b>	General public
	Scientists
	Policy-makers
	Regulators
	Industry
	Researchers
	Educators
	Students
	Not specified
	General public
<b>Potential target audience (subjective analysis)</b>	Scientists
	Policy-makers
	Regulators
	Industry
	Researchers
	Educators
	Students
	Non-specific
	Open access
<b>User access</b>	Restricted access
	User registration
	Free access
	Fee-based access
	Licence [text]
<b>Updating frequency</b>	[text box]

Knowledge Characterisation	
<b>3Rs relevance</b>	Replacement
	Reduction
	Refinement
<b>Purpose</b>	Fundamental studies

	Toxicological and safety evaluation
	Production and quality control
	Efficacy testing
	Diagnosis
	Education and training
	Documentation and information
	Regulatory testing
	Animal welfare
	Validation
	Method development
	Funding
<b>Legislative framework</b>	Directive 2010/63/EU
	Cosmetics Regulation (EC) No 1223/2009
	REACH Regulation (EC) No 1907/2006
	CLP Regulation (EC) No 1272/2008
	Biocidal Products Regulation (EC) No 528/2012
	Plant Protection Products Regulation (EC) No 1107/2009
	Food and feed legislation
	Medicines legislation
	Other
<b>Technology/Tools</b>	Alternative test methods ( <i>in vitro</i> )
	Non-testing methods ( <i>in silico</i> )
	Animal testing ( <i>in vivo</i> )
	Stem cells
	Omics
	Integrated approaches to testing and assessment (IATAs)
	High throughput screening
	High content screening
	3D printing
	Tissue engineering
	Analytics

**Annex 2.** Questions used for the survey on 3Rs Knowledge Sharing

**Survey Questions: Accelerating progress in the Replacement, Reduction and Refinement of animal testing through better knowledge sharing**

1. Please select and briefly describe the knowledge sources that are important to you:

Websites

Web search engines

Webinars

E-learning resources

Training courses (face to face)

Databases

Academic or educational organisations

External experts

Journals and peer-reviewed publications

Industry organisations or initiatives

Research consortia

Text books

Conferences or workshops

Online communities or social media

Other knowledge sources not covered in the list above

2. How often do you consult any of these 3Rs knowledge sources?

Daily

Weekly

Monthly

Several times per year

Less often

3. For which purpose do you consult 3Rs knowledge sources?

Experimental design

Regulatory activities

Biomedical research

*In vitro* method development

Project preparation/evaluation

Teaching or training

Other/specify

4. What benefits has the use of 3Rs knowledge sources brought to your activities?

5. How would you describe yourself or your organisation as a 3Rs knowledge source?

6. Do you proactively share your knowledge? [If yes, then: Please select, give specific

examples and briefly describe how you share your knowledge]

Websites

Webinars

Web search engines

E-learning resources

Training courses (face to face)

Databases

Guidance documents

Academic or educational courses

Peer-reviewed journal publications

Initiatives you or your organisations undertake

Text books

Conferences or workshops

Online communities or social media

Other means of sharing your knowledge not covered in the list above

7. What knowledge sources are lacking that you feel would be relevant to your activities?

8. Do you think you have reasonable access to 3Rs knowledge sources that are relevant to your activities? [If yes, please explain why].

9. What means do you find most effective for exchanging knowledge with others?

10. Do you think current means of sharing knowledge is adequate? [If no, please explain why].

11. What ideas do you have for better sharing of knowledge that would benefit the 3Rs?

12. What are the most promising new non-animal technologies or approaches that you think have the potential to shape the future of areas where animals are used today, including biomedical research, chemical hazard assessment, efficacy testing, and education and training?



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