Report on the systematic, European-wide Institutional Stakeholder Survey on Orphanet in 2017

14. June 2017

Orphanet Institutional Stakeholder Survey (2017)

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1. Introduction

Orphanet was established in 1997 in Paris at the Inserm (Institut national de la santé et de la recherche médicale) by the French Ministry of Health. Its goal was to collect knowledge and information on rare diseases in order to improve diagnosis, treatment/care, and the situation of rare disease patients in general. In 2000, funded by the European Commission, Orphanet was expanded to several other European countries. Since then, it has grown to a consortium of 40 countries in and outside of Europe, still coordinated by the Inserm in Paris. It now constitutes the most comprehensive and reliable information source on all aspects of rare diseases worldwide and is currently funded by the Inserm, the French Ministry of Health, and the European Commission with contributions from member states participating in the European Joint Action "RD-Action".

Orphanet offers a wide range of services on rare diseases and orphan drugs which are freely accessible via the internet and mostly available in at least seven languages. The core of Orphanet is an inventory and classification of all rare diseases known to date, each labeled with a unique identifier, the OPRHA code. Other main services include the collection of scientific data on rare diseases (genes, phenotypes, and disabilities); the directory of expert resources like clinics, diagnostic laboratories, patients' organisations etc.; an encyclopedia with expert-validated texts on rare diseases; an inventory of Orphan drugs; the Orphanet report series, providing information on different aspects of rare diseases in a printable format; and Orphadata including ORDO, providing Orphanet datasets for download.

All Orphanet services are evaluated on an annual basis via an online survey, where a pop-up window opens to Orphanet users on the first page they access. This survey is translated into all seven Orphanet languages (English, French, Spanish, Italian, Portuguese, Dutch, German). It is accessible for several weeks and usually yields a few thousand responses (2016: 4071; 2015: 3795; 2014: 3224). Questions in this regular user survey focus on the professional activity of the users, their habits when visiting the Orphanet website, their opinion of the content as well as their overall satisfaction and suggestions for improvement (for more details, please refer to the Orphanet Reports Series page at http://www.orpha.net/consor/cgi-bin/Education_Home.php).

However, as Orphanet has become increasingly important as an information and data source for official authorities and institutions at a European level and within Member States, it is now necessary to analyze its use with a specific focus on this particular audience. This includes also potential users who may not yet be familiar with Orphanet and its services, but might find it useful for their own professional use or for their institutions in the future. Therefore, within the frame of Work package 3 of "RD-Action", a stakeholder survey was launched, targeting professionals at national authorities, umbrella organisations of the pharmaceutical industry, patients' organisations, and other institutions. In addition to querying the usefulness of the different Orphanet services, the survey contains a section on the general funding of Orphanet, as well as possible institutional contributions to funding of the different Orphanet services (for a detailed description of the current funding situation, please refer to the Orphanet Sustainability Plan, prepared in parallel to this report and soon available on the RD Action website at http://www.rd-action.eu/leaflet-and-documents/). In the following sections, methodology, results and main conclusions of the survey are presented.

2. Methodology

2.1. General remarks

The survey was designed using the professional version of the online program "SurveyMonkey" (www.surveymonkey.com). In order to be able to provide some country specific information regarding the national access frequencies for the different Orphanet services, as well as to include some further specific questions addressed only to the stakeholder subgroup of "Patients' organisations", altogether 32 individual versions of the survey were created, each adapted to the specific needs outlined above. Each survey version was linked to an individual collector, allowing for a separate data retrieval and analysis for each participating Member State.

Since neither additional capacities nor any type of funding were available to translate the survey in all the languages of the different countries selected to participate, and since it was directed mainly to representatives of national authorities and organisations with at least some international links in their professional field, the survey versions of this first round of the survey were available only in English.

2.2. Country and stakeholder selection and identification of relevant contact persons

Being the first European-wide systematic stakeholder survey since Orphanet was launched in 1997 with the main goal to assess the use frequencies of the different services offered by Orphanet and the individual opinions and judgements on the quality and the personal, as well as institutional relevance of these services at a stakeholder level not covered by previous voluntary user surveys (launched annually on the Orphanet website), altogether 28 European Member States including Norway were selected to be included in the survey. This corresponds to a targeted coverage rate of 96,5% of the theoretically eligible European countries. The only Member State not addressed in this first round of the survey was Greece, were currently neither a country team nor even a focal point/contact person for Orphanet exists.

All Orphanet country coordinators – and all contact persons in countries were no Orphanet team is established at the moment – were then (when needed repeatedly) asked to provide contact information for the following groups of addressees in their respective Member State:

- The Ministry of Health or other central governmental Health Authority,
- The Ministry of Social Affairs or equivalent governmental authority,
- The Ministry of Science or equivalent governmental authority,
- The umbrella organisation of the pharmaceutical industry,
- The umbrella organisation of rare disease patients' organisations.

These institutions were to be addressed obligatorily. In addition, each Orphanet country coordinator was asked to identify and nominate further optional institutions, wherever applicable, that might have a particular relevance for Orphanet in their country, like:

- The umbrella organisations of the social insurance system,
- Public and/or private insurance corporations,
- Rare diseases centres at university hospitals,
- Other institutions of specific national interest.

This strategy should allow to identify and subsequently to contact – in a systematic way – the broadest possible range of stakeholders / contact persons in all selected Member States, forming an essential basis and prerequisite to achieve the most comprehensive institutional and geographical coverage across Europe for this survey.

2.3. Principal design of the survey

In general, apart from the first page “Introduction” briefly describing Orphanet and the main goals of the intended survey, the survey is subdivided into the following main chapters and subchapters:

- **General information**: collecting basic data from the individual participant including the country of residence, the type of institution and the link between the professional field of activity and rare diseases.

- **Use of Orphanet services**: collecting general information about the use of Orphanet including general use frequency, awareness of and familiarity with Orphanet and reasons to not use Orphanet (if applicable).

  After this general information, the “Use of Orphanet services” chapter is further partitioned into the following subchapters each requesting information on some aspects of a specific Orphanet services including use frequency, awareness of this service, evaluation of the personal, as well as the institutional usefulness, satisfaction with the quality of the service, and reasons not to use the service. These services comprise:

  - Inventory of rare diseases and classification system
  - Collection of scientific data on rare diseases
  - Directory of expert resources
  - Encyclopaedia (texts on diseases)
  - Inventory of Orphan drugs
  - Orphanet report series
  - Orphadata including the Orphanet rare diseases ontology (ORDO)

- **General use and relevance of Orphanet**: collecting information on how the participants evaluate the country-specific use numbers and, deduced from this, the national relevance of Orphanet.

- **Long-term funding and sustainability of Orphanet**: collecting information on different strategic funding options and concrete funding aspects for Orphanet.

- **Request for improvement and/or information**: collecting individual comments and requests from the participants to be forwarded to the national and/or the central Orphanet team

In order to firstly adjust the length and contents of the survey as good as possible to the needs and restricted time resources of the intended participants, and to secondly keep the number of drop-outs as low as possible, a multiaxial survey design with several response pathways was developed using the question skip logic tool from SurveyMonkey. Thus, participants were only asked those questions in the survey that seemed logical based on their responses to previous questions. For example, as outlined in **Figure 1 A**, when participants indicated that they were experienced in using Orphanet and would access a specific service in the database (in this case the directory of expert resources) on a regular basis (at least a few times a year), they were directed to a group of questions assessing the personal and institutional usefulness of this service and their overall satisfaction with its quality, while respondents that declared to never use the service were first asked whether they are aware of this service at all, and if not, received a brief description of the background and intended uses for this service, followed by two questions evaluating their opinion on the likelihood that they themselves or

their institution might use this specific service in the future. On the other hand, if participants replied to know the service but nevertheless not to use it, they were asked on their particular reasons why this service was obviously not helpful for them.

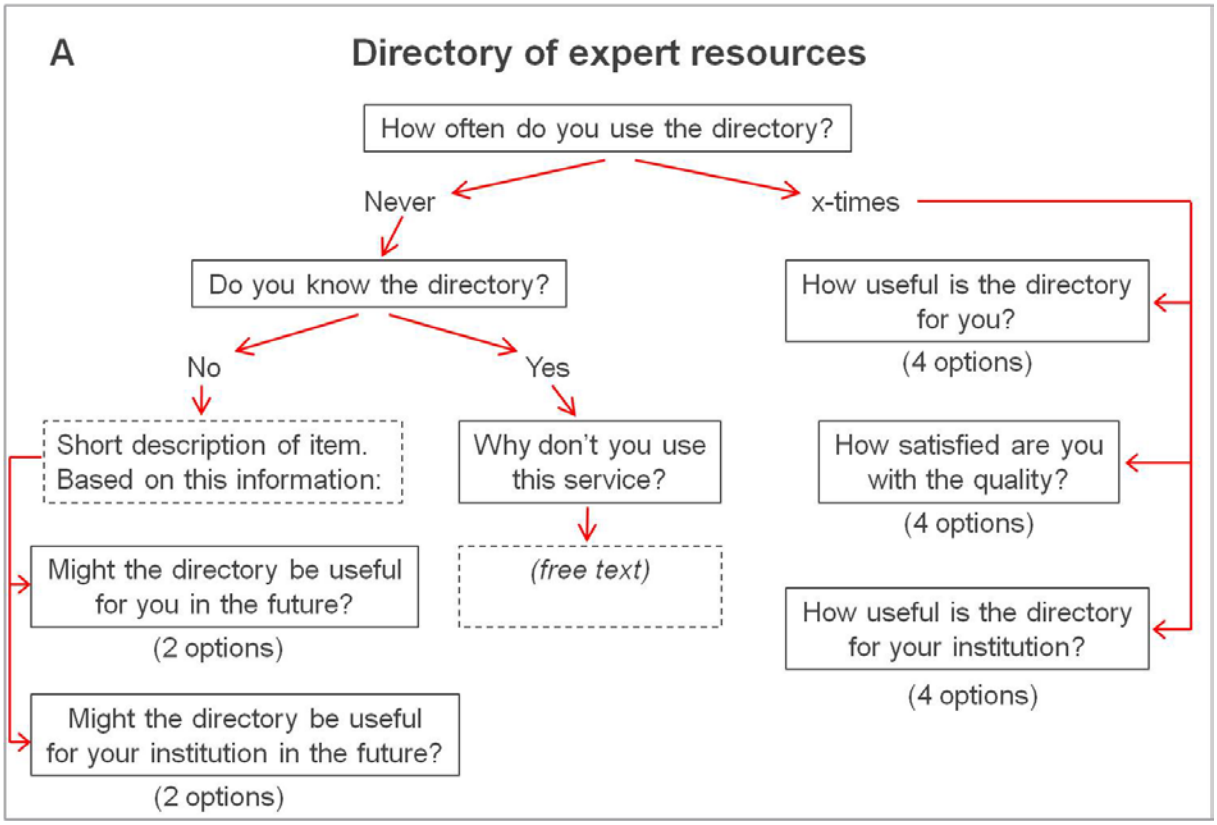

Figure 1 A: Schematic representation of the multiaxial structure of the survey and the question skip logic applied for all questions in the second chapter of the survey ("Use of Orphanet services") including all subchapters, using the example of the directory of expert resources.

This multiaxial design was applied to all questions in the second chapter "Use of Orphanet services" including the related subchapters (see above), thus separating the respondents for each individual service into several response pathways depending on their personal experience with, as well as their needs of this specific service.

The questions in all other chapters ("General information", "General use and relevance of Orphanet", "Long-term funding and sustainability of Orphanet" and "Request for improvement and/or information"), in contrast, were uniformly addressed to all participants. As shown in **Figure 1 B** with the example of the evaluation of possible funding options for Orphanet, all participants replying to the first question ("In your opinion, by which institution(s) should Orphanet be funded in the future?") were directed to the next triplet of questions, independent of their responses to the first (introductory) question.

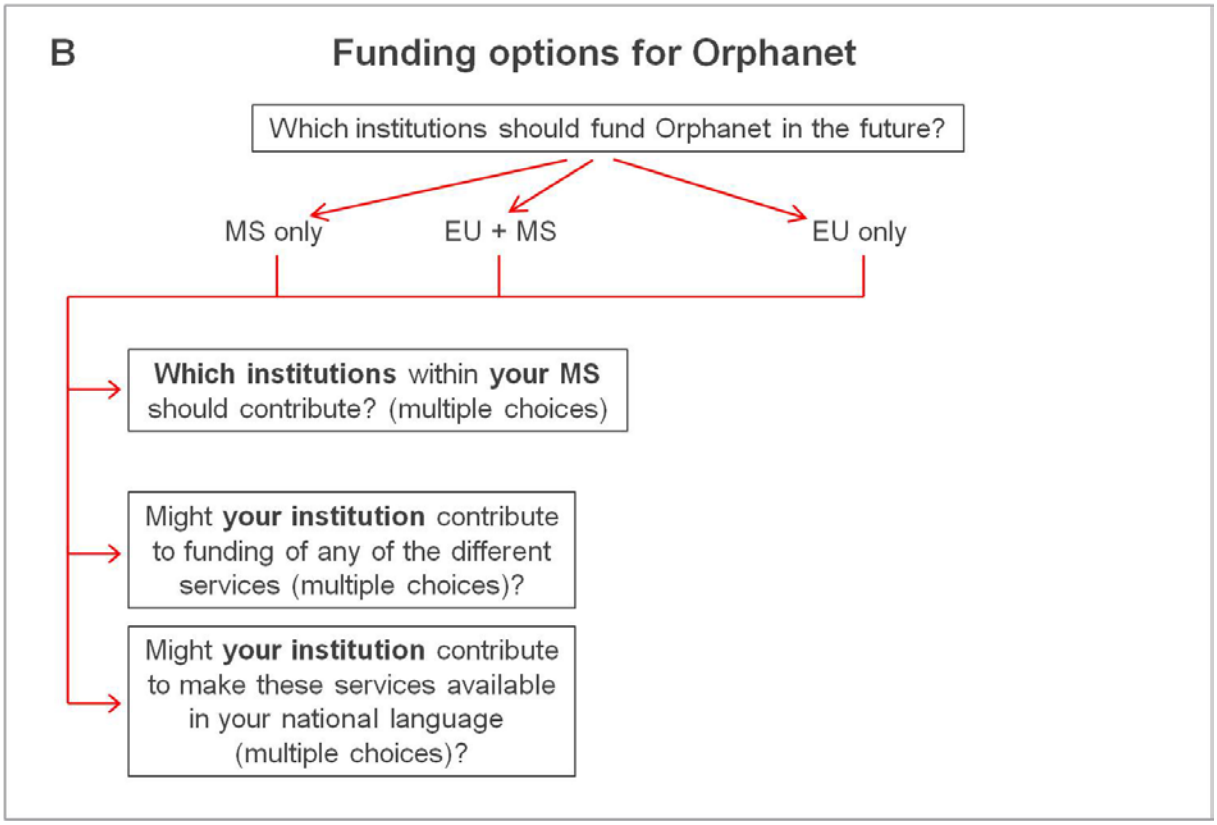

Figure 1 B: Schematic representation of the unidirectional structure of the survey for all questions in the first, third, forth, and fifth chapter of the survey ("General information", "General use and relevance of Orphanet", "Long-term funding and sustainability of Orphanet" and "Request for improvement and/or information"), using the example of the long-term funding of Orphanet.

An example of a complete stakeholder survey for all institutions/organisations except patients' organisations, covering all possible questions (in this case using the example of Austria), is provided in Annex 1 to this report. Looking at the whole document, it is important to bear in mind that due to the multiaxial approach no single stakeholder had to respond to all questions shown in this printed version when filling out the survey online.

3. Results

3.1. Introduction

In the time frame of the first round of this survey, 16 Orphanet country teams from 16 Member States[1] (Austria, Belgium, Bulgaria, Czech Republic, Estonia, Finland, France, Germany, Ireland, Italy, Latvia, Lithuania, Poland, Slovakia, Spain, UK) provided contact details in time for 151 representatives of altogether 129 different institutions and/or organisations, ranging from 3 to 29 institutions and/or organisations per Member State. All 151 representatives were subsequently contacted by personalized email in March 2017 by the Austrian Orphanet team, in charge for this task, with a further brief introduction to the survey, the request to complete it within the next four weeks, if possible, and the respective country- and stakeholder-specific link to the survey. All representatives were additionally informed that they could disseminate the survey further within their institution, either to a colleague more eligible to answer the survey or to further persons within their institution or organisation providing additional views on Orphanet.

Data presented here represent the merged results of all response files available as of May 16th, 2017.

Out of the 151 representatives contacted, replies from 53 participants from 35 institutions and/or organisations from 13 Member States were collected within the first round of the survey. 44 respondents completed all questions they were asked within their specific response pathway within the multiaxial survey, while 9 participants omitted answers to one or more questions. Altogether, these 53 survey participations correspond to a response rate of 35,1 %, spread across 13 Member States so far.

Putting this relative limited number of respondents to the first call in perspective, one has to consider the following aspects:

- The selection process for the stakeholders to be included in this survey, that was chosen to ensure a systematic European-wide opinion survey of key institutions and organisations involved in the health care and research systems of the Member States, automatically limited the number of possible participants to representatives closely linked to these institutions/organisations and with a direct or indirect link to the rare disease field within their institution/organisation;
- Additionally, the number of key stakeholder institutions/organisations varies considerably within the Member States, with some Member States where the responsibilities for instance for the healthcare, the health scientific and the social care areas are spread across three ministries, while in other Member States the same responsibilities are concentrated in one institution only. This in turn further limits the number of potential participants in the survey;
- Compared to the voluntary user survey of Orphanet that is performed on an annual basis running for several days with approximately 40.000 visitors daily, yielding in 2016 altogether 4071 responses, a number that translates into a participation rate of far less than 10% and probably approaching 1%, the relative response rate of around 35% in the stakeholder survey is significantly higher.

However, the still low absolute number of responses has two implications for the data analysis:

Firstly, in some instances the number of participants in the pre-defined stakeholder groups (see chapter 2.2, page 4) is limited to so few individuals only (**Figure 2**) that a re-sorting and aggregation of

[1] Out of the 28 European Member States, 24 have a dedicated Orphanet team in place, while 4 either only have a pp person or no representation at all.

the participating stakeholders to four main subgroups was necessary in order to assess the opinions received in a meaningful way. These subgroups that will be used throughout this chapter are as follows:

- **Ministries** (comprising all participants from the Ministries of Health, Social Affairs and Science, or from the related equivalent governmental authorities);
- **Pharmaceutical Industry** (comprising all participants from the pharmaceutical industry);
- **Other institutional Stakeholders** (further referred to as "**Other Stakeholders**", comprising the following institutions:
    - RD Center head/director
    - Governmental Science Funding agency
    - Rare diseases unit, university hospital and member of temporary working group on rare diseases, Ministry of Health
    - Head of the Unit for Rare diseases and member of rare disease group under the Ministry of Health
    - French National Institute of Health and Medical Research
    - Association pharma industry[2]
    - Hospital association
    - Board of private insurance companies
    - Charity[3]
    - Riga Stradins university
    - NHS Genomic Advisory Organisation
    - Healthcare provider/commissioner organisation
- **Patients' organisations** (comprising all participants from patients' organisations).

Secondly, it needs to be stressed that due to the low absolute numbers of respondents the results presented in this report represent opinion trends only making it impracticable to analyse any dataset in a statistical sense. However, as will become apparent in the subsequent subchapters, in particular the more institutional stakeholder subgroups often reveal a largely similar opinion profile in the different questions, underlining the robustness of the data in general independent of the limited participation figures in some stakeholder subgroups.

3.2. Distribution of and general information on the participants

Figure 2 displays the proportional distribution of the different stakeholder groups in the survey, highlighting the relative good coverage of representatives from the Ministries of Health, the pharmaceutical industry and the group of other stakeholders, as well as the low participation rate of representatives from the Ministries of Sciences and Social Affairs that finally led to the decision of the data aggregation of all ministries into one subgroup (see above). With this rearrangement, the more institutional subgroups ("Ministries", "Pharmaceutical industry" and "Other institutional stakeholders") form three similar sized participant blocks, ranging between 24%-36% of all respondents, while the subgroup of "Patients' organisations" constitutes a relative small block encompassing only 7% of all participants.

[2] According to its name, this association seems to belong to the subgroup of the "Pharmaceutical industry"; however, since the representative of the association answering the survey deliberately chose the choice box "Other institution" and not "Umbrella organisation of the pharmaceutical industry" that was also offered as a response option, we decided to follow the participants' request and choice.

[3] Similarly, the Charity probably belongs to the subgroup of "Patients' organisations"; however, since its representative again deliberately chose the choice box "Other institution", we respected this request when aggregating the stakeholders.

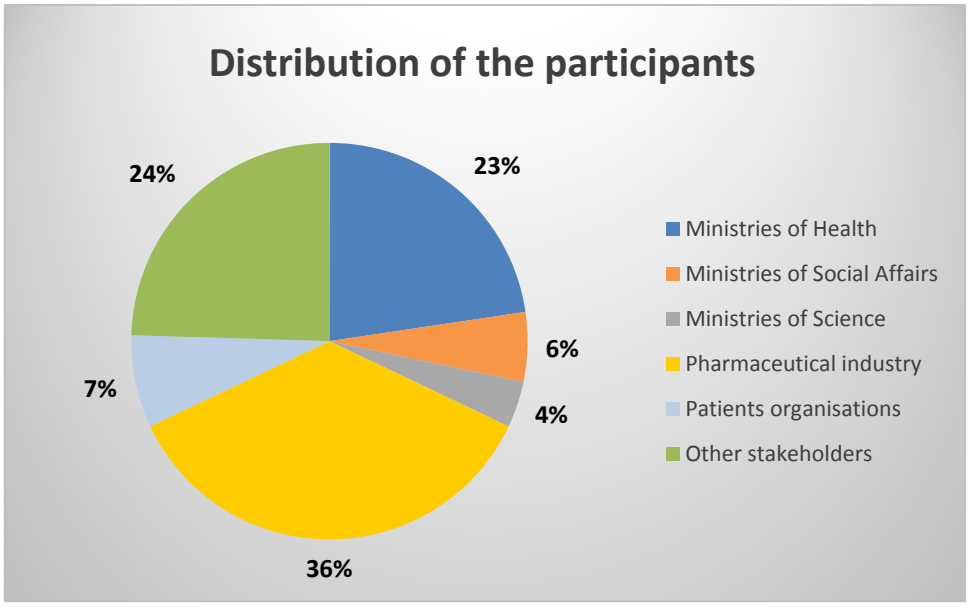

Figure 2: Relative distribution of the survey participants sorted by stakeholder category (n = 53).

Further asked to indicate their level of professional involvement in the field of rare diseases, an almost two-third majority of respondents replied that activities related to rare diseases constitute one part of their day-to-day work but that they have other obligations, too, while another one-third of participants declared that activities in the rare disease area represent the main part of their professional activity. Only 4% of the respondents stated to have no professional link to the rare diseases field at all (**Figure 3**).

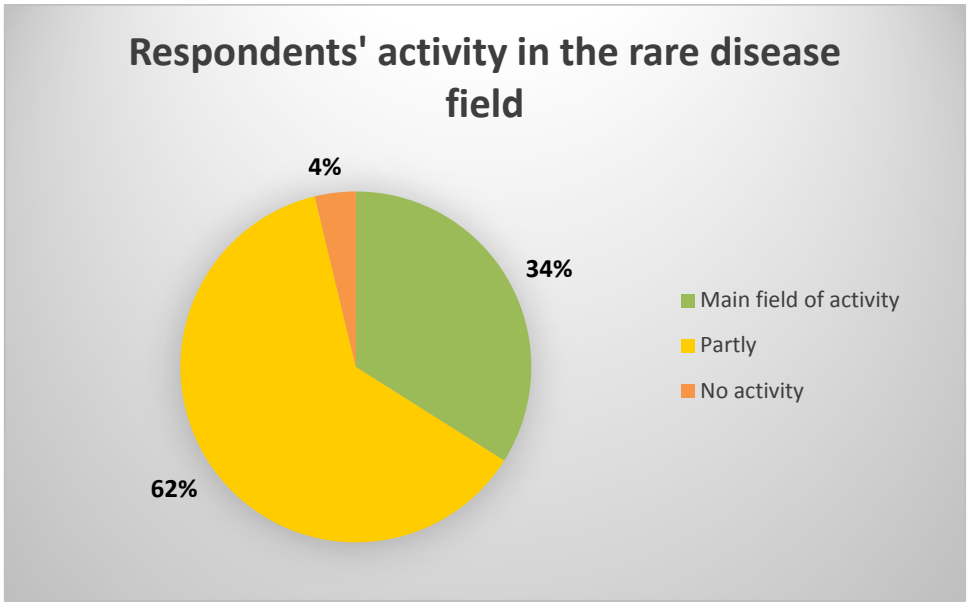

Figure 3: Relative distribution of the participants' professional link to and activity in the rare diseases field (n = 53).

3.3. General use of Orphanet

Before analysing the access rates for specific services offered by Orphanet, as well as the personal and institutional opinion on the usefulness and quality of these services, participants were asked to indicate how often they use Orphanet in general. As shown in **Figure 4 A-C**, three out of the four stakeholder subgroups, the “Ministries”, the “Pharmaceutical industry” and the “Other institutional stakeholders”, display a relatively similar picture regarding their use of Orphanet: While a small fraction, based on individual users, consult the database several times a week or at least weekly, approximately two-thirds of the respondents access Orphanet either monthly or, even more often, only few times a year.

This use profile might be explained by the fact that for the majority of participants (66%) rare diseases constitute only a part, or are not part at all, of their professional activities (see **Figure 3**). Thus, depending on the specific demands of the individual stakeholders, only a limited number of website visits seems to be necessary to gain the information needed. However, as will be shown in subchapter 3.8 (“General use and relevance of Orphanet”), these limited access rates do not diminish the high level of acknowledgement and appreciation these stakeholder subgroups exhibit regarding Orphanet (see **Figure 27** on page 50).

Participating patients’ organisations on the other hand, the fourth stakeholder subgroup, show a significantly different general use profile, with 100 % of the respondents accessing Orphanet at least weekly. While patients’ organisations and patients are certainly not the only addressee of Orphanet, they constitute, complementary to medical experts and general and more specialised physicians, one of the main target groups of the database, and the high access frequency indicates that Orphanet here indeed serves a high demand (**Figure 4 D**).

However, as pointed out in the introduction to this chapter, these access numbers originate from obviously active patients’ organisations participating in the survey following the first call. It needs to be corroborated in the follow-up phase of the survey, when further patients’ organisations have been recruited to participate in the survey by further calls, whether these figures indeed hold true or whether they might decrease when the opinion profiles of probably less strong and active patients’ organisations are included in the analysis.

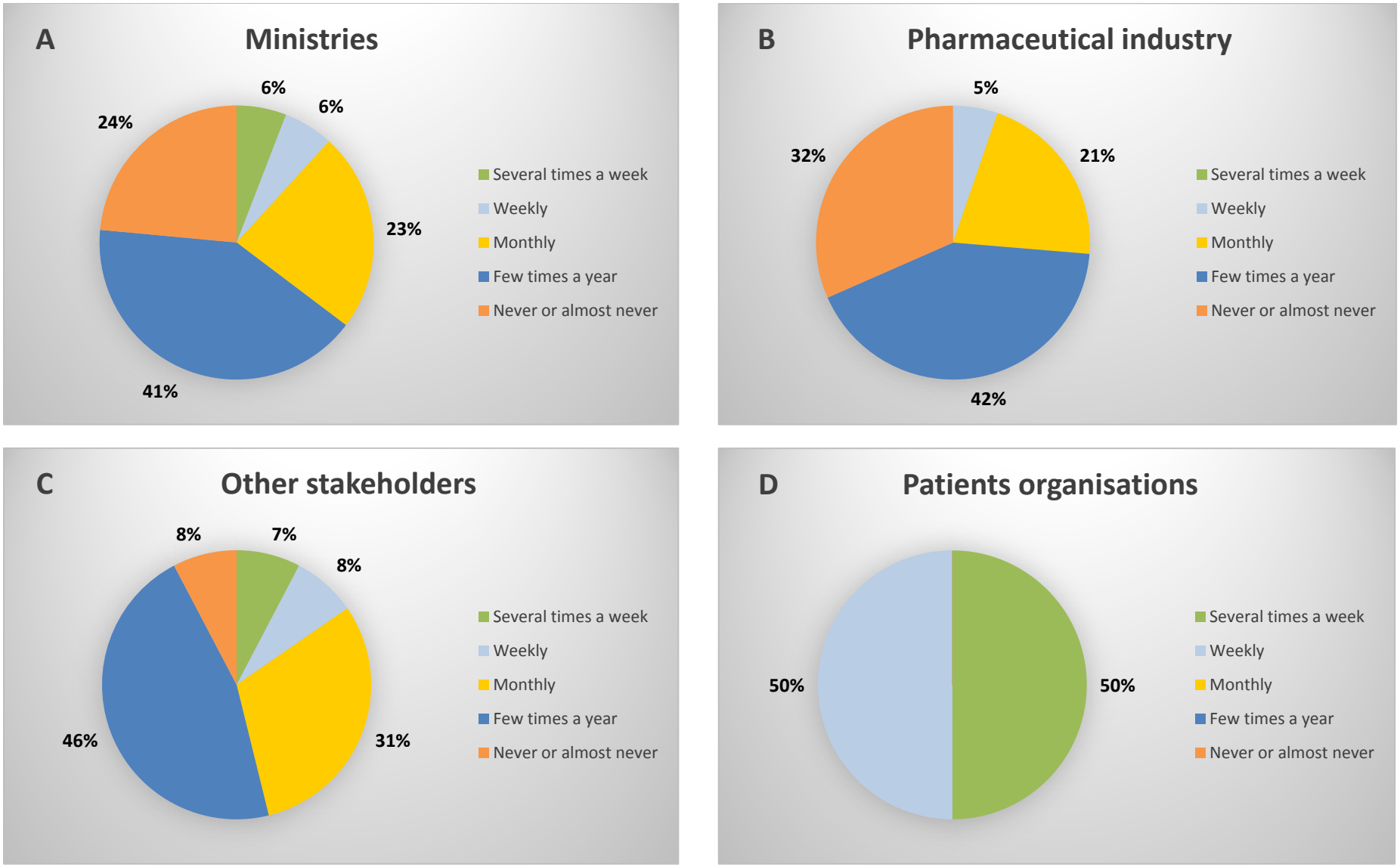

Figure 4: General use frequencies of Orphanet by (**A**) Ministries (n = 17), (**B**) Pharmaceutical industry (n = 19), (**C**) Other institutional stakeholders (n = 13) and (**D**) Patients' organisations (n = 4).

Apart from their institutional/organisational background, all participants were further asked whether they are aware of Orphanet and its services in general in order to get a better picture in particular of those respondents that indicated in the previous question – and/or will indicate this in the following questions covering the different services of Orphanet – to never or almost never use Orphanet. As outlined in **Figure 5 A**, 87% of the respondents in this survey are aware of Orphanet and its services, while 13% did not read or hear about the database before.

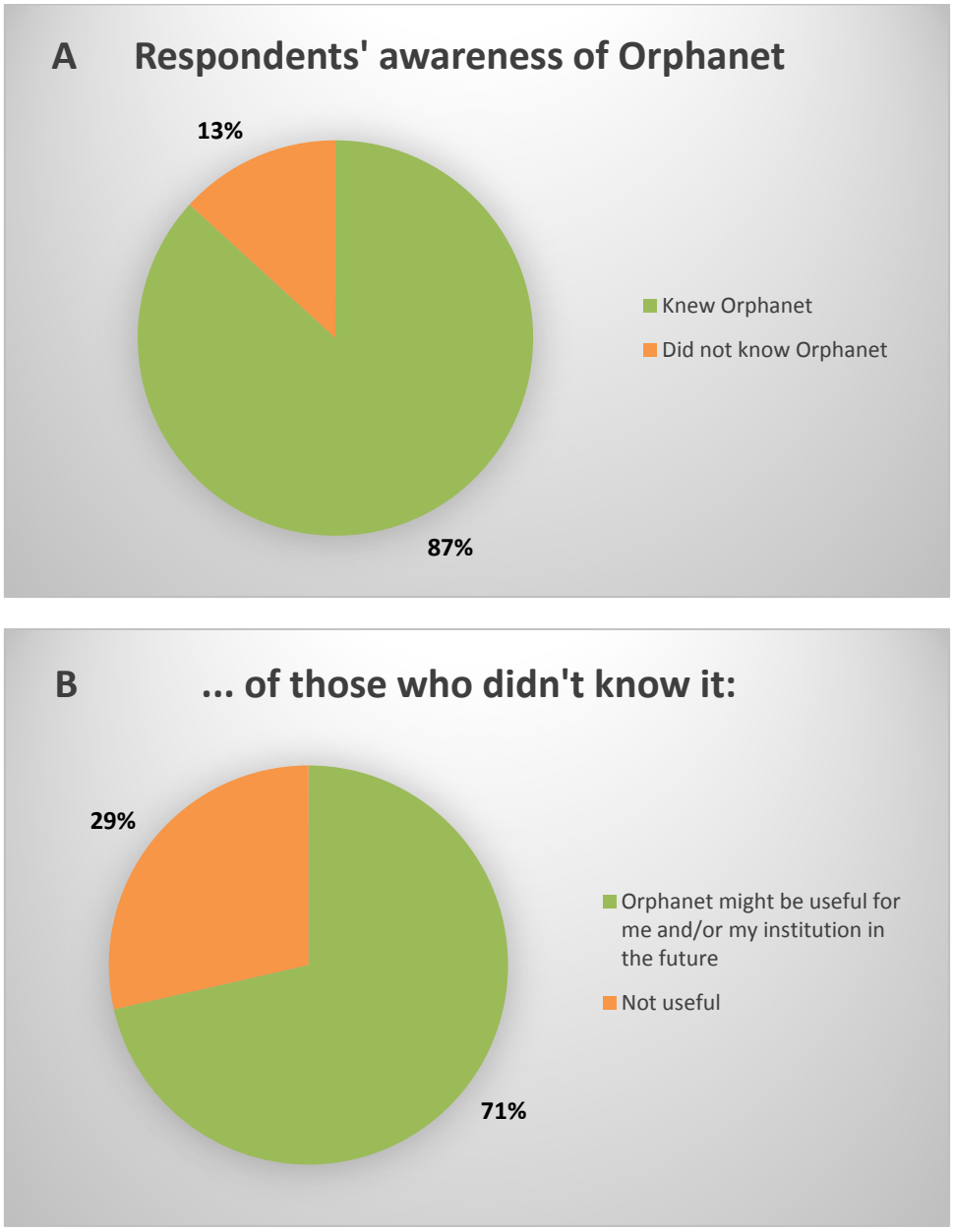

Figure 5: **A** Level of awareness on Orphanet of all participants independent from their stakeholder affiliation (n = 53). **B** Percentage of participants previously not aware about Orphanet that could imagine to use Orphanet and to benefit from its services in the future (n = 7).

That means, for instance, that the 21% of all participants that declared in the previous question to never or almost never use Orphanet in general (24% from the ministries, 32% from the pharmaceutical industry and 8% from the group of "Other institutional stakeholders"; see **Figure 4**) resemble two separate cohorts: one group comprising around 8% that either rarely access Orphanet, or does not use Orphanet at all despite knowing the database, because they have no professional demand in seeking that type of specific information offered by the database, and a second group covering this

13% of participants in the survey that in-fact never used Orphanet since they did not know about the database.

Those 13% of respondents being unaware of Orphanet so far were automatically directed to a different question pathway and first received the following basic information on Orphanet:

> Orphanet (www.orpha.net) is the only available database worldwide providing comprehensive validated, quality-controlled, expert-reviewed information on rare diseases. Orphanet is now the official reference-database for rare diseases of the European Union. It offers a wide range of freely accessible services on rare diseases and orphan drugs, most of them in at least seven languages:
>
> - inventory and classification of all rare diseases known to date with a numeric identifier (ORPHAcode)
> - information on genes, phenotypes and disability facts related to rare diseases
> - epidemiological data on rare diseases (i. e. prevalence, incidence, birth prevalence)
> - encyclopedia of rare diseases
> - inventory of orphan drugs
> - directory of expert resources on rare diseases (expert centres, medical laboratories, patient organisations, research projects, clinical trials, registries, networks, research infrastructures) for each of the member states and beyond (40 countries)
> - an assistance-to-diagnosis tool allowing users to search by signs and symptoms
> - encyclopedia of recommendations and guidelines for clinical practice, emergency medical care and anaesthesia, and of disabilities related to rare diseases
> - bi-weekly newsletter in English and French
> - a collection of thematic reports free for download on the Orphanet website
>
> For more information, please go to the Orphanet national website (*specific link to the respective national website*) and/or contact the Orphanet national team at (*specific e-mail address of the contact person(s) in the respective national team*).

Subsequently, when asked whether they could imagine, based on this information, that one or several services might be useful for them personally and/or for their institution in general, 71% of the respondents indicated to see a potential use of the database and its services in the future, while the remaining 29% declared to see no further benefit for their day-to-day work or that of their colleagues in their institution (**Figure 5 B**).

3.4. Inventory of rare diseases and classification system

Basic information:

Orphanet provides a comprehensive inventory of rare diseases classified according to a polyhierarchical classification system. To date, almost 6,000 diseases are listed. Entries are cross-referenced with ICD-10, OMIM, UMLS, MeSH, and MedDRA. The Orphanet rare disease inventory and classification system is available in seven languages and is constantly updated based on documented sources and expert advice.

Each disease entity listed in Orphanet is assigned a specific, unique identifier, the so-called Orpha number or Orpha code. This Orpha number can be found in the list of rare diseases, directly below the name of the respective disease. It allows for an unambiguous coding of each rare disease according to the Orphanet classification of rare diseases and can therefore, after integration into the respective Health information systems, serve as ideal tool to identify RD patients unambiguously.

Survey results[4]:

Analysing the answers obtained for the use frequencies of the inventory of rare diseases and the Orphanet classification system, a similar picture emerges as already observed in the previous category assessing the general use rates. Again, three out of the four stakeholder subgroups (the "Ministries", the "Pharmaceutical industry" and the "Other institutional stakeholders") display comparable profiles with 64%-77% using the inventory of rare diseases and the classification system monthly to few times a year, with individual stakeholders within the subgroup "Other stakeholders" consulting this service in part far more often (**Figure 6 A-C**), while the remaining respondents (between 36% of the participants from the pharmaceutical industry and 8% from the subgroup "Other stakeholders") never/almost never consult this service. Participating patient organisations, on the other side, are set apart, with 75% accessing the inventory of rare diseases and the classification system at least weekly and no responding patient organisation that does not use this service at all (**Figure 6 D**).

Again, these results illustrate that those stakeholders that are most deeply involved in the matter of rare diseases – in the context of this survey the patients' organisations – also show the highest use frequencies, while the other stakeholders, for whom rare diseases are only part of their range of responsibilities, if they belong to it at all, have lower information needs and accordingly lower access rates to the database.

Importantly, when further asked about their level of satisfaction with the quality of the inventory of rare diseases and the Orphanet classification system, all stakeholder subgroup show a similar high level of satisfaction, with percentages ranging from 86%-100% of respondents being quite to very satisfied, and no participant that declared to be not satisfied at all with the quality of this service (**Figure 7 A-D**).

Finally asked about the usefulness of the inventory of rare diseases and the Orphanet classification system for their personal work, 86%-100% of the respondents rate this service to be quite (in the majority of answers) to very useful (in some cases), with only one individual denying any reasonable use at all (**Figure 8 A-D**). Similarly, 73%-100% of participants rate this service also quite to very useful for the work in their institution in general, again with one individual assigning this service a limited value only (**Figure 8 E-H**). These on average high values highlight the fact that even stakeholders with lower use frequencies highly acknowledge and appreciate the existence of this service, when needed.

[4] Of note, the following questions were directed only to those participants that previously had indicated to be familiar with Orphanet and to use the database at least a few times a year.

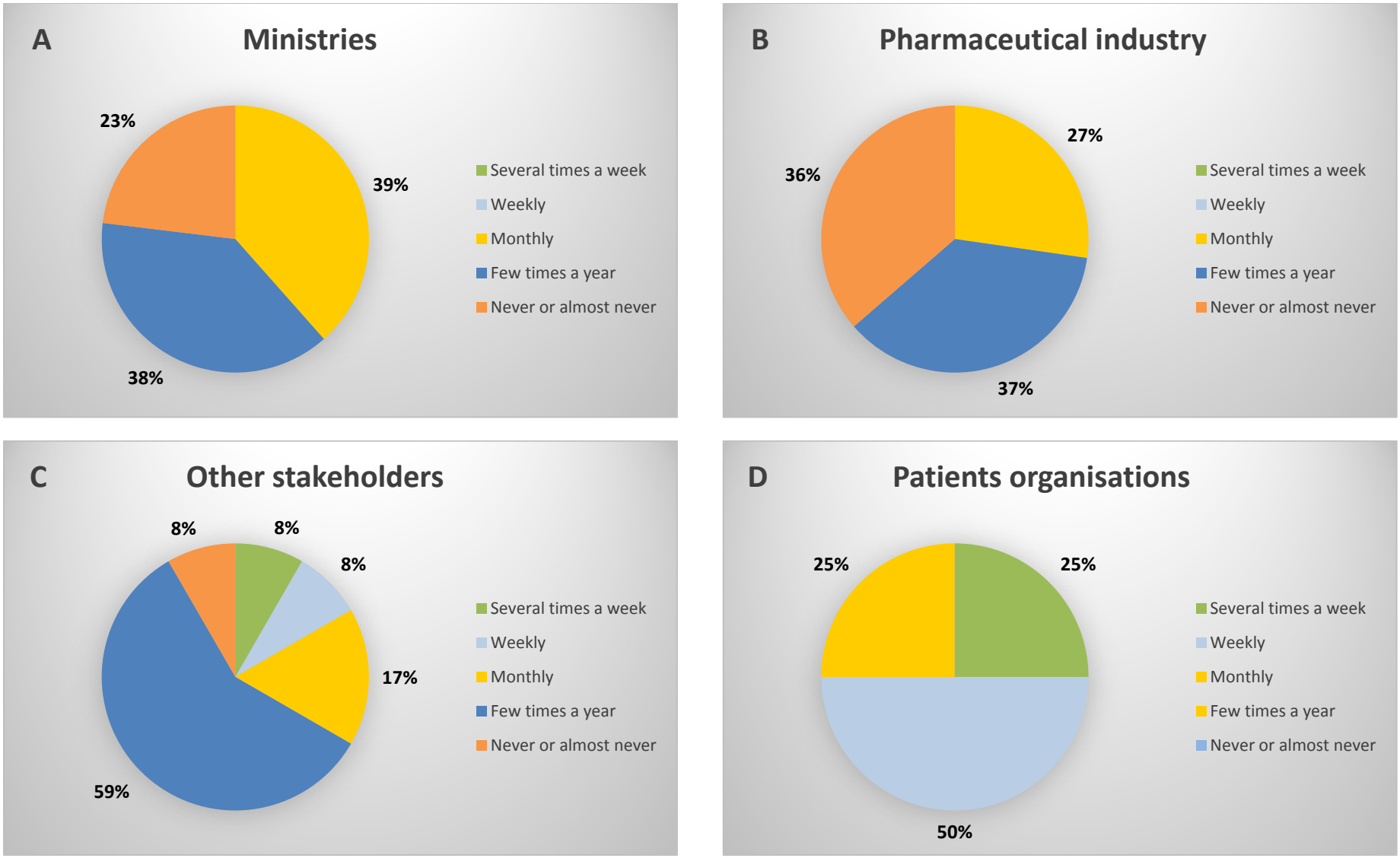

Figure 6: Use frequencies of the inventory of rare diseases and the Orphanet classification system by (**A**) Ministries (n = 13), (**B**) Pharmaceutical industry (n = 11), (**C**) Other institutional stakeholders (n = 12) and (**D**) Patients' organisations (n = 4).

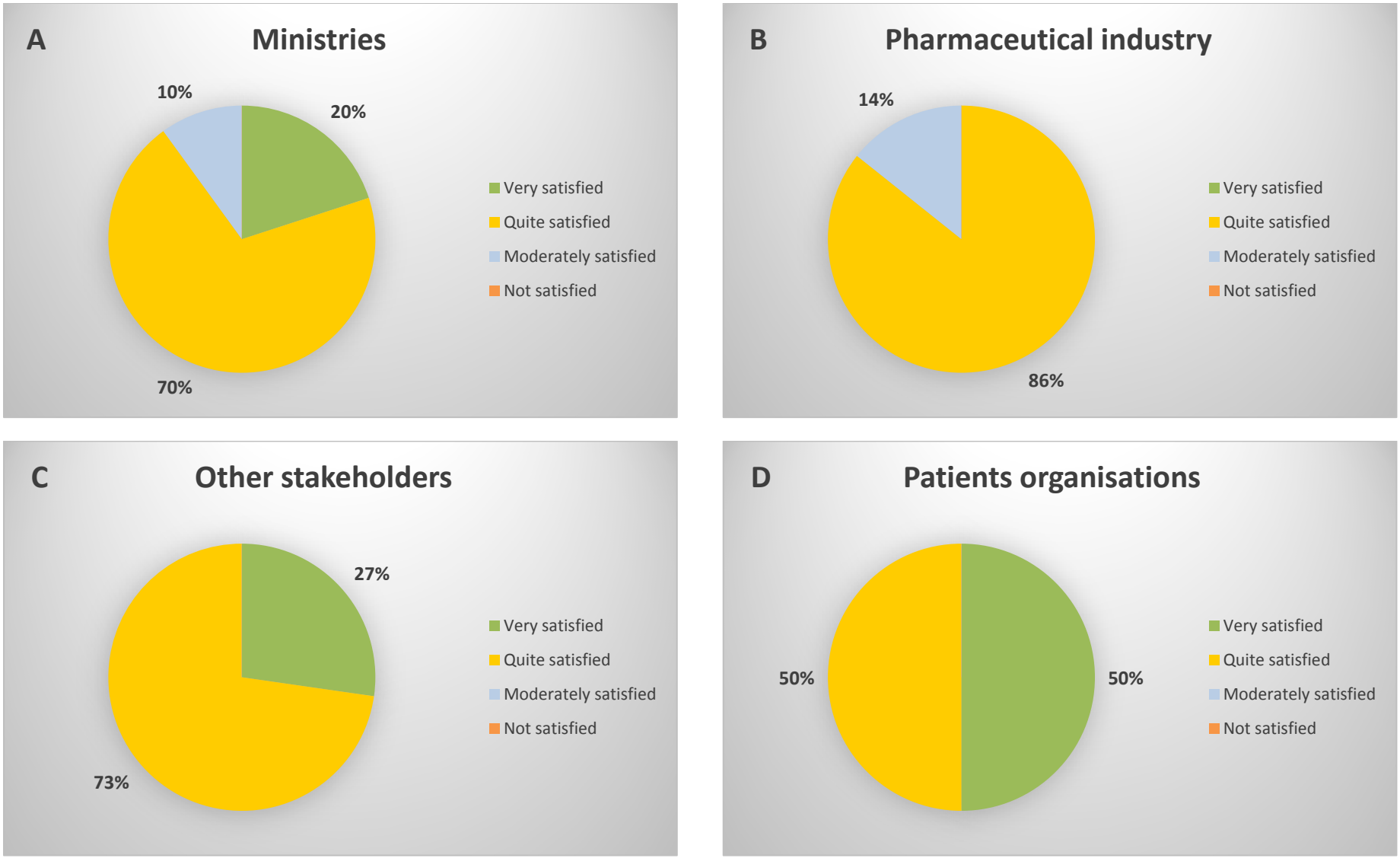

Figure 7: Level of satisfaction with the quality of the inventory of rare diseases and the Orphanet classification system by (**A**) Ministries (n = 10), (**B**) Pharmaceutical industry (n = 7), (**C**) Other institutional stakeholders (n = 11) and (**D**) Patients' organisations (n = 4).

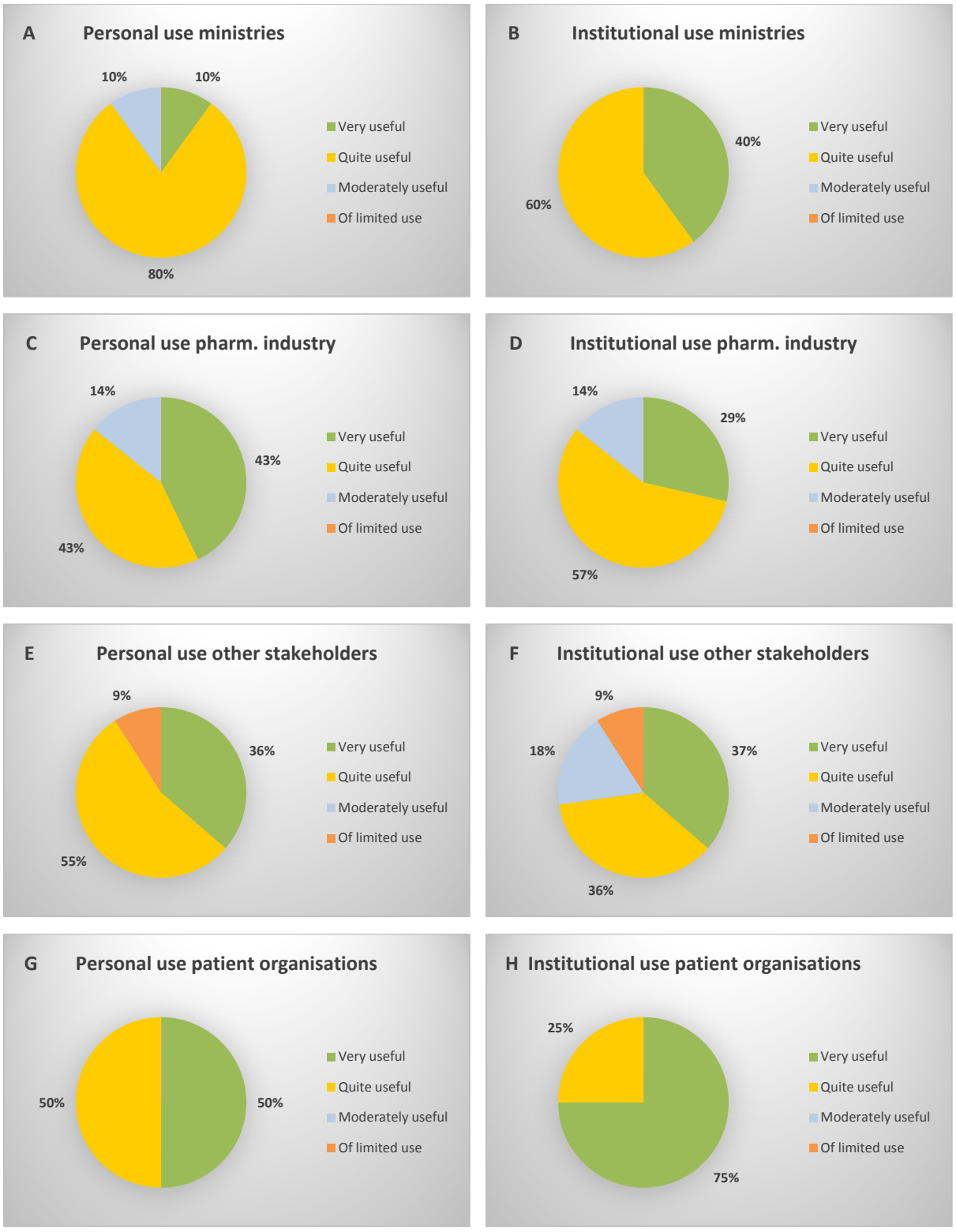

Figure 8: Evaluation of the personal (left) and institutional (right) usefulness of the inventory of rare diseases and the Orphanet classification system by (**A,B**) Ministries (n = 10), (**C,D**) Pharmaceutical industry (n = 7), (**E,F**) Other institutional stakeholders (n = 11) and (**G,H**) Patients' organisations (n = 4).

3.5. Collection of scientific data on rare diseases

Basic information:

Orphanet provides several collections of scientific data on rare diseases (including data collections on genes, phenotypes, and disability facts). In order to increase their scientific value and their usability, these datasets are cross-referenced to a range of other databases.

This includes the annotation of the Orphanet inventory of rare diseases with:

- The corresponding terms of the Human Phenotype Ontology (HPO), a standardized and controlled terminology covering phenotypic abnormalities in human diseases;
- Associated genes, with a characterization of the relationship between the gene and the disease (causative, modifier, susceptibility or playing a role in the phenotype) and the kind of mutation (germline or somatic);
- Functional consequence(s) recorded by frequency in the patients' population, temporality, degree of severity and loss of abilities (if applicable).

Furthermore, the inventory of rare diseases is cross-referenced with other medical languages (OMIM, ICD-10, MeSH, MedDRA and UMLS), while the inventory of genes is cross-referenced with genetic databases (HGNC, OMIM, UniProtKB, IUPHAR, and Genatlas), thereby ensuring interoperability between databases and registries.

Collectively, this service is designed to increase the knowledge on rare diseases, to support research, and to ensure interoperability between databases and registries.

Survey results[5]:

Asked about their use frequency of the various collections of scientific data on rare diseases in Orphanet, 70%-90% of the survey participants from the stakeholder subgroups “Ministries”, “Pharmaceutical industry” and “Other institutional stakeholders” indicated to consult this service at least few times a year (the majority of respondents) or monthly, with an individual higher access rate in the “Ministries” subgroup, while 10%-30% never or almost never connect to this service (**Figure 9 A-C**). Taking into account that the subgroups “Ministries” and “Other institutional stakeholders” include many stakeholders from the health policy and health care level, it seems plausible that the high proportion of non-users in these stakeholder subgroups is related to the more limited demand of this type of data in their daily work (in contrast to the “Pharmaceutical industry” subgroup, where the proportion of users is generally slightly higher and of non-users significantly lower, when compared to the other two institutional subgroups).

Participating patients’ organisations show a slightly different, evenly distributed access profile with equal use frequencies ranging from few times a year to several times a week. Again, no patients’ organisation indicated to never use the various collections of scientific data on rare diseases (**Figure 9 D**). However, apart from the fact that patients’ organisations have at least some interest in this service, the number of participating organisations and the spread of individual answers do not allow to distil any further tendencies out of these replies.

Asked about their level of satisfaction with the quality of the various collections of scientific data on rare diseases in Orphanet, all stakeholder subgroup show a similar high level of satisfaction, with percentages ranging from 78%-100% of respondents being quite to very satisfied, and no participant being not satisfied at all with the quality of this service (**Figure 10 A-D**).

[5] Again, the following questions were directed to those participants only that previously had indicated to be familiar with Orphanet and to use the database at least a few times a year.

Assessing the personal and the institutional usefulness of the various collections of scientific data on rare diseases, 67%-90% of respondents declare that they rate this service to be quite (in the majority of answers) to very useful (in some cases) for their personal work, with only few selected individuals in the "Other institutional stakeholders" subgroup seeing only a limited demand for the collections of scientific data in their personal work (**Figure 11 A-D**). A similar picture is revealed when analysing the opinion of the respondents about the usefulness of the collections of scientific data on rare diseases for the different institutions in general. Here, 55%-100% of the participants rate this service quite to very useful for the work in their institution, with no stakeholder denying any usefulness at all (**Figure 11 E-H**). Like before, these on average high values highlight the fact that even stakeholders with lower use frequencies highly acknowledge and appreciate the existence of this service, when needed.

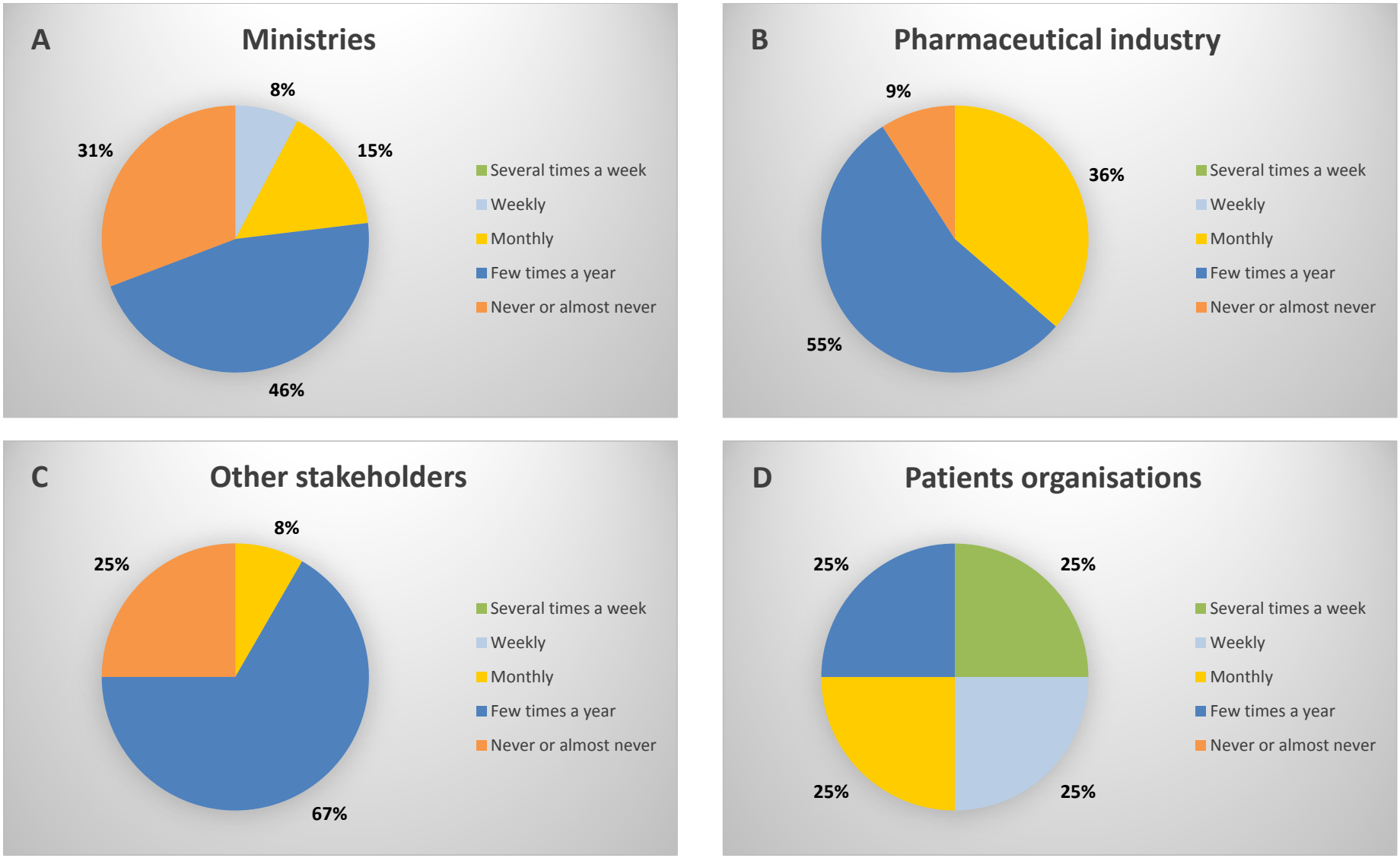

Figure 9: Use frequencies of the various collections of scientific data on rare diseases by (**A**) Ministries (n = 13), (**B**) Pharmaceutical industry (n = 11), (**C**) Other institutional stakeholders (n = 12) and (**D**) Patients' organisations (n = 4).

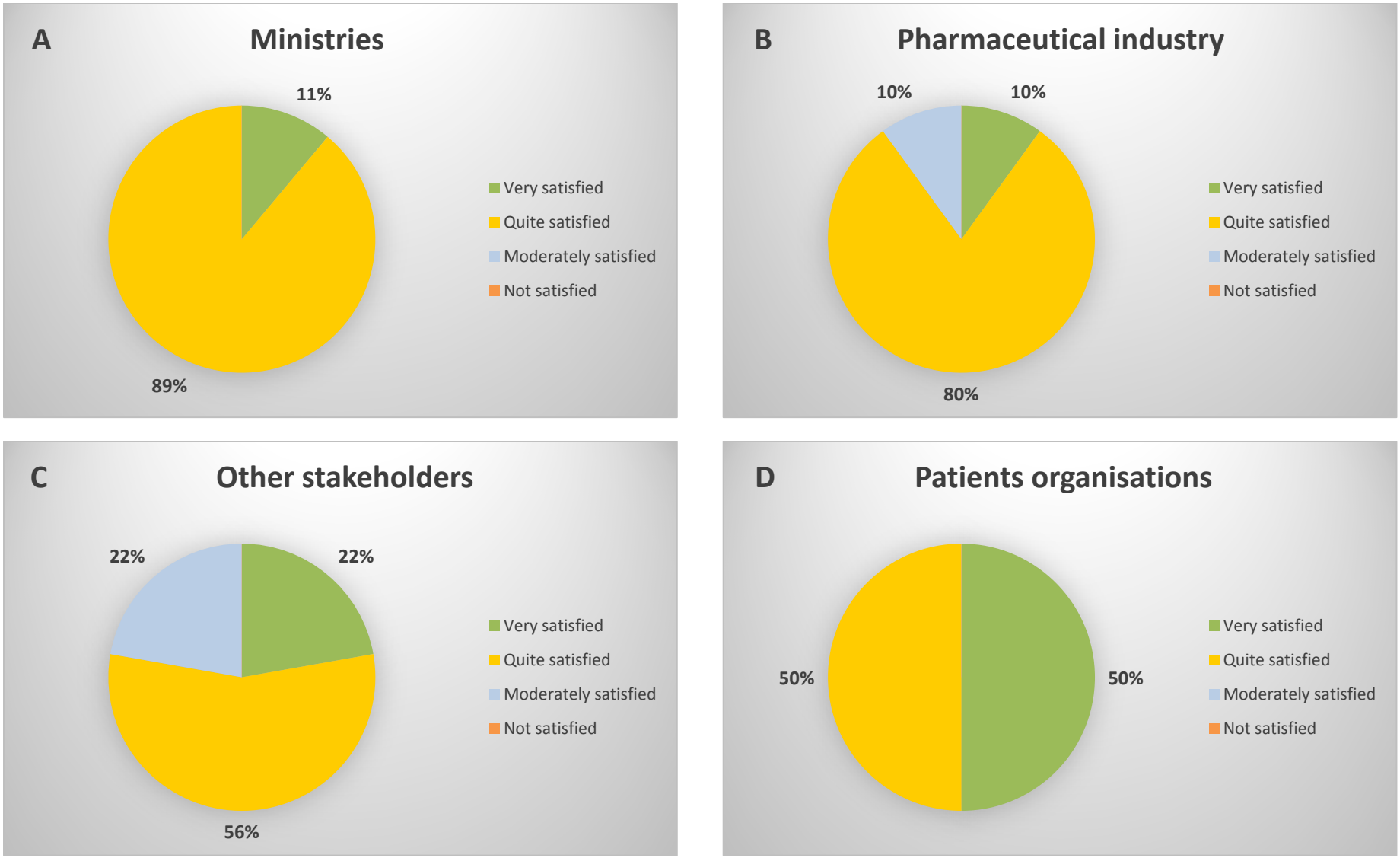

Figure 10: Level of satisfaction with the quality of the various collections of scientific data on rare diseases by (**A**) Ministries (n = 9), (**B**) Pharmaceutical industry (n = 10), (**C**) Other institutional stakeholders (n = 9) and (**D**) Patients' organisations (n = 4).

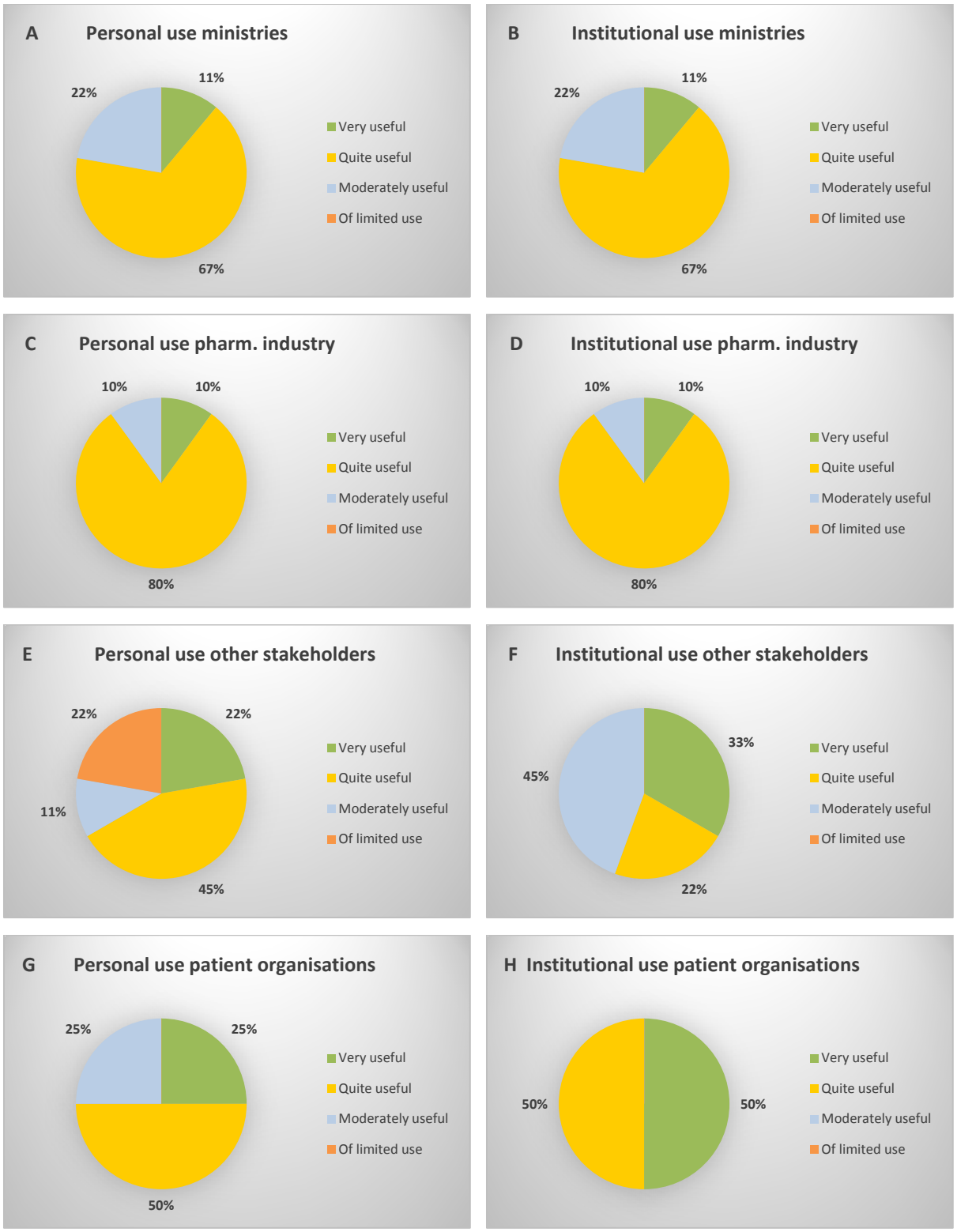

Figure 11: Evaluation of the personal (left) and institutional (right) usefulness of the various collections of scientific data on rare diseases by (**A,B**) Ministries (n = 9), (**C,D**) Pharmaceutical industry (n = 10), (**E,F**) Other institutional stakeholders (n = 9) and (**G,H**) Patients' organisations (n = 4).

3.6. Directory of expert resources

Basic information:

Countries participating in Orphanet collect data on national expert resources (expert centers/outpatient clinics, diagnostic laboratories and tests, patient organisations, clinical trials, research projects, registries, and infrastructures) specializing in rare diseases. All information is validated, quality controlled, and published in the national language, as well as in English.

The resulting directory of expert resources dedicated to rare diseases provides a comprehensive representation of healthcare, diagnostics and research services and activities specific for each rare disease in each participating country, for referrals as well as for analyses supporting policy making.

Survey results[6]:

Looking at the use frequencies of the directory of expert resources, again a significantly different use pattern is observed when comparing the three subgroups "Ministries", "Pharmaceutical industry" and "Other institutional stakeholders" with the forth subgroup, the "Patients' organisations". In the former set of subgroups, 50%-80% of the respondents consult the directory of expert resources few times a year (the majority of answers) to monthly, while the remaining 20%-50% never or almost never access this service to search for information (**Figure 12 A-C**). In contrast, patients' organisations use this service significantly more extensive, with 50% of the participants accessing the directory of expert resources at least weekly, if not several times a week, and another 50% accessing it monthly (**Figure 12 D)**.

These results further corroborate the close link between the use frequency for a specific service and the demands of the respective stakeholder subgroup. Information on expert resources is – in the context of and the stakeholder selection for this survey – most important for the group of patients and patients' organisations, which consequently display the highest access rates, while the other stakeholders have lower information needs and accordingly lower access rates to the database.

The latter conclusion does however not explain the particular high rate of non-users in the "Other stakeholders" subgroup that indicate to never or almost never consult the directory of expert resources. Although this subgroup is a mixture of different institutions, its composition includes many participants with (close) links to the national healthcare systems, thus also not explaining this high figure of non-users. The reason for this remains unclear at the moment and needs to be established in the future processing of the survey.

Analysing the level of satisfaction with the quality of the directory of expert resources shows a slightly more heterogeneous picture. Although between 60%-100% of the respondents declare to be quite to very satisfied with this service, a closer look to the different subgroups reveals that none of the participants from the "Ministries" and the "Pharmaceutical industry" subgroups rate the quality of the expert resources directory very satisfactory. In addition, around 30% are only moderately satisfied and an individual respondent is even not satisfied at all with this service. In the other two subgroups, "Other institutional stakeholders" and "Patients' organisations", the satisfaction levels are significantly higher (**Figure 13 A-D**).

Similarly, the assessments of the personal and the institutional usefulness of the directory of expert resources by the different stakeholder subgroups differ depending on the subgroup analysed. The highest values acknowledging the usefulness of this service are found in the subgroup of "Other

[6] Like in the previous two sub-chapters, the following questions were directed only to those participants previously indicating to be familiar with Orphanet and to use the database at least a few times a year.

institutional stakeholders", where 100% of the respondents rate this service quite to very useful, with a particularly high scoring for the institutional use in general (**Figure 14 E-F**). In the subgroups "Ministries" and "Pharmaceutical industry", 50%-67% of the participants describe this service as being quite useful for their personal work, as well as for their institution in general (only in this latter case, selected individuals from the pharmaceutical industry rate the value for the general institution even very useful). On the other hand, a relevant proportion of 33%-50% of the respondents indicate that this service is only moderately useful (the majority of answers) or of limited use only for their personal work and the work profile in their institution in general, marking each time the lowest levels of usefulness for these stakeholder subgroups (**Figure 14 A-D**). The last subgroup, "Patients' organisations", although satisfied with the service in general, displays a completely divers profile when assessing the personal and institutional usefulness, with 50% of the respondents rating this service personally, as well as institutionally at least quite useful, and another 50% rating it only moderately useful or of limited use at all (**Figure 14 G-H**).

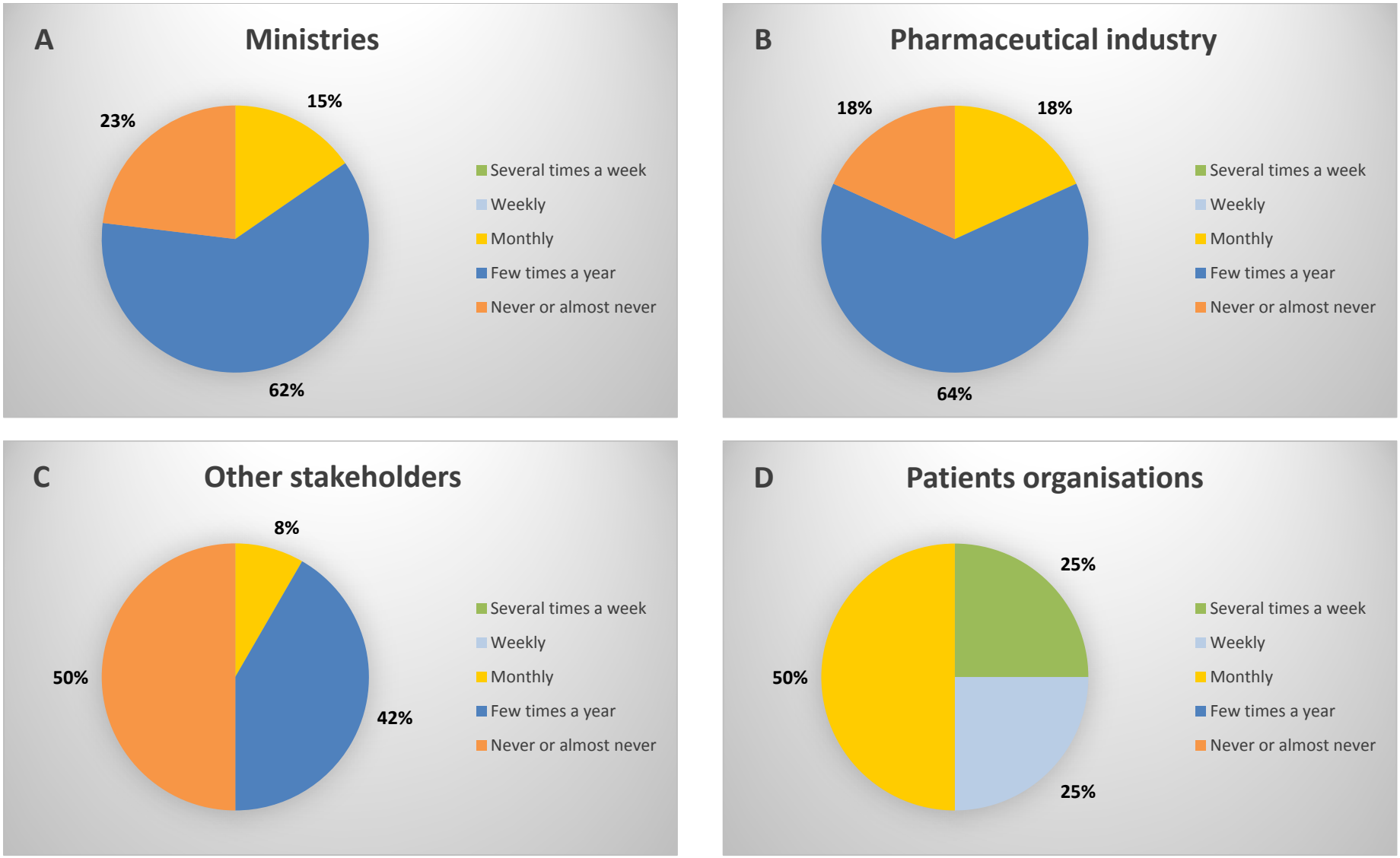

Figure 12: Use frequencies of the directory of expert resources by (**A**) Ministries (n = 13), (**B**) Pharmaceutical industry (n = 11), (**C**) Other institutional stakeholders (n = 12) and (**D**) Patients' organisations (n = 4).

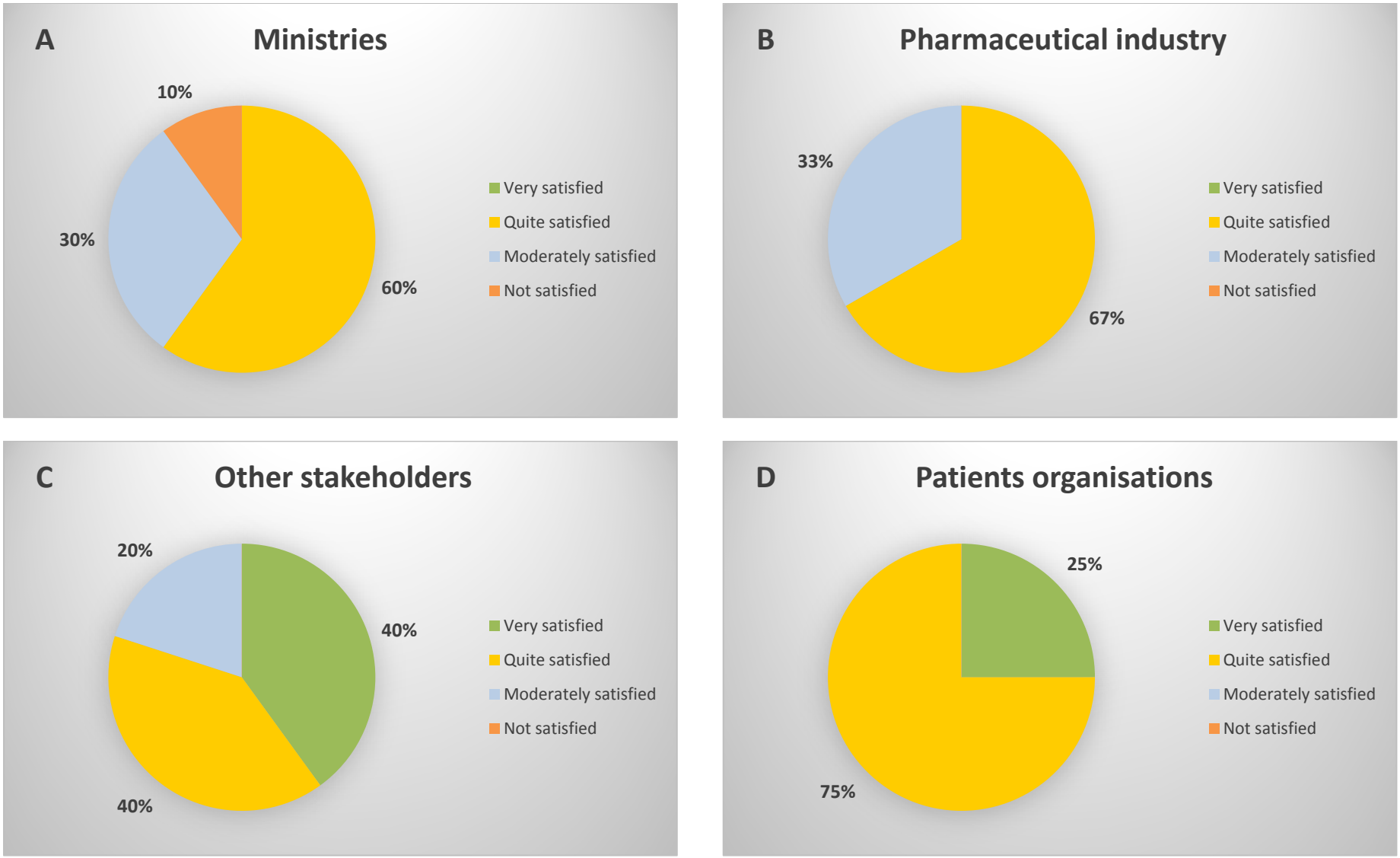

Figure 13: Level of satisfaction with the quality of the directory of expert resources by (**A**) Ministries (n = 10), (**B**) Pharmaceutical industry (n = 9), (**C**) Other institutional stakeholders (n = 5) and (**D**) Patients' organisations (n = 4).

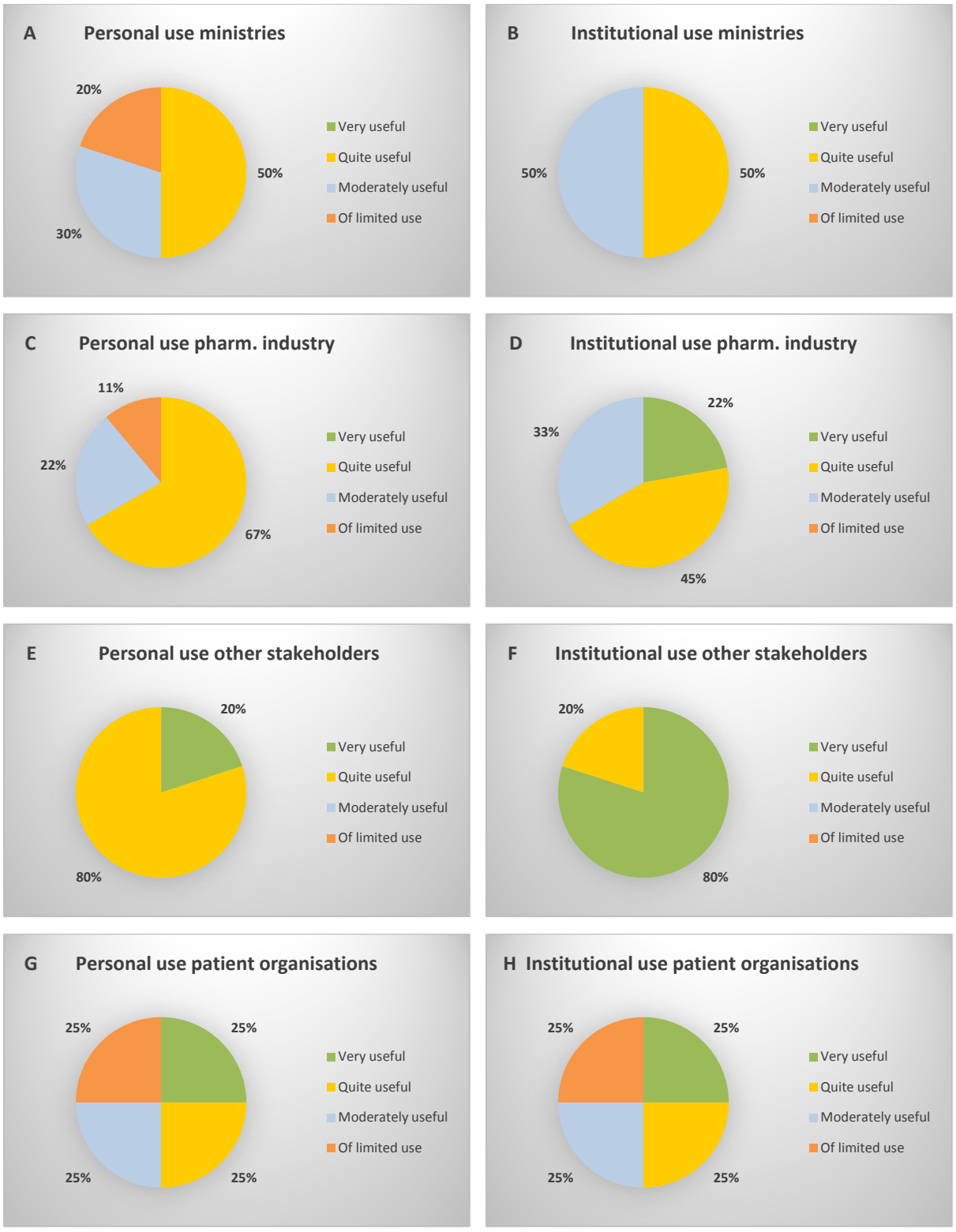

Figure 14: Evaluation of the personal (left) and institutional (right) usefulness of the directory of expert resources by (**A,B**) Ministries (n = 10), (**C,D**) Pharmaceutical industry (n = 9), (**E,F**) Other institutional stakeholders (n = 5) and (**G,H**) Patients' organisations (n = 4).

3.7. Orphanet Encyclopaedia (Texts on rare diseases)

Basic information:

The texts on diseases, altogether referred to as Orphanet encyclopaedia, provide information for health professionals, patients and relatives, social workers, and the general public on each rare disease.

In detail, Orphanet provides three distinct encyclopaedias on rare diseases:

- An encyclopaedia for health professionals (including review articles, practical genetics articles, emergency guidelines for the management of patients in emergency situations, and good practice guidelines issued by official organisations), expert-authored and peer-reviewed, available in eleven languages;
- An encyclopaedia for the general public, peer-reviewed by professionals and dedicated patient organisations, available currently mostly in French;
- Factsheets related to disabilities caused by the specific rare diseases, which mainly address professionals in the field of disability, as well as patients and their families.

In addition, there are links to externally produced literature on rare diseases in all languages.

Survey results[7]:

Analysing the use frequencies of the Orphanet encyclopaedia reveals a similar stakeholder pattern as seen before, with the subgroups “Ministries”, “Pharmaceutical industry” and “Other institutional stakeholders” clustering together with similar response profiles, clearly separated from the response pattern of the “Patients’ organisations” as the last subgroup. In detail, 54%-64% of the participants from the Ministries, the pharmaceutical industry and the group of other institutional stakeholders consult the Orphanet encyclopaedia few times a year (the majority of answers) or monthly (with rare individual higher access frequencies by single stakeholders), while between 36%-48% of the respondents never/almost never consult this service (**Figure 15 A-C**). On the other hand, 50% of the patients’ organisations access the content of the encyclopaedia at least weekly, if not several times a week, while the remaining 50% of the respondents consult this service monthly (**Figure 15 D**).

Once again, these results mirror the different needs and demands of the various stakeholder subgroups, with patients’ organisations having the highest needs for quality-assured information offered by the encyclopaedia within the frame of this survey, consequently consulting this service most often, while the other stakeholder subgroups have significantly lower specific information needs about specific diseases, therefore accessing this service less frequently.

The level of satisfaction with the quality of the Orphanet encyclopaedia is generally high. In three stakeholder subgroups, 83%-100% of the respondents declare to be quite to very satisfied with the quality of the service, only the subgroup of the “Pharmaceutical industry” shows a lower level of satisfaction, with 57% being quite to fully satisfied, whereas the remaining 43% are only moderately satisfied with the quality of this service, perhaps indicating that more pharmaceutical industry-relevant information is missing in the short abstracts constituting the encyclopaedia, or that for some diseases the relevant information is currently still missing. Importantly, none of the respondents was explicitely not satisfied with the quality of the encyclopaedia (**Figure 16 A-D**).

Similarly, the assessments of the personal, as well as institutional usefulness of the encyclopaedia revealed mostly high values, with 71%-100% of the respondents rating this service to be quite (in the

[7] Please note: The following questions were directed only to those participants that previously had indicated to be familiar with Orphanet and to use the database at least a few times a year.

majority of answers, except patients' organisations) to very useful (for patients' organisations the favourite answer) for their personal work and no individual denying any reasonable use at all (**Figure 17 A-D**). Likewise, 57%-100% of the participants rated this service also quite to very useful for the work in their institution in general, with the lowest score in the subgroup of the "Pharmaceutical industry", where almost half of the respondents (43%) only see a limited usefulness for their institution in general (**Figure 17 E-H**).

Collectively, however, these on average high values again underline the fact that even stakeholders with lower use frequencies highly acknowledge and appreciate the existence of this service, when needed.

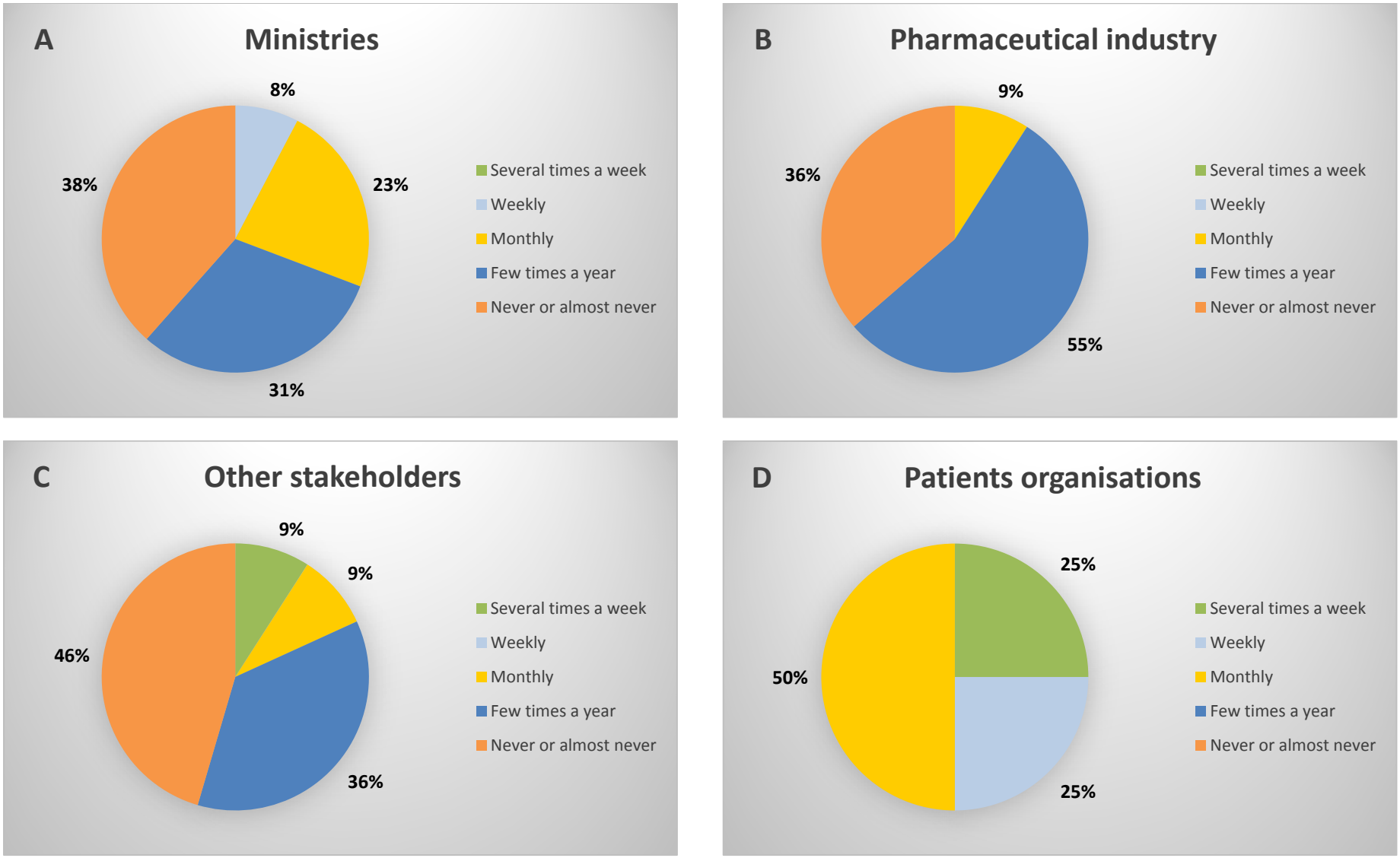

Figure 15: Use frequencies of the Orphanet encyclopaedia by (**A**) Ministries (n = 13), (**B**) Pharmaceutical industry (n = 11), (**C**) Other institutional stakeholders (n = 11) and (**D**) Patients' organisations (n = 4).

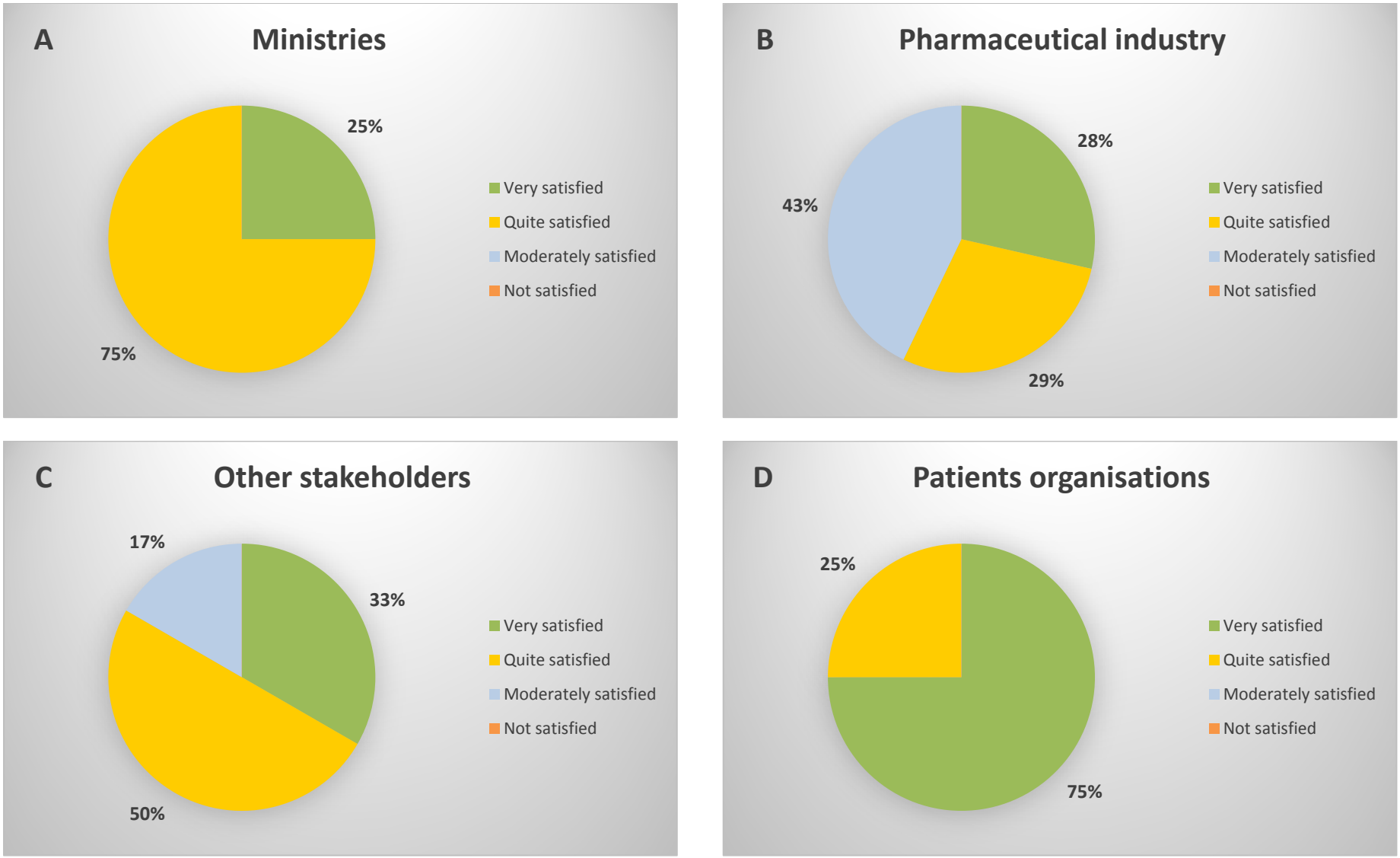

Figure 16: Level of satisfaction with the quality of the Orphanet encyclopaedia by (**A**) Ministries (n = 8), (**B**) Pharmaceutical industry (n = 7), (**C**) Other institutional stakeholders (n = 6) and (**D**) Patients' organisations (n = 4).

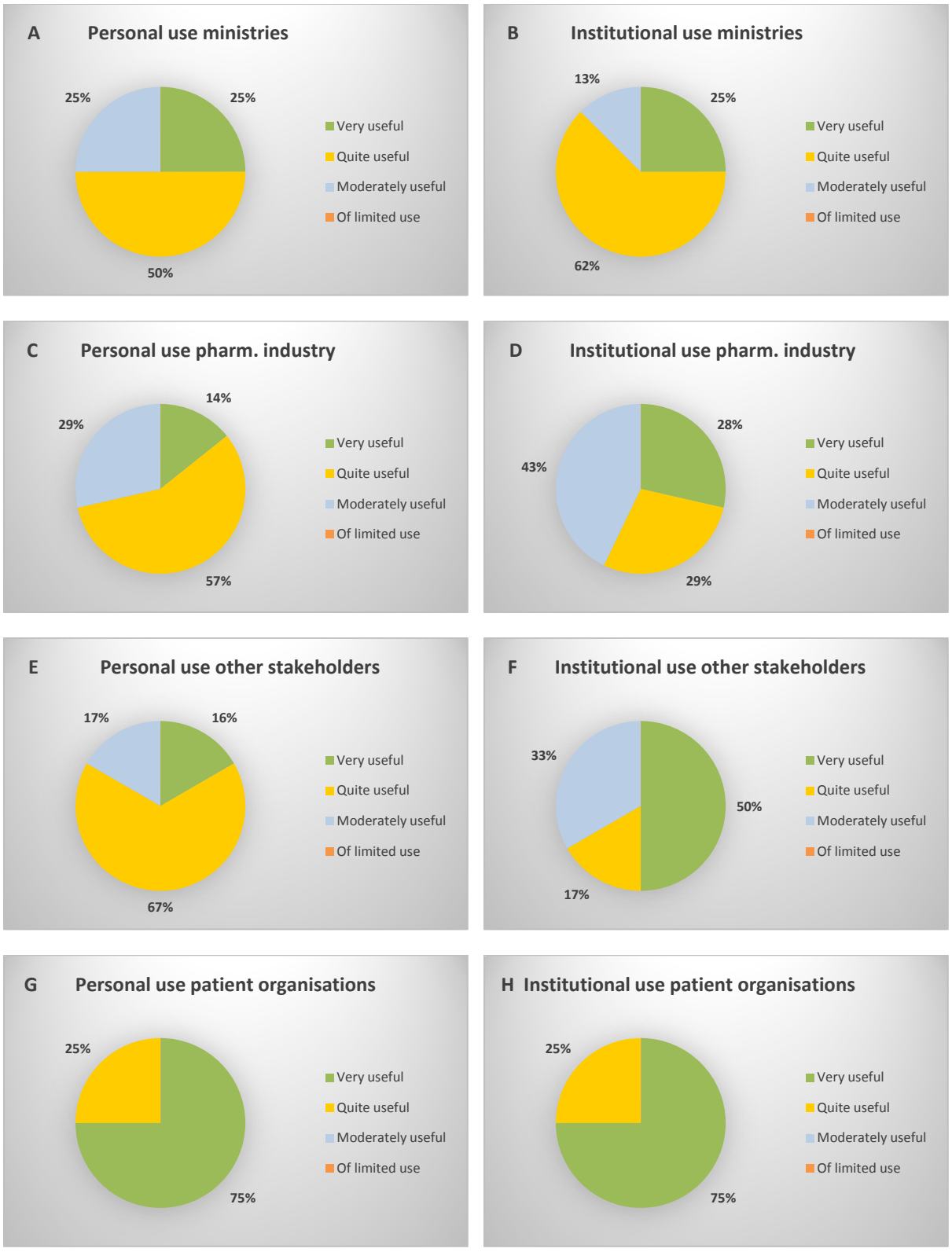

Figure 17: Evaluation of the personal (left) and institutional (right) usefulness of the Orphanet encyclopaedia by (**A,B**) Ministries (n = 8), (**C,D**) Pharmaceutical industry (n = 7), (**E,F**) Other institutional stakeholders (n = 6) and (**G,H**) Patients' organisations (n = 4).

3.8. Inventory of Orphan drugs

Basic information:

The inventory of Orphan drugs provides information on therapies, either approved or currently in development, that are specific for rare diseases.

To this end, the online-inventory allows the user to search for orphan drugs by:

- The substance or trade name,
- The diseases they are linked to,
- The ATC category (i. e. the WHO's Anatomical, Therapeutic, Chemical classification, which is used for the classification of medicinal substances),
- The name of the sponsor, or
- The name of the holder of the marketing authorization.

The list of orphan drugs includes all substances which have been granted an orphan designation for diseases considered rare in Europe. It also includes drugs without an orphan designation as long as they have been granted a marketing authorization with a specific indication for a rare disease.

Survey results[8]:

Asked about their use frequency of the inventory of Orphan drugs, 54%-73% of the survey participants from the stakeholder subgroups "Ministries", "Pharmaceutical industry" and "Other institutional stakeholders" consult this service primarily a few times a year, but to some extent also monthly, with an individual higher access rate in the subgroup of the "Other institutional stakeholders", while around 25%-40% never or almost never connect to this service (**Figure 18 A-C**). Patients' organisations, on the other hand, show again a significantly different use profile with 75% of the respondents consulting the inventory of Orphan drugs at least weekly, if not several times a week, and another 25%, that never or almost never use this service (**Figure 18 D**).

Despite the partially limited number of participants, these results illustrate again the close link between the individual personal or work-related demand within the stakeholder subgroups and the use frequency. Regarding Orphan drugs, patients and patients' organisations, directly confronted with the disease burden, as well as the existence or lack of pharmaceutical therapies and their concomitant circumstances and side effects, have higher and recurrent information needs and therefore access this service far more often than the other stakeholders that need the relevant information offered by Orphanet less frequently in their day-to-day work.

The close connection between the personal living and working environment and the personal assessment of this service gets also evident when participant are asked about their rating of the quality and the usefulness of the inventory of Orphan drugs. Evaluating the quality of the inventory, 100% of the respondents from the subgroups "Pharmaceutical industry", "Other institutional stakeholders" and "Patients' organisations" declare to be quite to very satisfied with the quality of this service, with the highest score (67% very satisfied) in the subgroup of the patients' organisations, while participants from the subgroup "Ministries" display a slightly lower satisfaction level with almost one third being only moderately satisfied. Importantly, none of the respondents indicated to be not satisfied at all **(Figure 19 A-D**).

Similarly, 100% of the participating representatives from the subgroups "Pharmaceutical industry" and "Patients' organisations" rate the inventory of Orphan drugs quite to very (the majority of answers)

[8] Again, the following questions were directed only to those participants previously indicating to be familiar with Orphanet and to use the database at least a few times a year.

useful for their personal use, as well as its usefulness for the institution in general (**Figure 20 C-D** and **G-H**), while respondents from the subgroups “Ministries” and “Other institutional stakeholders” show a slightly more variable reply profile, with 57%-87% assessing the Orphan drug inventory quite to be very useful for their personal situation and 71%-74% attesting this service a high to very high level of usefulness for their institution in general, while one individual participant from the group of the other stakeholders indicates to see only a limited use of this service for his institution (**Figure 20 A-B** and **E-F**).

Still, the on average high values for the quality and the personal and institutional usefulness underline the fact that all stakeholders, independent of their individual use frequency, highly acknowledge and appreciate the existence of this service, when needed.

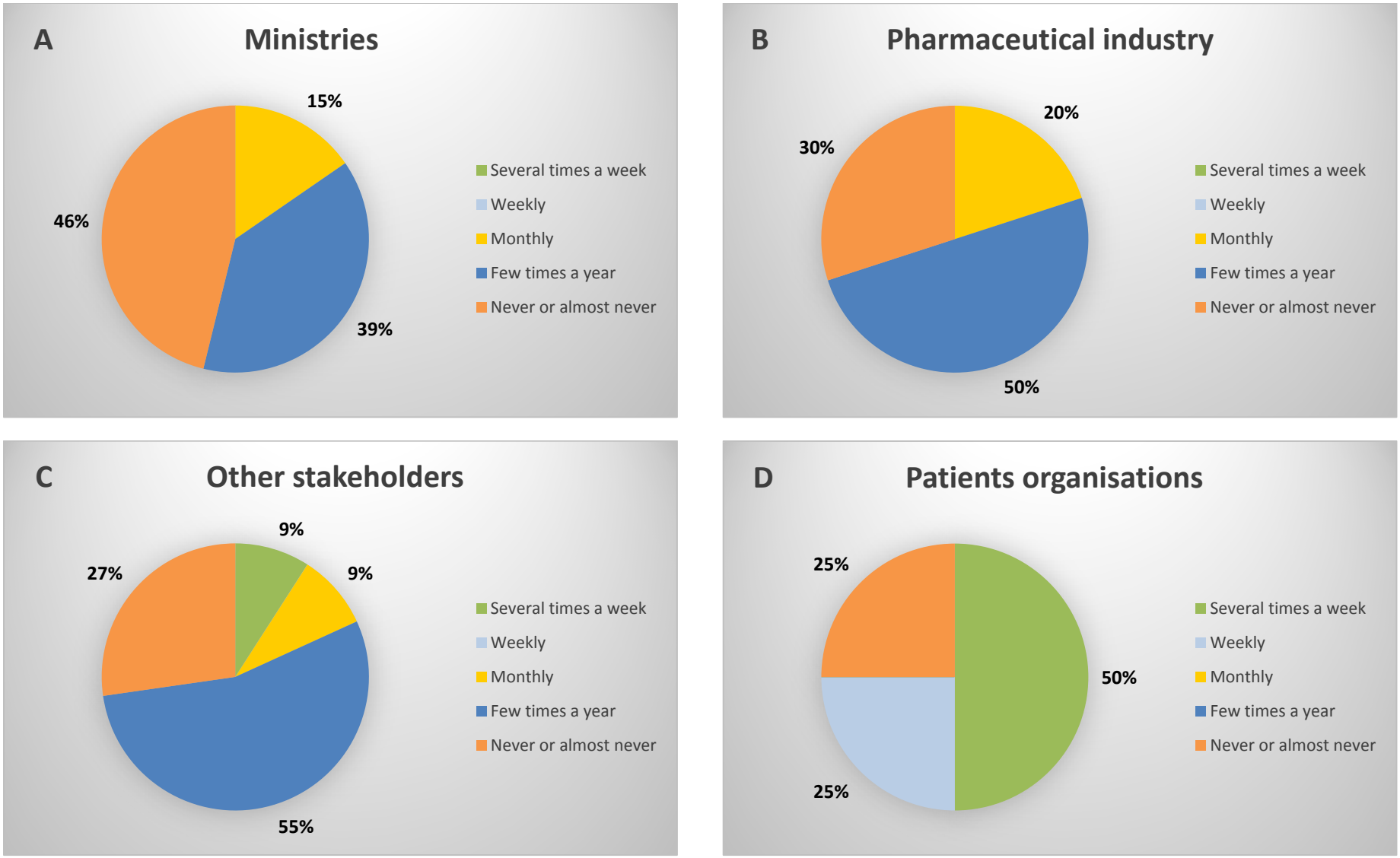

Figure 18: Use frequencies of the inventory of Orphan drugs by (**A**) Ministries (n = 13), (**B**) Pharmaceutical industry (n = 10), (**C**) Other institutional stakeholders (n = 11) and (**D**) Patients' organisations (n = 4).

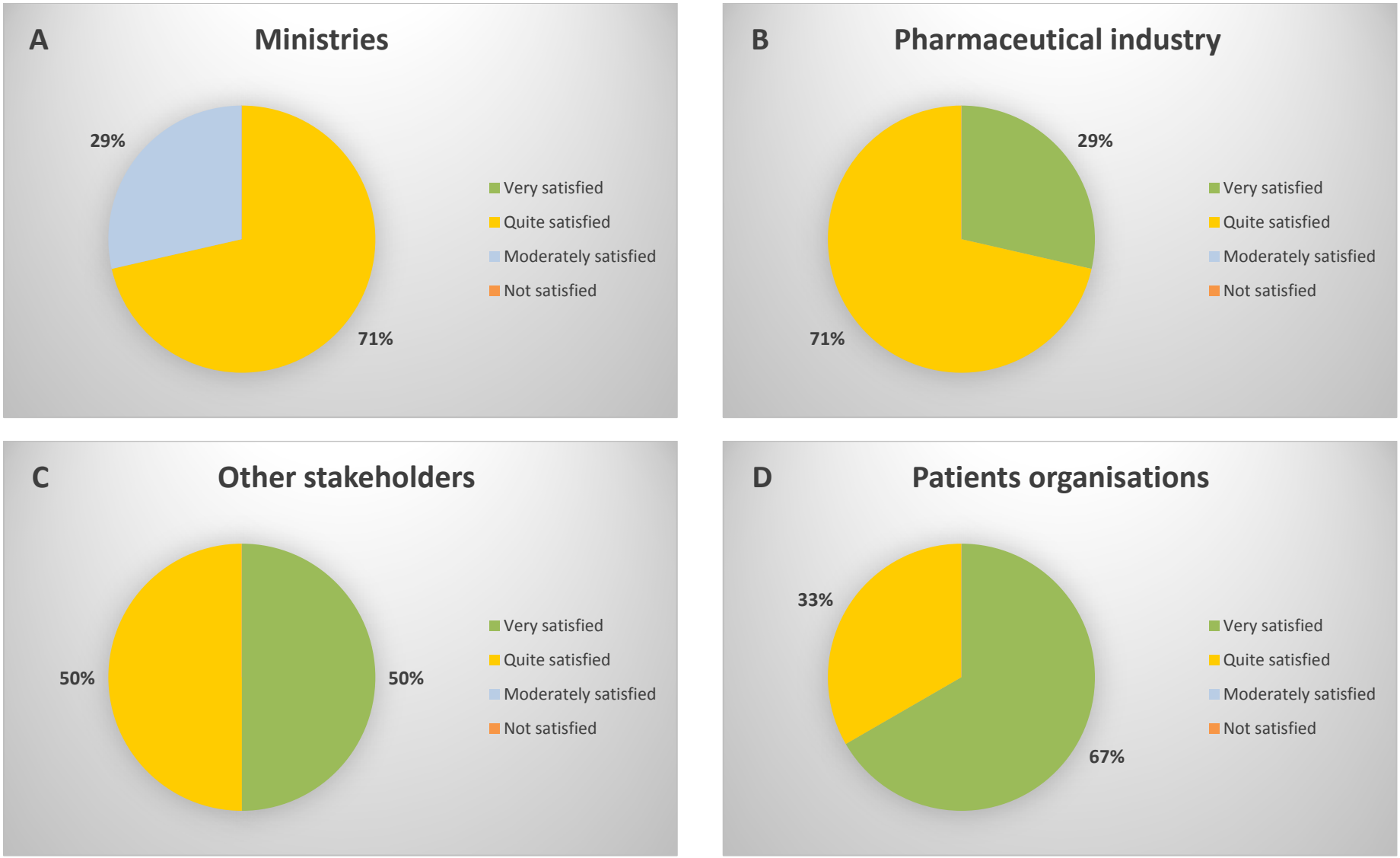

Figure 19: Level of satisfaction with the quality of the inventory of Orphan drugs by (**A**) Ministries (n = 7), (**B**) Pharmaceutical industry (n = 7), (**C**) Other institutional stakeholders (n = 8) and (**D**) Patients' organisations (n = 3).

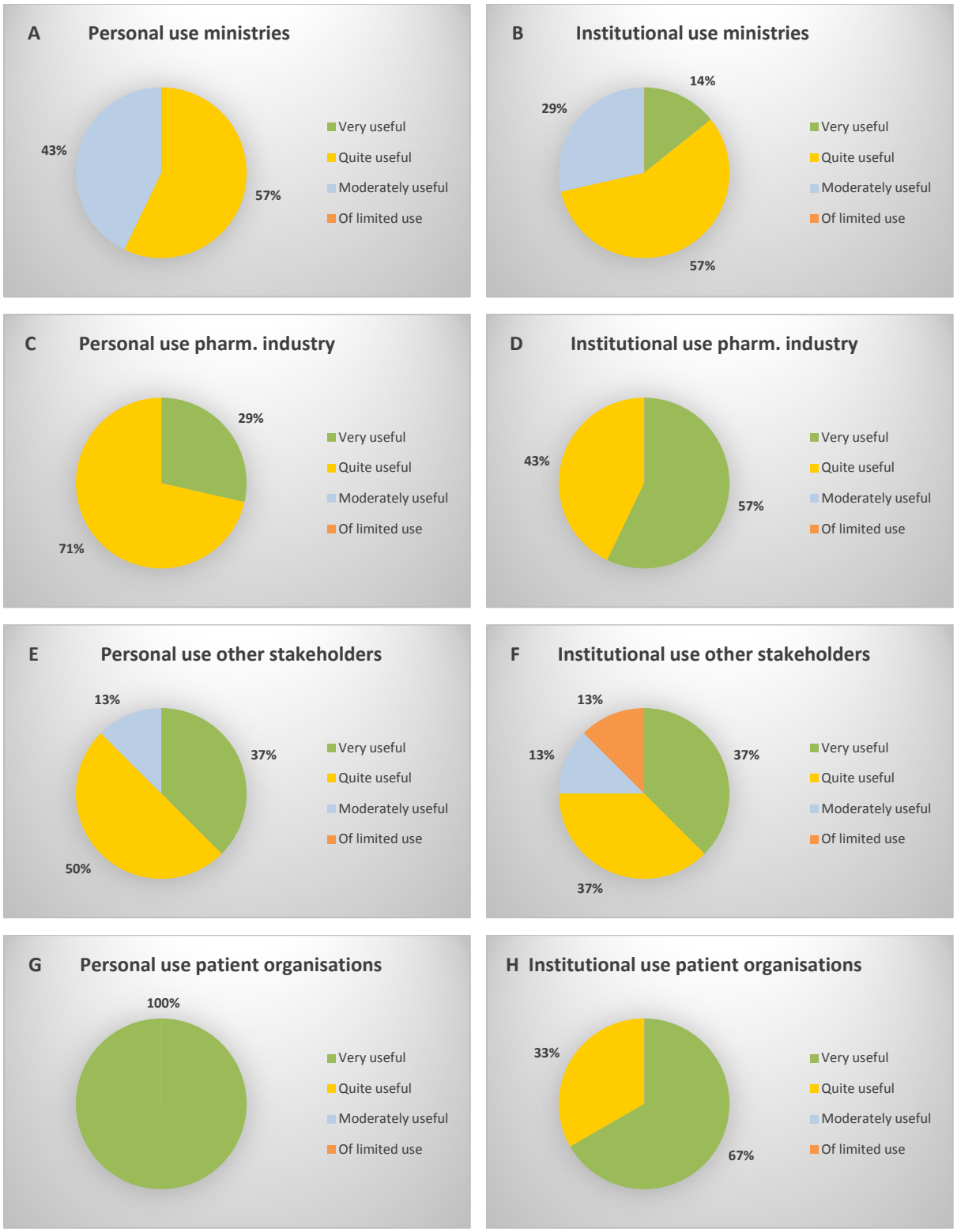

Figure 20: Evaluation of the personal (left) and institutional (right) usefulness of the inventory of Orphan drugs by (**A,B**) Ministries (n = 7), (**C,D**) Pharmaceutical industry (n = 7), (**E,F**) Other institutional stakeholders (n = 8) and (**G,H**) Patients' organisations (n = 3).

3.9. Orphanet report series

Basic information:

The Orphanet report series is a growing collection of reports currently comprising:

- A general list of rare diseases and synonyms,
- Lists of rare diseases with epidemiological data (sorted alphabetically or by decreasing prevalence)
- A list of Orphan drugs,
- A list of disease registries in Europe,
- A list of research infrastructures useful to rare diseases in Europe, and
- The annual Orphanet activity reports.

In general, the reports provide information on particular topics of interest for a variety of stakeholders in a printable format. Texts are either newly published or updated on a regular basis.

Survey results[9]:

Analysing the use frequencies of the Orphanet report series reveals a slightly different access profile as compared to most other services. In this instance, respondents from the subgroups “Ministries” and “Patients’ organisations” consult the report series significantly more often, with 83%-100% connecting to this service in the database at least few times a year, and no participant from the patients’ organisations and only 17% from the ministries indicating to never or almost never access to this service. In contrast, 40%-55% of the respondents from the other two subgroups, the “Pharmaceutical industry” and the “Other institutional stakeholders”, state to never or almost never use this service, followed by 36%-40% that consult the report series a few times a year only (**Figure 21 A-D**).

These findings suggest that the information offered by the different documents in the Orphanet report series is of particular interest to patients/patients’ organisations and ministries, resulting in correspondingly higher access rates to this service, while in the other two stakeholder subgroups with a broader professional spectrum of the participants, the demand for this service varies considerably more from individual to individual, probably based on the day-to-day working spectrum.

Interestingly, these obvious differences in the use frequency of the Orphanet report series between the four stakeholder subgroups are not mirrored in the level of satisfaction with the quality of this service. Here, 67%-100% of the participants of all stakeholder subgroups indicate to be quite to very satisfied with this service, with only few individuals in the groups of the pharmaceutical industry, the other institutional stakeholders and the patient organisations expressing a moderate satisfaction only regarding the report series (**Figure 22 A-D**).

And the assessments of the personal and the institutional usefulness of the Orphanet report series for the different stakeholder subgroups reveals an even more balanced picture. When asked about the personal usefulness of this service, 75%-83% off the participants rate the report series quite (in the majority of answers, except for the patient organisations) to very (the favourite answer of the patient organisations) useful, with only one individual from the ministries stating to have limited personal use for this service (**Figure 23 A-D**). Likewise, when asked to evaluate the institutional usefulness of the report series, 75%-90% rated the service quite to very useful, this time often with a preference on the highest possible score (**Figure 23 E-H**). Like in the previous sub-chapters, the on average high values for the quality and the personal and institutional usefulness demonstrate once more that all

[9] Please note: The following questions were directed only to those participants previously indicating to be familiar with Orphanet and to use the database at least a few times a year.

stakeholders, independent of their individual use frequency, highly acknowledge and appreciate the existence of this service, when needed.

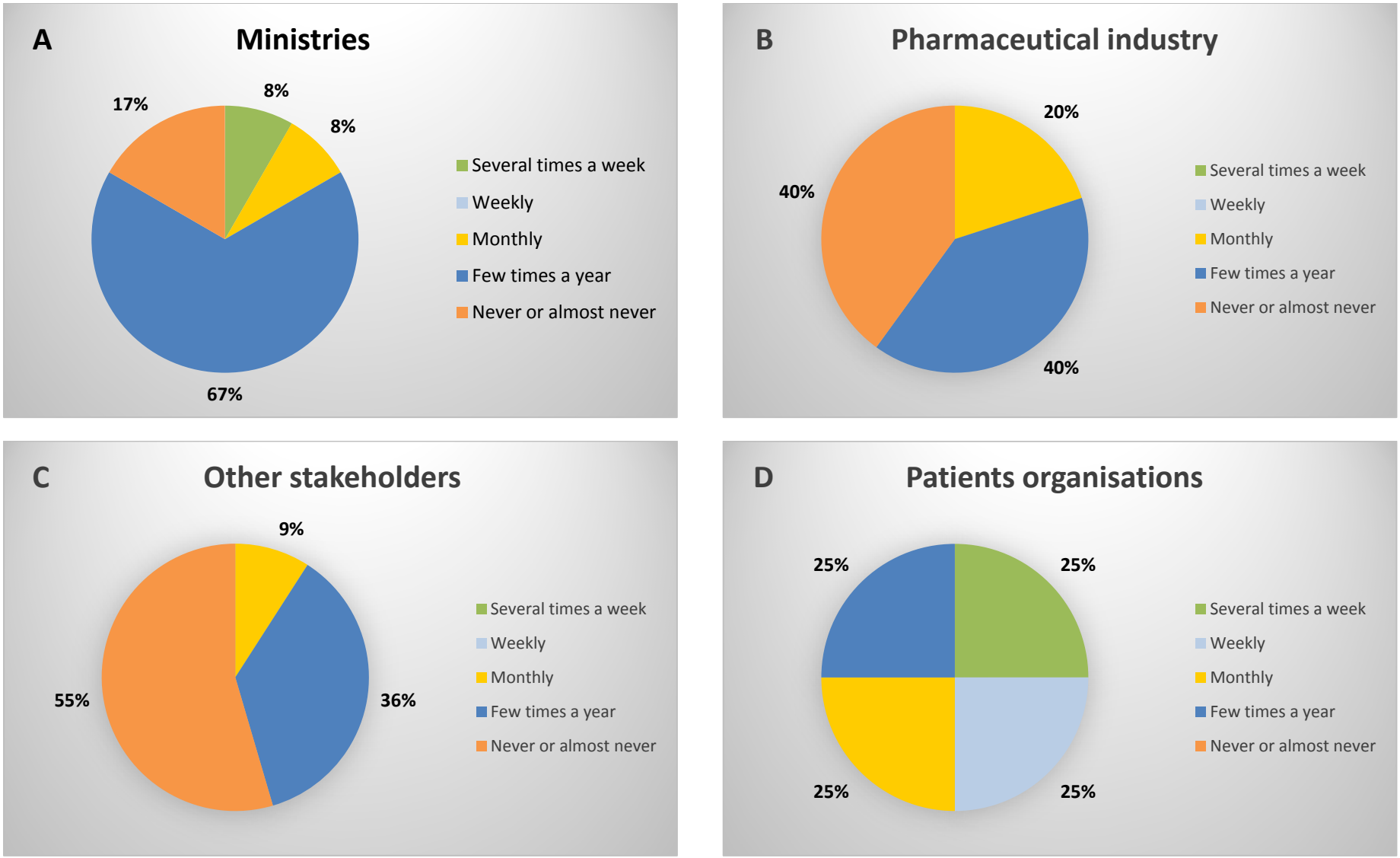

Figure 21: Use frequencies of the Orphanet report series by (**A**) Ministries (n = 12), (**B**) Pharmaceutical industry (n = 10), (**C**) Other institutional stakeholders (n = 11) and (**D**) Patients' organisations (n = 4).

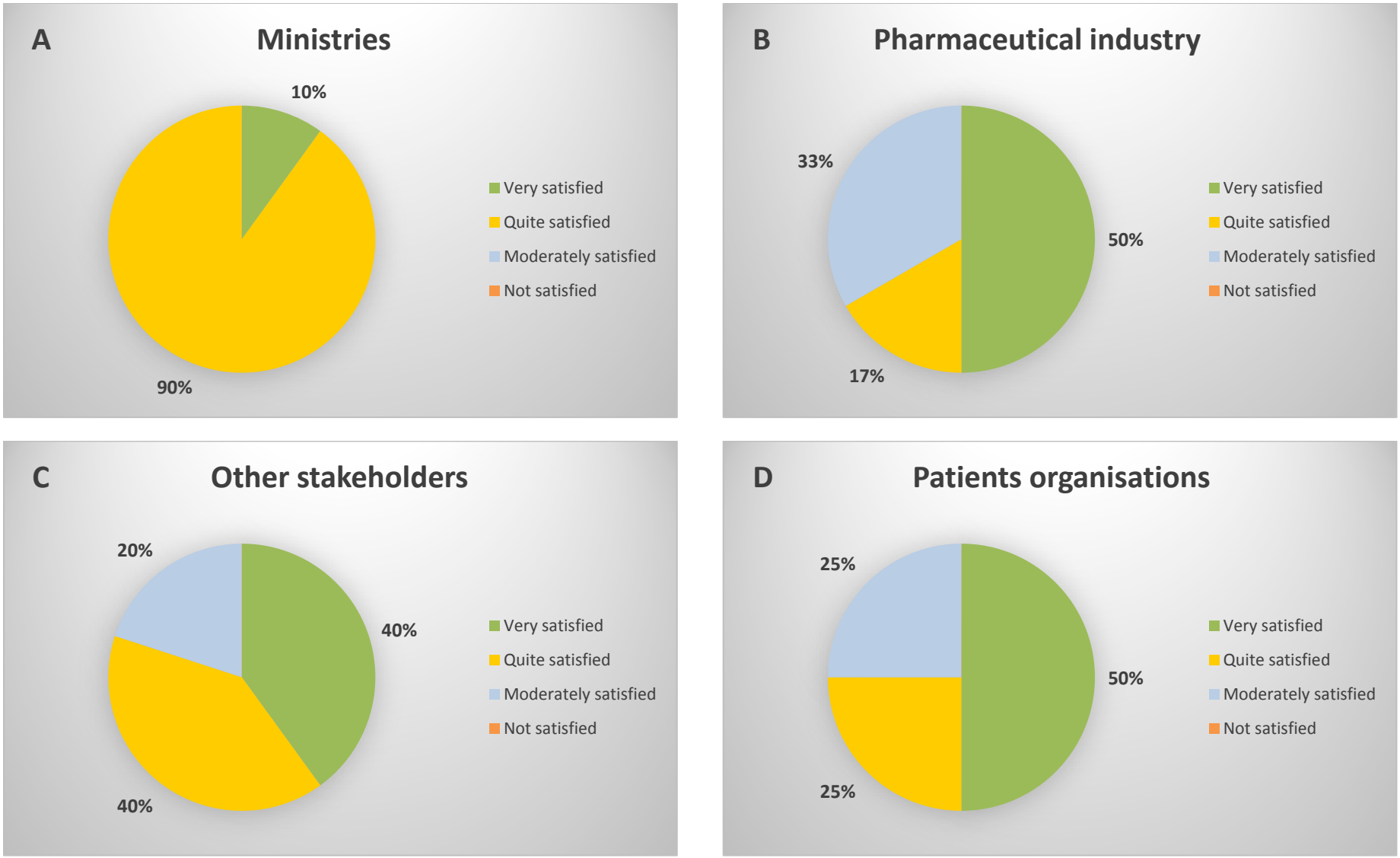

Figure 22: Level of satisfaction with the quality of the Orphanet report series by (**A**) Ministries (n = 10), (**B**) Pharmaceutical industry (n = 6), (**C**) Other institutional stakeholders (n = 5) and (**D**) Patients' organisations (n = 4).

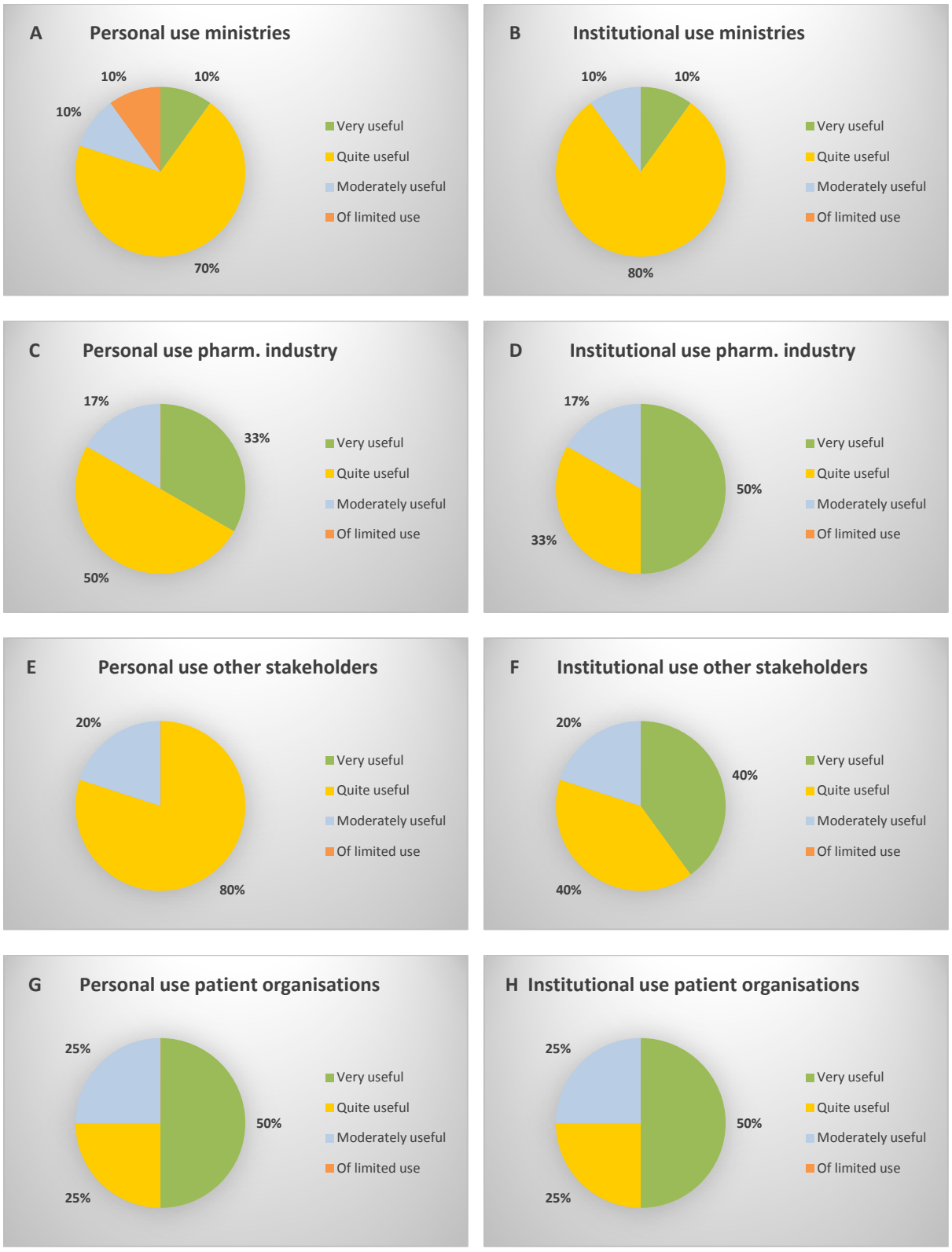

Figure 23: Evaluation of the personal (left) and institutional (right) usefulness of the Orphanet report series by (**A,B**) Ministries (n = 10), (**C,D**) Pharmaceutical industry (n = 6), (**E,F**) Other institutional stakeholders (n = 5) and (**G,H**) Patients' organisations (n = 4).

3.10. Orphadata including the Orphanet Rare Diseases Ontology (ORDO)

Basic information:

The website Orphadata (www.orphadata.org) provides downloadable Orphanet datasets including the Orphanet Rare Diseases Ontology (ORDO). The system allows mass-extraction and re-use of large datasets of the Orphanet database for research, analysis and decision-making purposes.

The datasets offered on Orphadata are comprehensive, high-quality datasets related to rare diseases and orphan drugs in a reusable, computable format. These datasets are a partial extraction of the data stored in Orphanet and are either accessible and downloadable for free, or available upon request and free for academia / available for a fee for industry.

Survey results[10]:

When assessing the use frequencies of the Orphadata service, three out of the four stakeholders subgroups, the "Ministries", the "Pharmaceutical industry" and the "Other institutional stakeholders" share again a similar use profile with a majority of respondents in each subgroup (64%-75%) never/almost never consulting this service and another 25%-30% of participants connecting few times a year to the database in order to download selected datasets of interest. These figures are complemented by one individual high-frequency user belonging to the group of "Other institutional stakeholders" (**Figure 24 A-C**). Participating patients' organisations, in contrast, show a slightly different use profile with again the majority (50%) of respondents never/almost never accessing the Orphadata website, while the other 50% of participants connect at least weekly to this service (**Figure 24 D**).

The in comparison to other Orphanet services globally high numbers of rare- to non-users of the Orphadata service (50%-75% of respondents in the various stakeholder subgroups) might be most easily explained by the fact that these datasets contain condensed, comprehensive information that is not designed to answer a specific question or demand, but instead is used for broader, more general types of analysis and comparison, thus limiting the need to access this service to very rare occasions and very specific tasks.

This and the fact that "almost never" does not solely mean "never", but also "rarely", is also reflected in the evaluation of the general satisfaction with and the personal and institutional usefulness of this service. Although 50% to 75% of respondents indicate to never or almost never use the Orphadata service, between 67%-100% declare to be quite to very satisfied with the quality of this service, with the highest satisfaction levels in the subgroups "Other institutional stakeholders" and "Patients' organisations" (75%-100% very satisfied). Additionally, no single user expresses any dissatisfaction with this service (**Figure 25 A-D**), underlining the fact that despite the partially very low use frequencies the Orphadata service serves any requirements well when it is needed.

Even higher scores are obtained when analysing the personal and institutional value of the Orphadata service. Here, 67%-100% of the participants of all stakeholder subgroups rate this service quite to very useful for their personal day-to-day work (with highest scorings in the subgroups "Ministries" and "Patients' organisations"), as well as for their institution in general (with highest scorings in the sub-groups "Ministries", "Other institutional stakeholders" and "Patients' organisations") (**Figure 26 A-H**).

These high ratings clearly demonstrate that all stakeholders, independent of their individual use frequency, highly acknowledge and appreciate the existence of this service, when needed.

[10] Please note: The following questions were directed only to those participants previously indicating to be familiar with Orphanet and to use the database at least a few times a year.

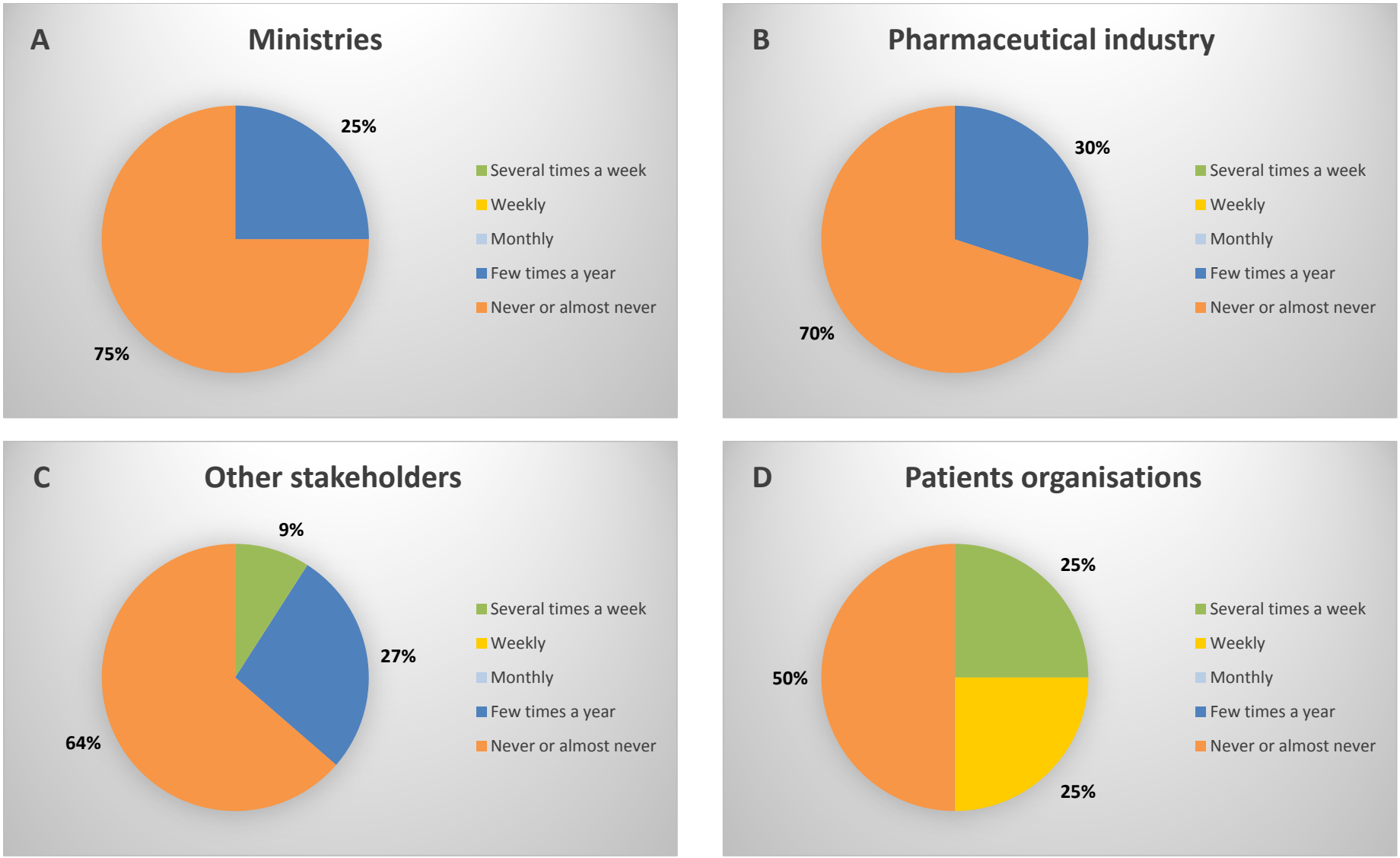

Figure 24: Use frequencies of the Orphadata service including the Orphanet Rare Diseases Ontology by (**A**) Ministries (n = 12), (**B**) Pharmaceutical industry (n = 10), (**C**) Other institutional stakeholders (n = 11) and (**D**) Patients' organisations (n = 4).

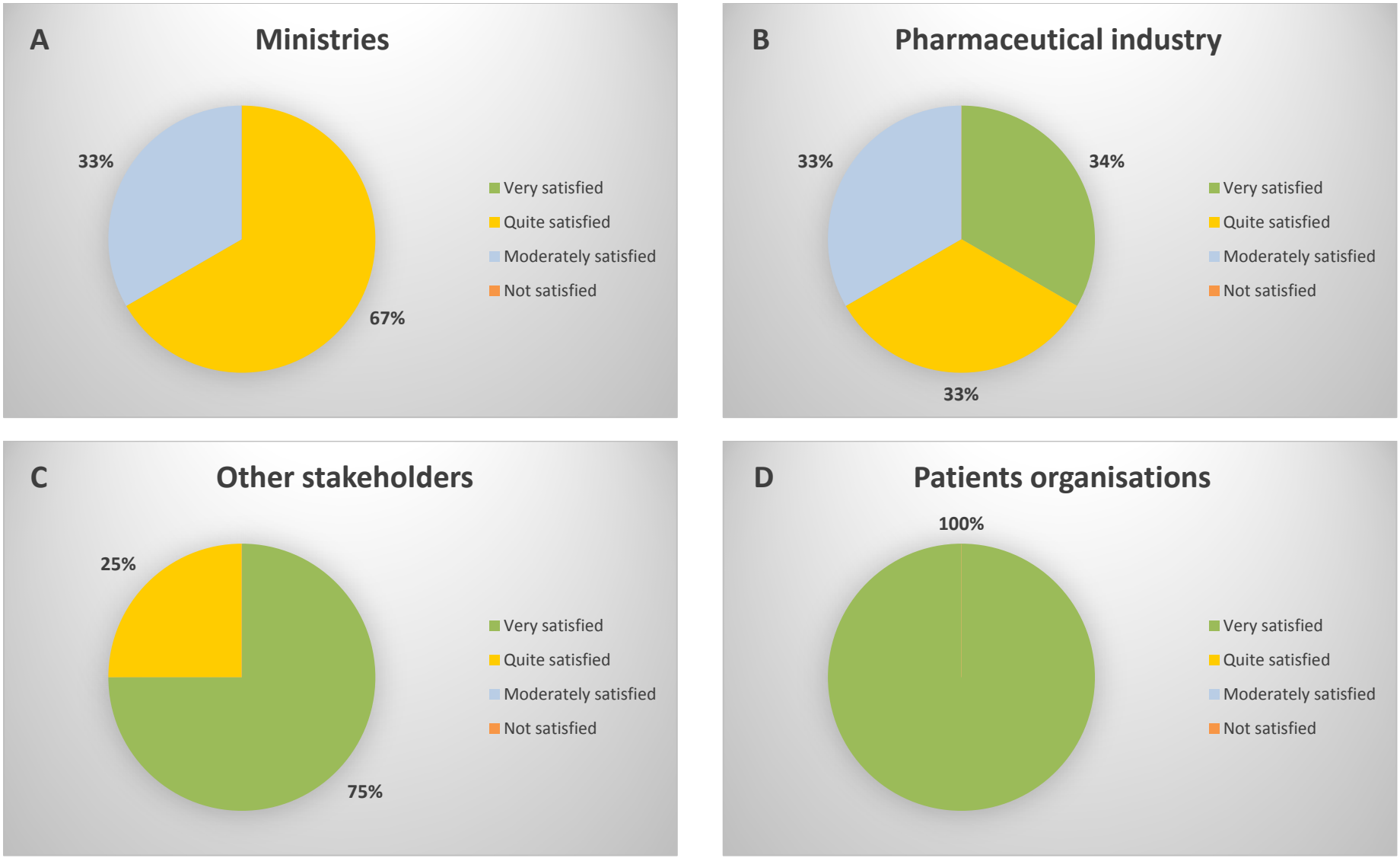

Figure 25: Level of satisfaction with the quality of the Orphadata service including the Orphanet Rare Diseases Ontology by (**A**) Ministries (n = 3), (**B**) Pharmaceutical industry (n = 3), (**C**) Other institutional stakeholders (n = 4) and (**D**) Patients' organisations (n = 2).

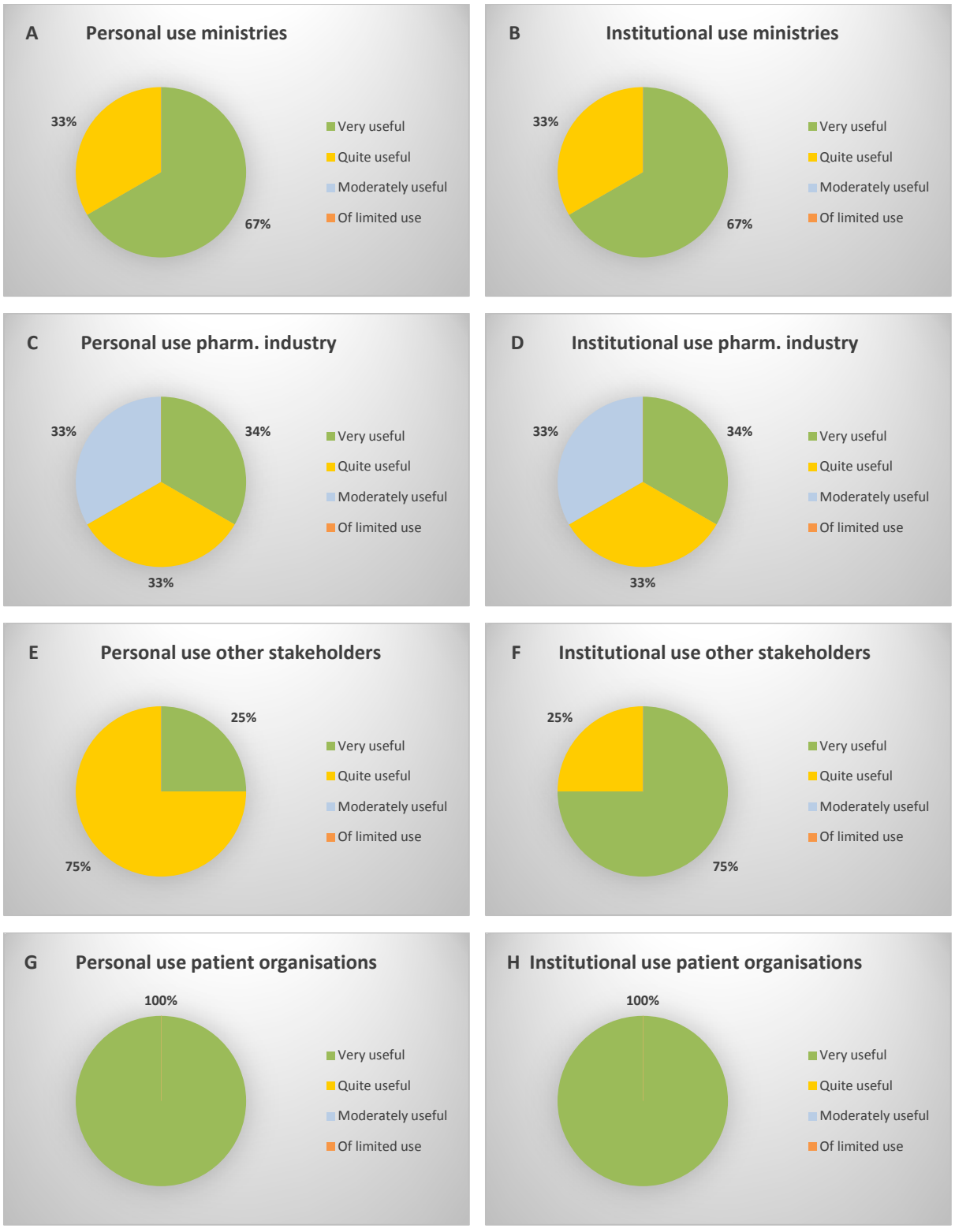

Figure 26: Evaluation of the personal (left) and institutional (right) usefulness of the Orphadata service including the Orphanet Rare Diseases Ontology by (**A,B**) Ministries (n = 3), (**C,D**) Pharmaceutical industry (n = 3), (**E,F**) Other institutional stakeholders (n = 4) and (**G,H**) Patients' organisations (n = 2).

3.11. General use and relevance of Orphanet

Basic information:

Since its foundation in 1997 in France, Orphanet constantly expanded its content, reach and geographical Member State coverage, constituting today the worldwide leading source for quality-assured information on most aspects of rare diseases. Accordingly, many users connect worldwide to the database each day, retrieving information from the different services offered by Orphanet.

For example, in September 2016, the date of the last comprehensive website use analysis, an average number of 969,729 users from 293 countries accessed Orphanet per day, visiting 4,123,930 pages. Based on the results obtained from the analysis of several online user surveys in the past years, these Orphanet users can be assigned to the following categories:

- Approx. 60 % health care professionals (including medical doctors and nurses, paramedical therapists, and medical students);
- Approx. 30 % patients (including parents and other relatives);
- Approx. 10 % other users (including social workers, policy makers, representatives from the pharmaceutical industry, journalists, and the general public).

These users consult different services, like for instance the inventory of expert resources. For this service, Orphanet currently (as of September 2016, data from 40 partner countries) provides information on:

- 7,172 Expert centres;
- 2,275 Patient organisations;
- 41,159 Diagnostic tests;
- 1,667 Medical laboratories;
- 2,489 Ongoing research projects;
- 2,123 Ongoing clinical trials.

And regarding the scientific content of the database (effective date September 2016, data from 40 partner countries) Orphanet currently lists for example:

- 6,008 Rare diseases (excluding sub-types and groups);
- 4,080 Texts on rare diseases;
- 3,573 Genes (including 3,179 known causative genes for 2,740 rare diseases);
- 2,636 Diseases annotated with clinical signs;
- 455 Diseases annotated with functional consequences.

Survey results:

Provided with these figures and asked, how they would value the benefit Orphanet offers for the individual Member States as a central, quality-assured, European tool for information on rare diseases, 87%-100% of the respondents of the different stakeholder subgroups stated that Orphanet plays a quite to very important role as comprehensive information source in the different countries, with highest values in the subgroups “Ministries”, “Other institutional stakeholders” and “Patients’ organisations” (63%-75% indicating a very important role) (**Figure 27 A-D**). On the other hand, only individual participants within the different subgroups rated Orphanet as a moderately important tool, and no respondent declared to see a limited importance only.

These high levels of acknowledgement across all stakeholders clearly demonstrate the high level of reputation Orphanet has gained over the last 20 years and the global confidence that all stakeholders have with regard to the quality and data accuracy of the database. And again – as has been shown in the previous sub-chapters when analysing the use frequencies versus the satisfaction level of the

different stakeholder subgroups with regard to the various specific services of Orphanet – these high levels of trust and appreciation are completely independent form the real-world use frequencies of any stakeholder. Even though for example the subgroups “Ministries”, “Pharmaceutical industry” and “Other institutional stakeholders” display a relatively low use profile of Orphanet in general with 41%-46% consulting the database only few times a year (the favourite choice within these three subgroups) and 24% of the respondents from the ministries, as well as 32% of the participants from the pharmaceutical industry never or almost never accessing Orphanet (see **Figure 4 A-D**, page 12), almost all respondents acknowledge the high importance that Orphanet plays in their Member States, serving an information demand of many other stakeholders including patients, general practitioners, medical experts and other people working in the healthcare sector, scientists, and the general public.

Taking into account the currently unresolved issue of the sustainability of the database and the actual fragile situation with a secured funding mechanism expiring in May 2018, these high levels of acknowledgement and appreciation might also be seen as an impulse for all stakeholders to thoroughly evaluate all possible options for a long-term funding of Orphanet (see next sub-chapter).

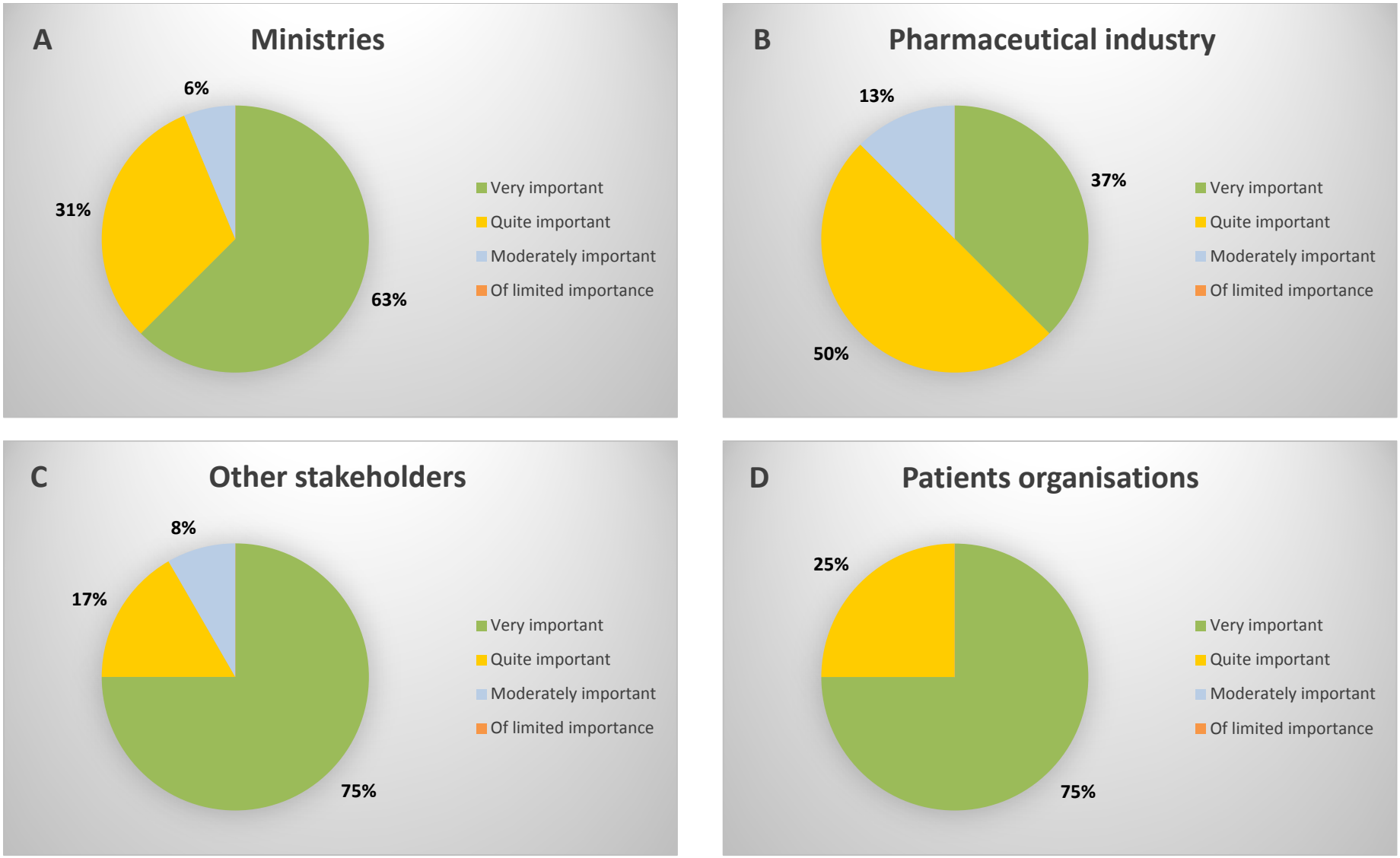

Figure 27: Relevance of Orphanet as assessed by the different stakeholders (**A**) Ministries (n = 17), (**B**) Pharmaceutical industry (n = 19), (**C**) Other institutional stakeholders (n = 13) and (**D**) Patient organisations (n = 4) across all Member States.

3.12. Long-term funding and sustainability of Orphanet

Basic information:

The last part of the survey addressed the question of a long-term funding mechanism, and thus a long-term sustainability of Orphanet.

Since its foundation in 1997 in France, Orphanet has been funded by several consecutive EU-projects, as well as huge contributions for the central coordinating team and infrastructure at the INSERM, France. Since 2011, Orphanet has been financed as a so-called Joint action, where funding is provided in part by the EU, and in part by the respective participating Member State. With the end of this funding period in 2018, new strategies will be necessary to ensure a sustainable continuation of Orphanet.

Like in the current Joint Action, where Member States are co-funders and end-users of the Orphanet database in parallel, Member States could participate in the continuation of Orphanet by funding of defined national activities (like keeping information on national expert resources up to date), joint activities (like the advancement of the encyclopaedia), and/or core activities (like the core infrastructure of Orphanet).

Survey results:

All participants of the survey were first asked to indicate whether, according to their institutional and/or personal opinion, Orphanet should be funded in the future in principle via (1) a merely EU-based budget and mechanism or (2) by a joint activity of the Member States and the European Commission or (3) by Member States only. As shown in **Figure 28**, three-quarter of the respondents favour a joint approach, where Member States and the European Commission share the costs to run Orphanet by a yet to be defined allocation formula, while around 25% of participants opted for a solution assigning the full responsibility for the funding and continuation of Orphanet to the European Commission only. No respondent from any stakeholder or Member State advocated for a funding concept solely supported by the Member States.

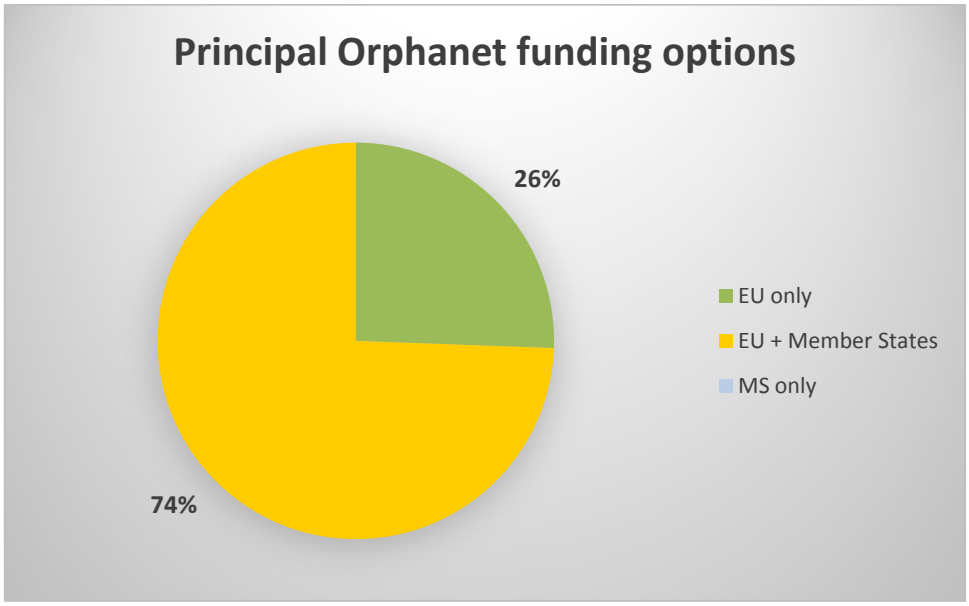

Figure 28: Relative approval of the different financing options for a long-term funding of Orphanet by all participating stakeholders (n = 47).

Subsequently, all participants were asked to indicate, which institutions within their countries should, in their opinion, contribute to any Orphanet funding. To this end, attendees were provided with a carefully arranged, comprehensive check-box list with various stakeholder institutions, fully resembling the list of institutions that had been invited to participate in this survey. Respondents had the possibility to select multiple choices and/or to add further suggestions in a free-text commentary field.

As outlined in **Figure 29**, the results obtained can be clustered into the following three main groups according to their relative frequency levels reached:

- Group 1: Funding institutions favoured by ≥ 50% of the respondents.

  The first group comprises only one possible funding institution, the Ministries of Health, resembling the preferred choice of 72% of all participants. This high preference level indicates that the predominant majority of respondents primarily see a close link between the Orphanet services and the healthcare sector, thus assigning the highest co-funding "responsibility" to the Health Ministries.

- Group 2: Funding institutions favoured by 19%-50% of the respondents.

  The second group consists of the other two ministries included in the stakeholder survey, the Ministries of Social Affairs and of Science, with preference levels of 30% and 38%, respectively, to participate in the Orphanet funding concept, and the European, as well as the national alliances of the pharmaceutical industry, both selected by 26% and 19% of the respondents to contribute to the future financing of Orphanet.

- Group 3: Funding institutions favoured by ≤ 18% of the respondents.

  Between 6%-15% of respondents finally indicated that also the national and European alliances of patient organisations, as well as the European alliances of learned societies and other stakeholder institutions like university hospitals or national funding agencies (INSERM as example) should participate in the joint funding of Orphanet.

It is important to note that these figures resemble the cumulated opinions of all stakeholders on all possible institutions, including, but not limited to their own organisation.

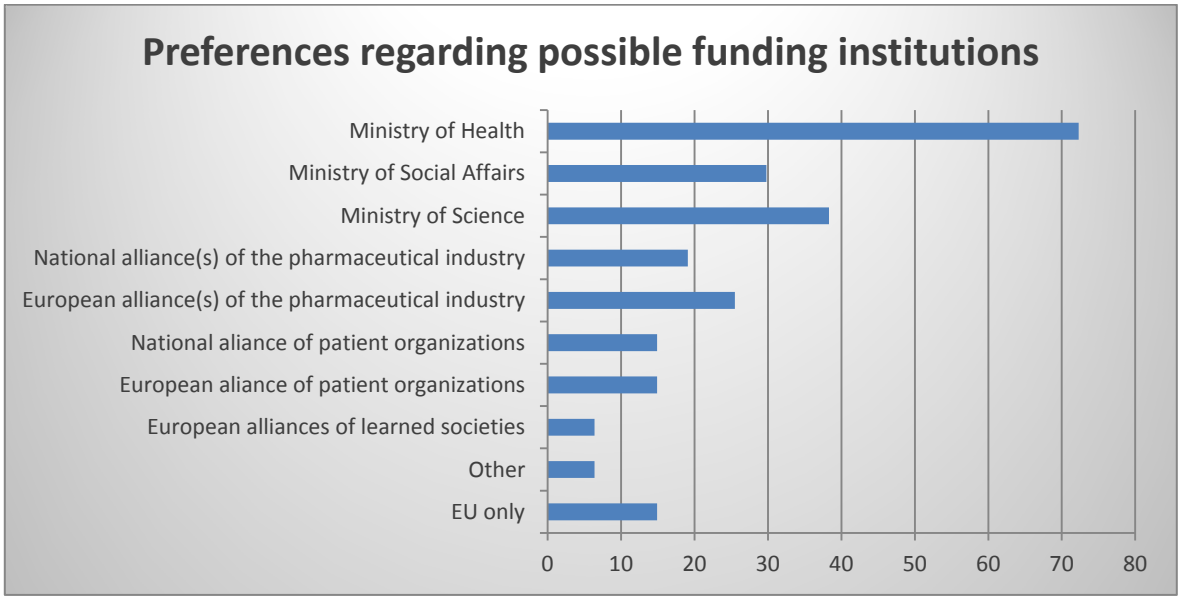

Figure 29: Cumulative preference levels regarding a possible participation of the different institutional stakeholders in the future co-funding of Orphanet by all responding stakeholders (n = 47).

As a side note, a slight shift in opinion within all respondents can be observed regarding the assessment of the funding option "EU only". While in the previous question 26% of the respondents favoured the EU only version, when the alternatives presented to the participants were "EU only", "EU plus Member States" and "Member States only", now, in the follow-up question, which offered more and multiple choices to the participants, this fraction decreased to 15% only that still opted for an exclusive funding by the European Union.

While **Figure 29** gives a global impression on the preferred order and relevance of possible co-funding institutions in a joint funding concept for Orphanet, based on the cumulative opinions off all respondents, **Figure 30** presents a more detailed analysis of all the replies received, now sorted by stakeholder/stakeholder subgroup.

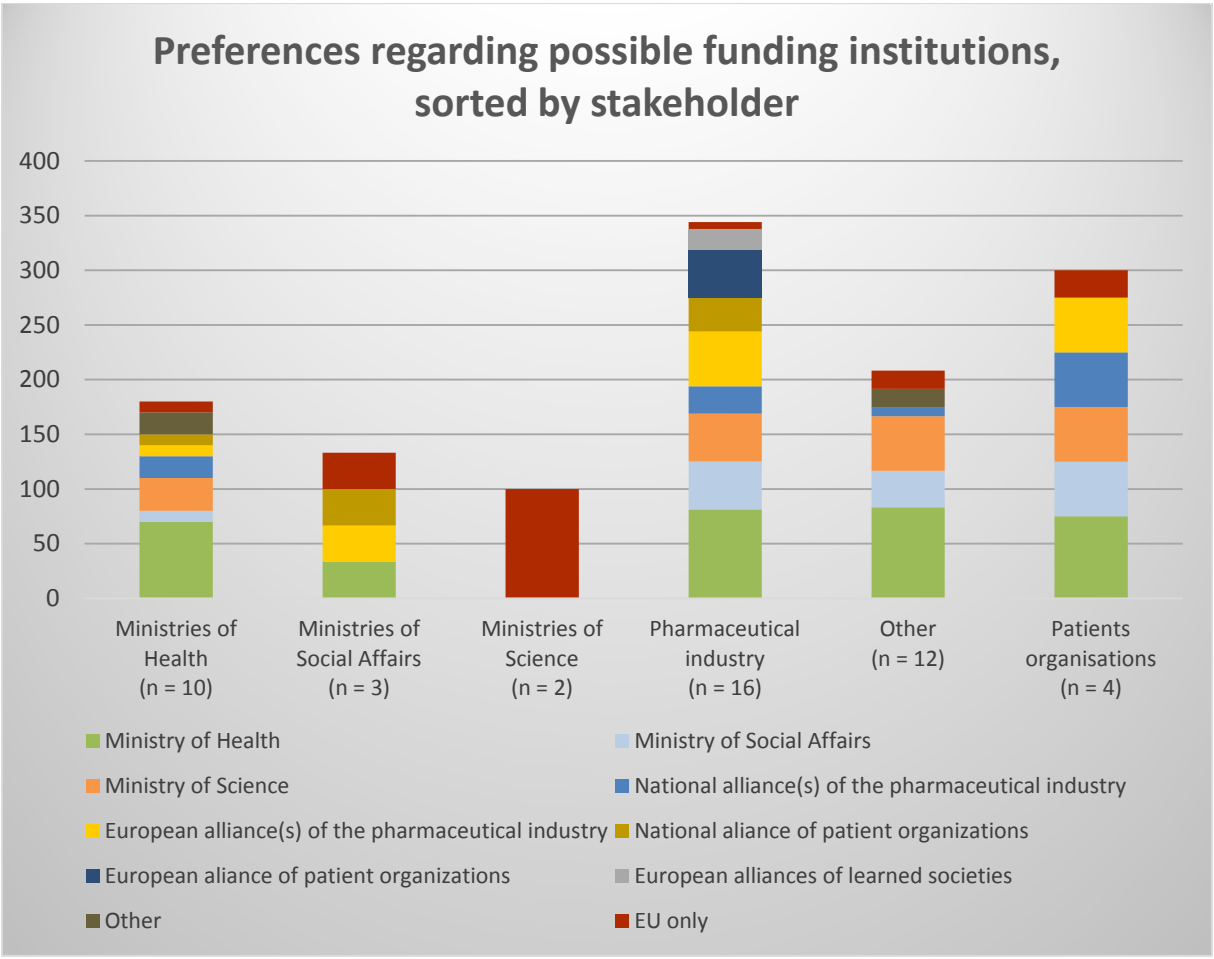

Figure 30: Cumulative preference levels regarding a possible participation of the different institutional stakeholders in the future co-funding of Orphanet sorted by stakeholder/stakeholder subgroup (n = 47).

The first thing to note is that except for the representatives of the Ministries of Science, which assign any funding responsibility to the European Union only, all other respondents favour by the majority a mixed funding approach with a sometimes more, sometimes less complex composition of participating institutions and organisations. Secondly, participants from four out of the six stakeholders/stakeholder subgroups (the "Ministries of Health", the "Pharmaceutical industry", the "Other institutional stakeholders" and the "Patients' organisations") would prefer the inclusion of all three ministries (the Ministries of Health, Social Affairs and Science) in a future funding concept, albeit to different degrees.

Importantly, except for the Ministries of Health, representatives of the other two ministries do not see any own involvement of their institution in the joint financing of Orphanet in this question (the situation is a bit different in the follow-up question, see below). Furthermore, respondents from all stakeholders/ stakeholder subgroups except from the Ministries of Science opt for a limited role of the pharmaceutical industry in the future financing of Orphanet, be it on the level of the national and/or the European alliances. Participants from three stakeholders (the Ministries of Health and Social Affairs, as well as the Pharmaceutical industry) also advocate for a limited participation of national alliances of patients' organisations in the funding concept, with respondents from the Pharmaceutical industry being the only ones to also include the European alliance of patients' organisations and European alliances of learned societies into their basket of potential funding institutions.

In the final question, all participants from the various stakeholders were asked about the possibilities that their own institution takes part in the co-funding of the different Orphanet services, either by supporting the national and/or the central Orphanet team or by making a specific service available in the national language. Again, multiple choices were possible.

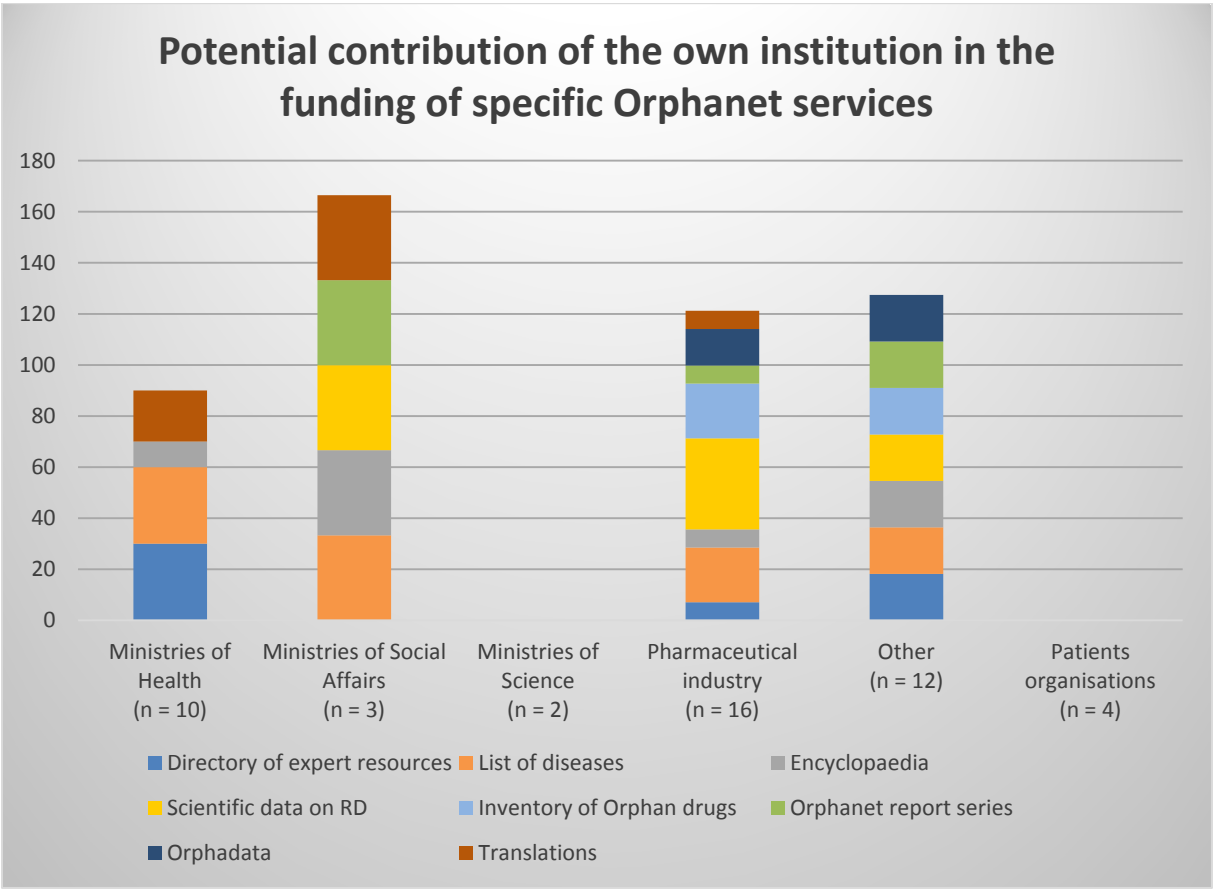

Figure 31: Cumulative preference levels regarding a possible future co-funding of specific Orphanet services, sorted by stakeholder/stakeholder subgroup (n = 47).

As depicted in **Figure 31**, the participants from two stakeholders, the "Ministries of Science" and the "Patients' organisations", unanimously refused the possibility of any contribution to the co-funding of any Orphanet service, completely in line with their preferences when selecting possible funding institutions in general (see **Figure 30**). Participants from the other stakeholders/stakeholder subgroups, on the other side, declared in part their principal willingness to support various Orphanet

services. The preferred services, mentioned by respondents from at least three stakeholders, comprise the directory of expert resources, the list of diseases, the encyclopaedia, the scientific data on rare diseases, the Orphanet report series, and translations into national languages. The other two selectable services, the inventory of Orphan drugs and Orphadata, were only selected by participants from the pharmaceutical industry and the group of other institutional stakeholders.

The data obtained in this question were finally also analysed with regard to the concrete willingness of the different stakeholder institutions and organisations to participate themselves in a future Orphanet co-funding concept (**Figure 32 A-F**).

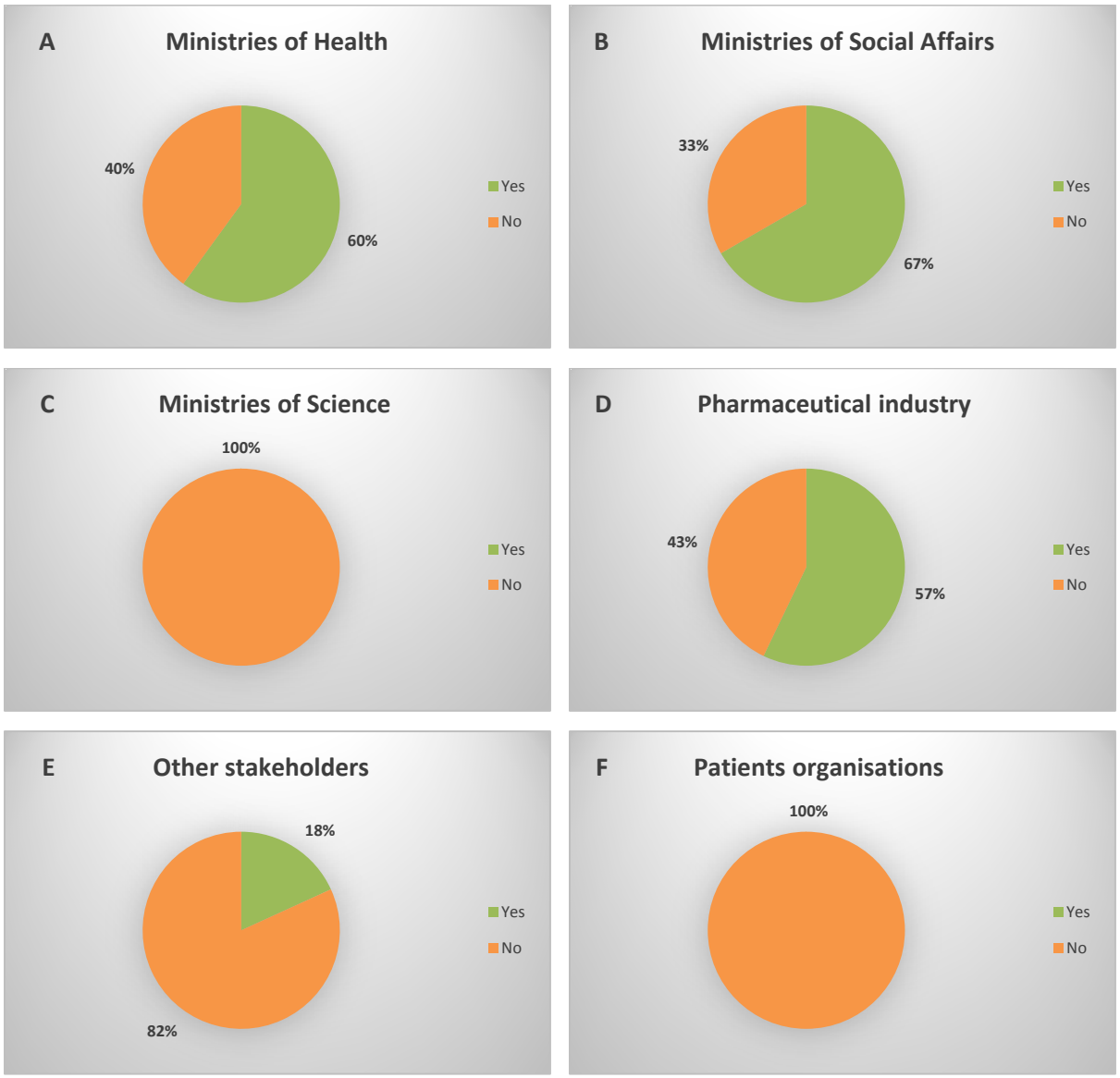

Figure 32: Principal willingness of the different stakeholders/stakeholder subgroups to participate in a future joint co-funding of Orphanet. Values describe the relative proportions of respondents per stakeholder/organisation, opting for either of the two choices (n = 47).

In general, a majority of 57%-67% of the respondents from the stakeholder groups “Ministries of Health”, “Ministries of Social Affairs” and “Pharmaceutical industry” indicate that their institutions could possibly contribute to the future funding of Orphanet (**Figure 32 A, B, D**), while in the subgroup of

"Other institutional stakeholders" only 18% of respondents belief that their institution might be willing to participate in any joint financing scheme (**Figure 32 E**). In the subgroups "Ministries of Science" and "Patients' organisations", no respondent opts for a contribution of their institution/organisation to any future Orphanet funding (**Figure 32 C, F**).

Of note, a few stakeholder subgroups show slight discrepancies within their answer profiles when asked about possible strategies and perspectives for the future financing of Orphanet. These differences are best explained by the fact that these questions were targeted once to the more global and once to the very concrete level of the individual institution. For example, in the stakeholder group of the "Ministries of Health", 70% of respondents agreed with a possible co-funding role of health ministries in general (**Figure 30**), while only 60% of participants declared to see an option that their own institution would contribute in reality to such a funding concept (**Figure 32 A**). On the other hand, respondents from the subgroup "Ministries of Social Affairs" did at first not include their own ministries in the list of potential funding institutions for Orphanet in general (**Figure 30**). However, when asked about possible concrete support for Orphanet services, 67% of the respondents indicated that their ministries might indeed be willing to participate in certain funding aspects of Orphanet (**Figure 32 B**).

Collectively, considering firstly the often high to very high levels of satisfaction with the Orphanet services, secondly the generally high acknowledgement and appreciation of the role that Orphanet plays in the healthcare and science field, and thirdly the general opinion, accepted by three-quarters of the participants, that any future long-term funding of Orphanet should be based on a joint approach with participation of the European Commission and the Member States (see **Figure 28**), the actual number of institutions and/or organisations indicating a principle willingness to possibly participate in such a joint financing concept falls slightly short to what could have been expected from the previous high rating of Orphanet, underlining that further discussions and conceptual work is necessary on the level of the European Commission and the Member States to finally elaborate and establish a joint funding model that ensures the necessary financial resources for a stable and long-term operation of the database.

4. General conclusions and outlook

Summarizing the results presented in the previous chapter, the following general conclusions can be drawn:

- Based on the contact details received from the national Orphanet teams, the survey was addressed to stakeholder institutions and organisations in 16 out of 24 Member States with a dedicated Orphanet team in place and 16 out of 28 European Member States altogether. This corresponds to a geographical "invitation coverage" of 67% (relating to Member States with Orphanet teams) and 57% (relating to all European Member States), respectively. Out of these 16 Member States, responses from at least one stakeholder were received from 13 Member States, corresponding to a response rate of 81% of the Member States, and a general geographical "response coverage" of 54% (relating to Member States with Orphanet teams) and 46% (relating to all European Member States).

  Focussing on countries with dedicated Orphanet teams in place, a two-thirds geographical coverage regarding the invitation to participate in the survey reaches the set target of a systematic *European-wide* survey in a borderline manner, while a 54% geographical coverage regarding responses received from the participants falls slightly short of the aim of this study, indicating that the European-wide aspect was only partially fulfilled.

- The relatively low number of actual participants in the survey (n = 53) also implies that the results obtained have to be interpreted as opinion trends only and not as statistically corroborated figures. However, in this context it needs to be stressed that reaching participant numbers in a range suitable for any statistical analysis was neither a goal of this study nor was it possible to recruit the necessary number of participants for such an analysis in a study purposefully designed to include only selected institutional and organisational stakeholders and excluding the broader public.

- The characterisation as opinion trends should not be misinterpreted as a challenge to the value of the data, implying the results obtained would be too weak and arguable to be of further use. To the contrary, the often very similar response profiles of the more institutional stakeholders (the ministries, the pharmaceutical industry and the group of "Other institutional stakeholders") demonstrate the particular robustness of the data clearly underlining the value of the results presented in this survey.

- The detailed analyses of the answers received from the different stakeholder subgroups regarding their individual use frequencies of the various services offered by Orphanet revealed that for most services these subgroups can be split into two response profiles: one comprising the subgroups "Ministries", "Pharmaceutical industry" and "Other institutional stakeholders", all exhibiting an on average limited to very limited access rate to the database, and the other one composed of the subgroup "Patients' organisations" displaying an on average high use frequency, indicating that the different stakeholder subgroups obviously have a different demand for the information offered by Orphanet and thus connect to the database to a varying extent.

- Importantly, this different demand and use behaviour does not have any influence on the general appreciation for Orphanet across all stakeholder subgroups. Independent whether accessing the database often or rarely, the clear majority of respondents almost always experienced the various services of Orphanet personally, as well as institutionally to be quite to highly useful and to be quite to very satisfied with the quality of these services. These constantly high scorings strongly underline the fact that all stakeholders, independent of their

individual use frequency, highly acknowledge and appreciate the existence of any of these services, when needed, and thus highly value the benefits offered by Orphanet.

- All stakeholders strongly encourage the objective to sustain Orphanet and to provide a framework allowing its continuation.
- Regarding the future financing of Orphanet, a clear majority of stakeholders recommends a joint funding mechanism with contributions from the European Commission, as well as from the Member States.
- And finally, regarding a concrete implementation of and participation in a co-funding model, only one half of the stakeholder subgroups indicates a concrete willingness to possibly contribute to a joint funding mechanism for Orphanet in a meaningful way, while in the other half the stakeholder subgroups either completely refuse to participate in any co-funding of Orphanet or show only a limited interest in supporting a joint financing of Orphanet, as expressed by a small minority within this subgroup.

Since all these conclusions are based on opinion trends extracted from a limited number of participants so far and despite the robustness of the data from the more institutional stakeholder subgroups, as explained above, the work package 3 and RD Action lead teams have decided to extent the survey on a voluntary basis in order to recruit more participants from further countries and stakeholders in a further call for participation, aiming to further broaden the base data of the survey as much as possible and subsequently, based on a further analysis including these newly collected data, to corroborate or correct and adapt the results obtained so far.

This document is part of the project / joint action '677024 / RD-ACTION' which has received funding from the European Union's Health Programme (2014-2020).

Annex 1

Printed version of a complete stakeholder survey for all institutions/organisations except patients' organisations using the example of Austria

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Orphanet survey (Austria)

Introduction

In the frame of the European Joint Action project "Rare Diseases Action (RD-ACTION)" and supported by the European Commission, Directorate General Food and Health, we cordially invite you to participate in the first European-wide systematic stakeholder survey on Orphanet, the most comprehensive and reliable information source for rare diseases worldwide.

As you might know, the European Union has defined rare diseases as those disease entities with a prevalence of not more than 5 affected persons per 10,000 inhabitants. Despite some significant progress during the past years, people living with rare diseases and those supporting and taking care of them like relatives and friends, as well as professionals including physicians, nurses and other health care personnel, are still confronted with numerous difficulties like, amongst others, lack of information and expert knowledge, scarcity of resources, lack of timely diagnostics and specific therapies, and insufficient awareness regarding their medical and social needs. In order to address these challenges, Orphanet (www.orpha.net) was established in 1997 in France and successively expanded throughout Europe and beyond. It now constitutes the most comprehensive and reliable information source on all aspects of rare diseases worldwide, positioning Orphanet as a potential official reference database for rare diseases in the European Union.

This outlook makes an evaluation of Orphanet on the level of main stakeholders in health-care, social systems and research in all European Member States necessary (in addition to the regular online user-survey which is carried out every year).

Therefore, this survey is addressed to representatives of the Ministries of Health, Social Affairs and Science, as well as national and European alliances of patient organizations, the pharmaceutical industry, social insurance institutions and selected learned societies. Its main objective is to evaluate the direct and indirect benefits of the different information services offered by Orphanet on the level of the above mentioned institutions, as well as their expected overall value for each Member State. In addition, it can help to further improve the usefulness and usability of Orphanet in the future.

Your participation in this survey is of great value, whether you have been using Orphanet or not, and regardless of your current knowledge of Orphanet and its services.

It will take approximately 15-20 minutes to complete the survey. Importantly, you do not have to complete the survey in one pass. Instead, you may save your entries at any point and come back

later to continue.

On behalf of all members of the Joint Action RD-ACTION, we thank you in advance for your efforts.

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Orphanet survey (Austria)

General information

* 1. Please indicate your country

* 2. Type of institution / affiliation / profession

- ◯ Ministry of Health or other central governmental Health Authority
- ◯ Ministry of Social Affairs or equivalent governmental authority
- ◯ Ministry of Science or equivalent governmental authority
- ◯ Social insurance
- ◯ Pharmaceutical industry
- ◯ Patient organizations
- ◯ European alliance of a learned society
- ◯ Other (please specify)

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General information

* 3. Are you:

- ◯ National alliance / institution
- ◯ European alliance / institution

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General information

* 4. Does your professional field of activity include rare diseases?

- ◯ main field of activity
- ◯ yes, partly
- ◯ no

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Orphanet survey (Austria)

Use of Orphanet services

* 5. How often do you use the Orphanet website / Orphanet services?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Use of Orphanet services

* 6. Do you know Orphanet and its services?

- ◯ yes
- ◯ no

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Use of Orphanet services

* 7. Why do you not use Orphanet?

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Use of Orphanet services

Orphanet (www.orpha.net) is the only available database worldwide providing comprehensive validated, quality-controlled, expert-reviewed information on rare diseases, thus positioning Orphanet as a possible future reference-database for rare diseases in the European Union. It offers a wide range of freely accessible services on rare diseases and orphan drugs, most of them in at least seven languages:

- **inventory and classification of all rare diseases known to date with a numeric identifier (ORPHAcode);**
- **information on genes, phenotypes and disability facts related to rare diseases;**
- **epidemiological data on rare diseases (i. e. prevalence, incidence, birth prevalence);**
- **encyclopaedia of rare diseases;**
- **inventory of orphan drugs;**
- **directory of expert resources on rare diseases (expert centres, medical laboratories, patient organizations, research projects, clinical trials, registries, networks, research infrastructures) for each of the Member States and beyond (40 countries);**
- **an assistance-to-diagnosis tool allowing users to search by signs and symptoms;**
- **encyclopaedia of recommendations and guidelines for clinical practice, emergency medical care and anaesthesia, and of disabilities related to rare diseases;**
- **bi-weekly newsletter in English, Italian and French;**
- **a collection of thematic reports free for download on the Orphanet website.**

For more information, please go to the Orphanet national website (http://www.orpha.net/national/AT-DE/index/startseite/) and/or contact the Orphanet national team at ursula.unterberger@meduniwien.ac.at.

* 8. Based on this information, do you think these services might be useful for you and/or your institution in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Inventory of rare diseases and classification system

Orphanet provides a comprehensive inventory of rare diseases classified according to a polyhierarchical classification system. To date, almost 6,000 diseases are listed. Each disease entity listed in Orphanet is assigned a specific, unique identifier, the so-called Orpha number or Orpha code.

* 9. How often do you use the inventory of rare diseases, the classifications and the Orpha code nomenclature?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Inventory of rare diseases and classification system

* 10. Do you know this service?

- ◯ yes
- ◯ no

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Inventory of rare diseases and classification system

* 11. Please specify why you do not use this service.

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Orphanet survey (Austria)

Inventory of rare diseases and classification system

Orphanet provides a comprehensive inventory of rare diseases classified according to a polyhierarchical classification system. To date, almost 6,000 diseases are listed. Entries are cross-referenced with ICD-10, OMIM, UMLS, MeSH, and MedDRA. The Orphanet rare disease inventory and classification system is available in seven languages and is constantly updated based on documented sources and expert advice.

Each disease entity listed in Orphanet is assigned aspecific, unique identifier, the so-called Orpha number or Orpha code. This Orpha number can be found in the list of rare diseases, directly below the name of the respective disease. It allows for an unambiguous coding of each rare disease according to the Orphanet classification of rare diseases and can therefore, after integration into the respective Health information systems, serve as ideal tool to identify RD patients unambiguously.

* 12. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 13. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Inventory of rare diseases and classification system

* 14. How useful is this service for you personally?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

* 15. How satisfied are you with the quality of this service?

- ◯ very satisfied
- ◯ quite satisfied
- ◯ moderately satisfied
- ◯ not satisfied

* 16. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

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Orphanet survey (Austria)

Collection of scientific data on rare diseases

The collection of scientific data on rare diseases (including data collections on genes, phenotypes, and disability facts) and the cross-referencing of these datasets to other databases are designed to increase the knowledge on rare diseases, to support research, and to ensure interoperability between databases and registries.

* 17. How often do you use the collection of scientific data on rare diseases?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Orphanet survey (Austria)

Collection of scientific data on rare diseases

* 18. Do you know this service?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Collection of scientific data on rare diseases

* 19. Please specify why you do not use this service.

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Orphanet survey (Austria)

Collection of scientific data on rare diseases

The Orphanet inventory of rare diseases is annotated with:

- **the corresponding terms of the Human Phenotype Ontology (HPO), a standardized and controlled terminology covering phenotypic abnormalities in human diseases;**
- **associated genes, with a characterization of the relationship between the gene and the disease (causative, modifier, susceptibility or playing a role in the phenotype) and the kind of mutation (germline or somatic);**
- **functional consequence(s) recorded by frequency in the patients' population, temporality, degree of severity and loss of abilities (if applicable).**

The inventory of diseases is cross-referenced with other medical languages (OMIM, ICD-10, MeSH, MedDRA and UMLS), while the inventory of genes is cross-referenced with genetic databases (HGNC, OMIM, UniProtKB, IUPHAR, and Genatlas), thereby ensuring interoperability between databases and registries.

This service is designed for research purposes, as well as to increase knowledge on rare diseases in general.

* 20. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 21. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Collection of scientific data on rare diseases

* 22. How useful is this service for you personally?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

* 23. How satisfied are you with the quality of this service?

- ◯ very satisfied
- ◯ quite satisfied
- ◯ moderately satisfied
- ◯ not satisfied

* 24. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

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Orphanet survey (Austria)

Directory of expert resources

The directory of expert resources dedicated to rare diseases provides a comprehensive representation of healthcare, diagnostics and research services and activities specific for each rare disease in each participating country, for referrals as well as for analyses supporting policy making.

* 25. How often do you use the directory of expert resources?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Orphanet survey (Austria)

Directory of expert resources

* 26. Do you know this service?

- ◯ yes
- ◯ no

Orphanet survey (Austria)

Directory of expert resources

* 27. Please specify why you do not use this service.

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Directory of expert resources

Countries participating in Orphanet collect data on national expert resources (expert centers/outpatient clinics, diagnostic laboratories and tests, patient organizations, clinical trials, research projects, registries, and infrastructures) specializing in rare diseases. All information is validated, quality controlled, and published in the national language, as well as in English.

* 28. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 29. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Directory of expert resources

* 30. How useful is this service for you personally?

- very useful
- quite useful
- moderately useful
- of limited use

* 31. How satisfied are you with the quality of this service?

- very satisfied
- quite satisfied
- moderately satisfied
- not satisfied

* 32. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- very useful
- quite useful
- moderately useful
- of limited use

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Orphanet survey (Austria)

Encyclopaedia (texts on diseases)

The texts on diseases, altogether referred to as Orphanet encyclopaedia, provide information for health professionals, patients and relatives, social workers, and the general public on each rare disease.

* 33. How often do you use the encyclopaedia?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Orphanet survey (Austria)

Encyclopaedia (texts on diseases)

* 34. Do you know this service?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Encyclopaedia (texts on diseases)

* 35. Please specify why you do not use this service.

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Orphanet survey (Austria)

Encyclopaedia (texts on diseases)

Orphanet provides three distinct encyclopaedias on rare diseases:

1. **An encyclopaedia for health professionals (including review articles, practical genetics articles, emergency guidelines for the management of patients in ermergency situations, and good practice guidelines issued by official organizations), expert-authored and peer-reviewed, available in eleven languages;**
2. **An encyclopaedia for the general public, peer-reviewed by professionals and dedicated patient organizations, available currently mostly in French;**
3. **Factsheets related to disabilities caused by the specific rare diseases, which mainly address professionals in the field of disability, als well as patients and their families.**

In addition, there are links to externally produced literature on rare diseases in all languages.

* 36. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 37. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Encyclopaedia (texts on diseases)

* 38. How useful is this service for you personally?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

* 39. How satisfied are you with the quality of this service?

- ◯ very satisfied
- ◯ quite satisfied
- ◯ moderately satisfied
- ◯ not satisfied

* 40. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

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Orphanet survey (Austria)

Inventory of Orphan drugs

The inventory of Orphan drugs provides information on therapies, either approved or currently in development, that are specific for rare diseases.

* 41. How often do you use the inventory of Orphan drugs?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Orphanet survey (Austria)

Inventory of Orphan drugs

* 42. Do you know this service?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Inventory of Orphan drugs

* 43. Please specify why you do not use this service.

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Orphanet survey (Austria)

Inventory of Orphan drugs

This online-inventory allows the user to search for orphan drugs by:

- **the substance or trade name,**
- **the diseases they are linked to,**
- **the ATC category (i. e. the WHO's Anatomical, Therapeutic, Chemical classification, which is used for the classification of medicinal substances),**
- **the name of the sponsor, or**
- **the name of the holder of the marketing authorization.**

The list of orphan drugs includes all substances which have been granted an orphan designation for diseases considered rare in Europe. It also includes drugs without an orphan designation as long as they have been granted a marketing authorization with a specific indication for a rare disease.

* 44. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 45. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Inventory of Orphan drugs

* 46. How useful is this service for you personally?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

* 47. How satisfied are you with the quality of this service?

- ◯ very satisfied
- ◯ quite satisfied
- ◯ moderately satisfied
- ◯ not satisfied

* 48. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

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Orphanet survey (Austria)

Orphanet report series

The Orphanet report series covers a growing collection of reports providing information on particular topics of interest in the field of rare diseases for a variety of stakeholders in a printable format.

* 49. How often do you use the Orphanet report series?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Orphanet survey (Austria)

Orphanet report series

* 50. Do you know this service?

- ◯ yes
- ◯ no

Orphanet survey (Austria)

Orphanet report series

* 51. Please specify why you do not use this service.

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Orphanet survey (Austria)

Orphanet report series

The Orphanet report series is a growing collection of reports currently comprising:

- **a general list of rare diseases and synonyms,**
- **lists of rare diseases with epidemiological data (sorted alphabetically or by decreasing prevalence),**
- **a list of orphan drugs,**
- **a list of disease registries in Europe,**
- **a list of research infrastructures useful to rare diseases in Europe, and**
- **annual Orphanet activity reports.**

In general, the reports provide information on particular topics of interest for a variety of stakeholders in a printable format. Texts are either newly published or updated on a regular basis.

* 52. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 53. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Orphanet report series

* 54. How useful is this service for you personally?

- very useful
- quite useful
- moderately useful
- of limited use

* 55. How satisfied are you with the quality of this service?

- very satisfied
- quite satisfied
- moderately satisfied
- not satisfied

* 56. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- very useful
- quite useful
- moderately useful
- of limited use

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Orphanet survey (Austria)

Orphadata including ORDO

The website Orphadata (www.orphadata.org) provides downloadable Orphanet datasets including the Orphanet Rare Diseases Ontology (ORDO). The system allows mass-extraction and re-use of large datasets of the Orphanet database for research, analysis and decision-making purposes.

* 57. How often do you use the Orphadata/ORDO?

- ◯ several times a week
- ◯ weekly
- ◯ monthly
- ◯ few times a year
- ◯ never or almost never

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Orphadata including ORDO

* 58. Do you know this service?

- ◯ yes
- ◯ no

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Orphadata including ORDO

* 59. Please specify why you do not use this service.

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Orphanet survey (Austria)

Orphadata including ORDO

The website Orphadata (www.orphadata.org) provides downloadable Orphanet datasets including the Orphanet Rare Diseases Ontology (ORDO). The system allows mass-extraction and re-use of large datasets of the Orphanet database for research, analysis and decision-making purposes.

The datasets offered on Orphadata are comprehensive, high-quality datasets related to rare diseases and orphan drugs in a reusable, computable format. These datasets are a partial extraction of the data stored in Orphanet and are either accessible and downloadable for free, or available upon request and free for academia / available for a fee for industry.

* 60. Based on this information do you think this service might be useful for you personally in the future?

- ◯ yes
- ◯ no

* 61. Based on this information do you think this service might be useful for YOUR INSTITUTION IN GENERAL in the future?

- ◯ yes
- ◯ no

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Orphanet survey (Austria)

Orphadata including ORDO

* 62. How useful is this service for you personally?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

* 63. How satisfied are you with the quality of this service?

- ◯ very satisfied
- ◯ quite satisfied
- ◯ moderately satisfied
- ◯ not satisfied

* 64. How useful would you rate this service for YOUR INSTITUTION IN GENERAL?

- ◯ very useful
- ◯ quite useful
- ◯ moderately useful
- ◯ of limited use

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Orphanet survey (Austria)

General use and relevance of Orphanet

In September 2016, the date of the last comprehensive website use analysis, anaverage number of 969,729 users from 293 countries accessed Orphanet per day, visiting 4,123,930 pages. Based on the results obtained from the analysis of several online user surveys in the past years, these Orphanet users can be assigned to the following categories:

- **approx. 60 % health care professionals (including medical doctors and nurses, paramedical therapists, and medical students);**
- **approx. 30 % patients (including parents and other relatives);**
- **approx. 10 % other users (including social workers, policy makers, representatives from the pharmaceutical industry, journalists, and the general public).**

In the Inventory of expert resources Orphanet currently (as of September 2016, data from 40 partner countries) provides information on:

- **7,172 Expert centres (274 in Austria);**
- **2,575 Patient organisations (67 in Austria);**
- **41,159 Diagnostic tests (973 in Austria);**
- **1,667 Medical labs (40 in Austria);**
- **2,245 Ongoing research projects (61 in Austria);**
- **2,435 Ongoing clinical trials (52 in Austria).**

Regarding the Scientific database (effective date September 2016, data from 40 partner countries) Orphanet currently lists:

- **6,008 rare diseases (excluding sub-types and groups);**
- **4,080 texts;**
- **3,573 genes (including 3,179 known causative genes for 2,740 rare diseases);**
- **2,636 diseases annotated with clinical signs;**
- **455 diseases annotated with functional consequences.**

Finally, the proportional number of Orphanet users from Austria, relative to the size and population of the country, lies above the median when comparing the user frequency between all 28 European Member States.

* 65. Looking at these figures, how important would you rate the benefit Orphanet provides for Austria as a central, quality assured, European tool for information regarding rare diseases?

- ◯ very important
- ◯ quite important
- ◯ moderately important
- ◯ of limited importance

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Long-term funding and sustainability of Orphanet

Since its foundation in 1997 in France, Orphanet has been funded by several consecutive EU-projects, as well as huge contributions for the central coordinating team and infrastructure at the INSERM, France. Since 2011, Orphanet has been financed as a so-called Joint action, where funding is provided in part by the EU, and in part by the respective participating Member State. With the end of this funding period in 2018, new strategies will be necessary to ensure a sustainable continuation of Orphanet.

Like in the current Joint Action, where Member States are co-funders and end-users of the Orphanet database in parallel, Member States could participate in the continuation of Orphanet by funding of defined national activities (like keeping information on national expert resources up to date), joint activities (like the advancement of the encyclopaedia), and/or core activities (like the core infrastructure of Orphanet).

* 66. In your opinion, by which institution(s) should Orphanet be funded in the future?

- ◯ EU only
- ◯ EU + Member States
- ◯ Member States only

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Long-term funding and sustainability of Orphanet

* 67. In your opinion, which institutions within Austria should contribute to Orphanet funding (multiple choices possible)?

- [ ] Ministry of Health or other central governmental Health Authority
- [ ] Ministry of Social Affairs or equivalent governmental authority
- [ ] Ministry of Science or equivalent governmental authority
- [ ] National alliance(s) of the pharmaceutical industry
- [ ] European alliance(s) of the pharmaceutical industry
- [ ] National aliance of patient organizations
- [ ] European aliance of patient organizations
- [ ] European alliances of learned societies
- [ ] None of the above, EU only
- [ ] Other (please specify)

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Orphanet survey (Austria)

Long-term funding and sustainability of Orphanet

* 68. Do you think your institution might contribute to funding of the following Orphanet services in the future and/or to make these services available in your national language (multiple choices possible)

- [ ] Directory of expert resources (clinics, medical laboratories etc.)
- [ ] List of diseases and classifications and Orpha code nomenclature
- [ ] Encyclopaedia (texts on diseases)
- [ ] Scientific data on rare diseases: genes, phenotypes, disabilities
- [ ] Inventory of orphan drugs
- [ ] Orphanet report series (list of rare diseases, epidemiology of rare diseases, list of orphan drugs, lists of registries and research infrastructure, Orphanet activity reports)
- [ ] Orphadata including ORDO (downloadable Orphanet datasets including the Orphanet Rare Diseases Ontology)
- [ ] Translation of the Orphanet website (complete or partially) into the national language
- [ ] Translation of the Orphanet nomenclature into the national language (for instance to be used for coding purposes)
- [ ] Translation of the Encyclopaedia (complete or partially) into the national language
- [ ] None of the above – my institution will not contribute to Orphanet funding

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Request for improvements and/or information

* 69. What should Orphanet improve to better serve your needs?

* 70. Do you want to be contacted by a member of the Orphanet team in your country to receive further information on Orphanet?

- ◯ yes
- ◯ no

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End of the survey

We would like to thank you very much for your time and your answers and opinions. This is of great importance to us and will help us to improve and secure Orphanet.