Survey on researchers' opinion about and experience with the Swiss Federal Act on Research involving Human Beings

Forschung im Geltungsbereich des Schweizer Humanforschungsgesetzes 2016/2017 (TPF6)

Report of Project part 2 (version corrected July 2019)

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List of abbreviations

BASEC	Business Administration System for Ethics Committees
ClinO	Clinical Trials Ordinance
CRO	Contract Research Organisation
CTU	Clinical Trial Unit
EC	Ethics Committee
ESOPE	Enquêtes de satisfaction et d'opinion des patient-e-s et des employé-e-s
EU	European Union
FOPH	Swiss Federal Office of Public Health
FUP	Further use project
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HFG	Humanforschungsgesetz (English: Human Research Act)
HRA	Human Research Act (German: Humanforschungsgesetz)
HRO	Human Research Ordinance
IQR	Interquartile range
KOFAM	Koordinationsstelle Forschung am Menschen
NA	“Not available” (missing data) or “Not applicable”. In the figures numbers for both groups are combined.
SAE	Serious Adverse Event
SM+	Projects with submission to Swissmedic
SM-	Projects without submission to Swissmedic & not further use projects

Executive summary

Background: The implementation of the new Human Research Act (HRA) in Switzerland since 2014 is being evaluated in a series of projects. One project (TPF6) comprises a quantitative description of research applications submitted for approval by Swiss Ethics Committees (ECs) through the central Business Administration System for Ethics Committees (BASEC) starting in January 2016 (Project part 1) combined with an online survey of researchers (project managers and investigators) who submitted projects in 2017 (Project part 2). Project part 2 is the focus of this report. In a further project (Project part 3), jurisdictional inquiries from researchers for clarification of the applicability of the HRA to their projects were investigated.

Objectives: We aimed to evaluate the implementation of the HRA from the researchers' perspective. The focus was on their perception of and experience with 1) the current legal framework, 2) the implementation concerning ethical and regulatory approval of research projects, and 3) the usefulness of the BASEC electronic submission system. We aimed to understand the researchers' views about how this legislation had been implemented and any impact it may have had on the design, planning and conduct of research involving human beings in Switzerland.

Methods: We conducted an online survey of researchers who submitted an application through BASEC during the year 2017. In June 2018 they were invited to complete two separate (but interlinked) parts of a questionnaire developed for this purpose. Part A was for project managers and Part B for investigators. This questionnaire included subsets of questions for three distinct types of studies (i.e. studies requiring approval by Swissmedic, studies not eligible for approval by Swissmedic and studies with further use of biological material or health-related data) and allowed entering comments and suggestions in free text.

Main findings: We contacted researchers who submitted a total of 2187 research projects in 2017. They returned 770 valid questionnaires Part A (response rate 35.2%) and 750 questionnaires Part B (34.3%). The respondents for both parts were identical for 87% of the surveyed projects.

A range of aspects of the current legislation was deemed appropriate by most researchers. However, about 40% affirmed a statement that the HRA hinders scientific research and about two thirds supported the view that many researchers do not know the current legislation very well. About a quarter of respondents regarded the current Swiss legislation as more burdensome than in other countries and another quarter did not (50% undecided). Researchers with industry-initiated projects perceived it as less burdensome than those with investigator-initiated projects. For various professional, structural and private reasons 13% had decided to conduct research projects abroad and specifically not in Switzerland. In a separate question, some researchers (15%) answered that they had been excluded from an international multi-site study once or several times.

Overall, there was a high level of agreement with the current processes. However, about half of the researchers mentioned difficulties with selected aspects of the HRA when designing and planning their study; this was most pronounced for chapters of the Human Research Ordinance (HRO). In cases where ECs or Swissmedic made changes to the type of study (in <10%) researchers mostly agreed with the change and found that explanations were clear and sensible. Most researchers responded that the EC in charge had given adequate weight to a range of criteria relevant for ethical approval according to the HRA and that it had the necessary expertise for this task. However, 20% or more disagreed for some of these criteria (e.g. scientific relevance/quality or funding). More generally, researchers identified the role and expertise of ECs as being mostly in the traditional core domains such as protection of study participants but to a lesser extent in ensuring study quality and feasibility. Less than half of the respondents answered that they felt ECs evaluate projects to a common standard; the majority was either undecided or expressed the opinion that standards differed. More than 70% would welcome more standardisation of processes across ECs, and almost half opted for two models with a reduced number of ECs (either one per language region or one national committee).

Most respondents rated the submission process using the BASEC portal and contacts with either ECs or Swissmedic as good or very good. However, they consistently described several problematic areas, e.g. the requirement to submit complex application dossiers for research projects deemed “small” or “simple” (e.g. collection of retrospective data) or procedures deemed inadequate for research projects other than clinical trials.

Strengths and limitations: In a comprehensive online survey of clinical researchers, we used up-to-date technology and several methodological safeguards to foster participation and to obtain valid data. The achieved response rates were satisfactory given the substantial time and effort that we asked the researchers to invest. Our findings should be interpreted cautiously keeping in mind that:
(i) respondents needed to work in a language other than their mother tongue and were asked about critical issues in a non-anonymised survey, (ii) about 20% of responses were given by researchers who responded for more than one project, and (iii) some findings are based on a small number of responses (in particular, for specific types of projects).

Conclusions: The results of this survey confirm that researchers active in human research in Switzerland are appreciative and satisfied with their interaction with the competent authorities and that they regard the current framework of the HRA and related ordinances as adequate, in general. Consequently, substantial changes to the legislation do not seem necessary. Nevertheless, some findings and the multiple comments point to areas in which improvements in the implementation of the law may be warranted. This might include measures to reduce delays, improve communication between authorities and researchers, streamline pertinent information resources, reduce redundancy in the study information requested at time of submission, and better tailor requirements to the type and nature of submitted research projects. Any such improvements are likely to strengthen Switzerland’s profile as a place for relevant high-quality health research.

1. Introduction

The implementation of the new Federal Act on Research involving Human Beings (Human Research Act, HRA) from 1st January 2014 onwards was accompanied by a series of evaluation projects mandated by the Federal Office of Public Health (FOPH). One of these projects analysed human research projects submitted for approval by Swiss Ethics Committees (ECs) according to the Human Research Act (HRA) in 2016 and 2017. This project has three parts. The present project part 2 was an online survey of researchers who had submitted a research project for approval in 2017 ("Befragung der Forschenden zur Umsetzung des HFG").

2. Objectives

The goal was to evaluate the implementation of the HRA (incl. related ordinances) and the derived processes from the researchers' perspective. We aimed to capture the perceptions and experience of researchers with the revised legal framework, in particular in the context of ethical and regulatory approval of research projects. The focus was on the respondents' opinions about 1) the current framework of the HRA in general, 2) its enforcement by the competent authorities, and 3) the usefulness of the BASEC electronic submission system for the ethical approval of research projects. Because researchers may face difficulties with the current processes for ethical approval, we also aimed to capture feedback on how this legislation had been implemented and what impact it may have had on the design, planning and conduct of research involving human beings in Switzerland.

3. Methods

We conducted an online survey among all researchers who applied for ethical approval at one of the cantonal ECs in Switzerland in 2017.

3.1. Preparation of survey questionnaire

In order to identify key themes and to develop a first draft list of items and the overall structure of the questionnaire, we conducted interviews with several stakeholders of clinical research in Switzerland including staff of Clinical Trial Units (CTUs) and researchers. In an iterative process with FOPH and swissethics and with additional input from the Institute for Political Science (University of Zurich) and Büro BSS (Zurich) the draft questionnaire was refined. This step included the decision to split the questionnaire in two parts. Questions in the first part (Part A) concerned the submission process in BASEC and were tailored to the persons who actually entered the data and submitted the application in the BASEC portal. This could have been a project manager/coordinator or a (principal) investigator. Questions in the second part (Part B) concerned the overall experience with the Swiss human research regulation and its enforcement and were directed to the (principal) investigators who took overall responsibility for the submitted project in Switzerland. A subset of questions in both parts were phrased identically to allow comparison between both respondent groups. Part A and B of the final questionnaire are included in Appendix 1. The questionnaire was in English only, and we refrained from translating and validating versions in other languages. We strived to simplify the text as much as possible to improve its readability.

We assigned each project to one of three groups (see 'Definition' box below) following criteria defined in the HRA and related ordinances, in particular the risk classification. For this purpose, we used the project information available from the BASEC dataset held by swissethics. The questionnaire included subsets of conditional questions that were specific to these three groups.

Definition of groups with subsets of questions:	
SM+	Clinical trials in risk category B or C involving a submission to Swissmedic (ClinO chapters 2 and 3);
SM-	Clinical trials in risk category A (ClinO chapters 2-4), "other" clinical trials in risk category B (ClinO chapter 4), and research involving persons according to Human Research Ordinance (HRO) chapter 2, i.e. not involving a submission to Swissmedic;
FUP	Projects with further use of already available personal data/biological material according to the HRO chapter 3 (so-called "further use" projects).

An overview of the various types of research that are distinguished in the current Swiss legislation and how they map to these three groups is provided in Appendix 2.

The questionnaire was programmed using the software SphinxOnline Manager (sphinx-survey, Erding/Germany). It was then tested in a small group of researchers, and their comments and suggestions were incorporated. We did not pilot the questionnaire in a larger group because this would have considerably delayed the full survey.

3.2. Survey population

The survey population comprised all researchers who had submitted human research projects to a cantonal EC through the BASEC portal between 1st January and 31st December 2017. Projects that were still under review at the end of 2017 were also included. Studies on deceased, embryos or foetuses were excluded. The unit of analysis was the research project entered in the BASEC database. For each project, separate responses by project managers and investigators were possible in Part A and B of the questionnaire. The decision to complete or forward one part of the questionnaire to another person was made by the recipient of the invitation email. The programming of the online survey allowed respondents to start with filling in Part A or Part B and then to pass on the remaining part to the second person (or to fill in themselves when appropriate). In the following we use the generic term "researcher" to describe the respondents for one or both parts.

3.3. Conduct of survey

Using an extract of the BASEC database provided by swissethics, we prepared a list of contact email addresses. There were 2246 entries in total. We drafted an invitation email in four languages (D / F / I / E) which contained a personalised web link to access the online questionnaire. It was sent on behalf of FOPH and swissethics through SphinxOnline Manager from the ESOPE group's generic e-mail address. The first mailing was on 6 June 2018. There were 59 invalid email addresses in return and 2187 valid invitations sent to the researchers. We sent reminders on 20 June 2018 and 3 July 2018. We tracked automated error messages and individual responses in order to identify the suitable respondent for any included project, to resolve any uncertainties (e.g. about who should answer) and to maximise the overall response rate. The survey closed on 25 July 2018.

3.4. Data management & analysis

The dataset was prepared for analysis using standard plausibility checks (e.g. for quantitative data entered) and by removing data from questionnaires that were only partially filled in, i.e. for less than half of the overall number of applicable questions (including sub-items). This step was done separately in questionnaire Parts A and B.

The quantitative analyses used standard descriptive methods and were conducted with the statistical software R (version 3.5.1). Stratification was used where appropriate (e.g. by type of project or role of respondent). We did not aim to identify correlations between answers in Parts A and B given the substantial overlap between both respondent groups (see Results). Information entered in the free-

text fields was assigned to broader aspects; we summarised this type of information by counting and tabulating how often the various aspects occurred. We selected quotes to illustrate certain points that were recurrently raised by the respondents and, where appropriate, added them to the Results section below. A formal qualitative analysis of the text information was not part of this project.

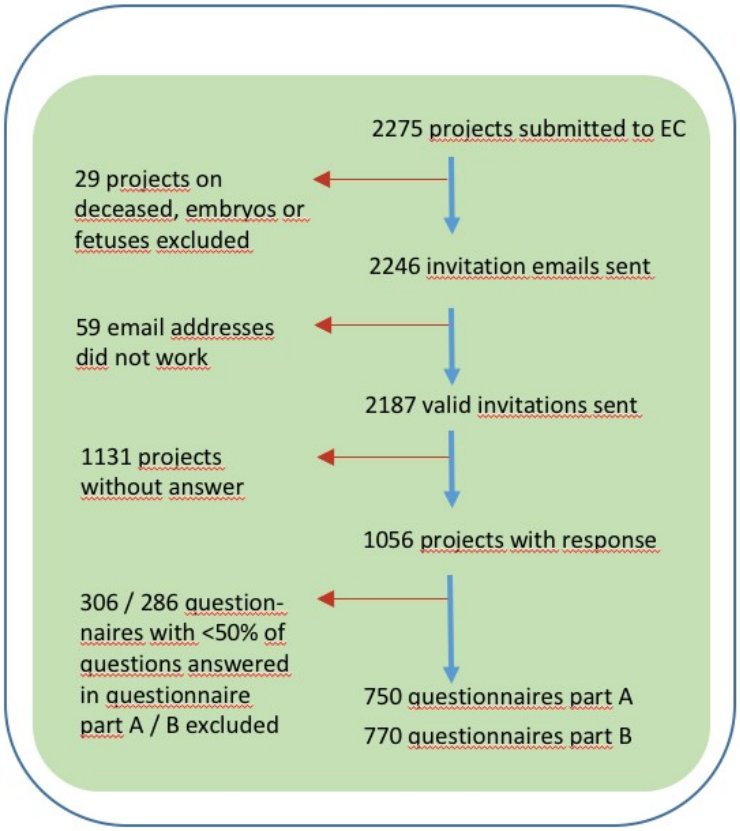
4. Results

Note: In the figure labels, the codes in parentheses refer to the numbering of the corresponding sections in the Survey Questionnaire Part A and B (Appendix 1).

4.1. Response rates and clustering

Following the invitations sent out to valid email addresses for 2187 research projects, researchers returned 770 valid questionnaires Part A (Figure 1). This accounts for a response rate of 35.2%. For Part B, researchers returned 750 valid questionnaires accounting for a response rate of 34.3%.

Figure 1: Flowchart of participant projects

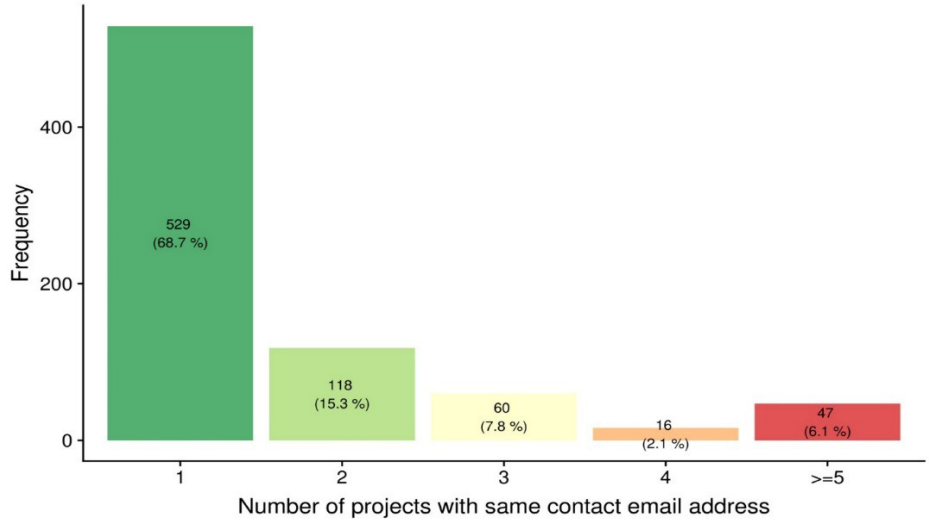


For 667 (87%) of the 770 projects, respondents in Part A und Part B were the same person, and in 103 (13%) projects they were different. The detailed survey responses from both parts of the questionnaire are given in the "Full report of survey results" (Appendix 3).

We analysed whether projects with a response in the survey differed from all eligible research projects: There were no important differences between eligible and respondent projects. Clinical trials (according to ClinO) and research projects with persons (according to HRO chapter 2) were slightly overrepresented whereas "further use" projects (according to HRO chapter 3) were slightly underrepresented among survey responses. A comparison of eligible and respondent projects with regard to several study characteristics is provided in Appendix 4.

Several research projects could have been submitted during the course of the year 2017 by the same individual or by different individuals using the same contact email address. We assessed whether clustering of survey responses by person (i.e. one person answering questionnaires for more than one research project) was sufficiently frequent to warrant a sensitivity analysis. For 69% of projects one single contact email address was used (Figure 2). For the remaining 31%, clustering with identical contact emails addresses ranged from two projects for the same email address (15%) to nine projects (n=1) for one single email address.

Figure 2: Clustering of research projects by respondent email address



Consequently, there were 619 unique persons completing 770 questionnaires in Part A and 607 unique persons completing 750 questionnaires in Part B. This means that the questionnaires for 151 projects (20%) in Part A and for 143 projects (20%) in Part B were answered by researchers who responded more than once (clustering). We decided against any sensitivity analyses because, most likely, they would have been futile due to a relatively limited amount of clustering.

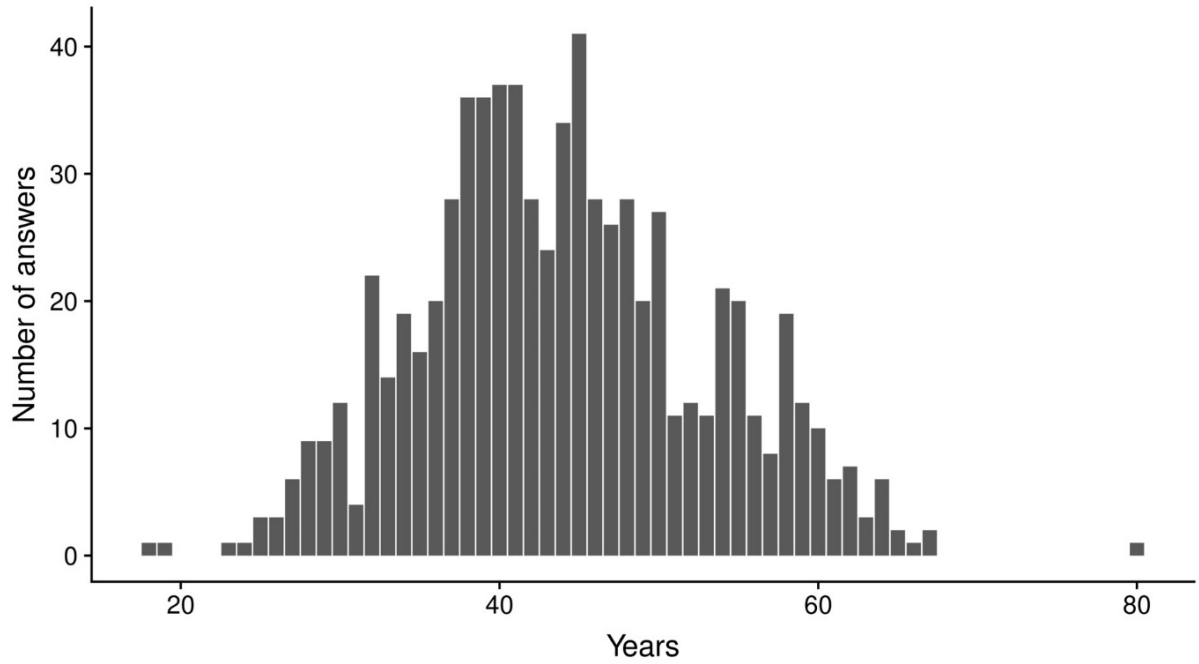
We calculated alternative response rates based on the number of unique respondents. For questionnaire Part A, it was 40.2% (619 unique persons), and for Part B 39.5% (607 unique persons).

4.2. Description of survey population

The following description of the survey population refers to the 750 respondents of questionnaire Part B. Because the 770 respondents of questionnaire Part A are identical to a large extent (87%) their demographic data are provided in the "Full report of survey results" (Appendix 3) only.

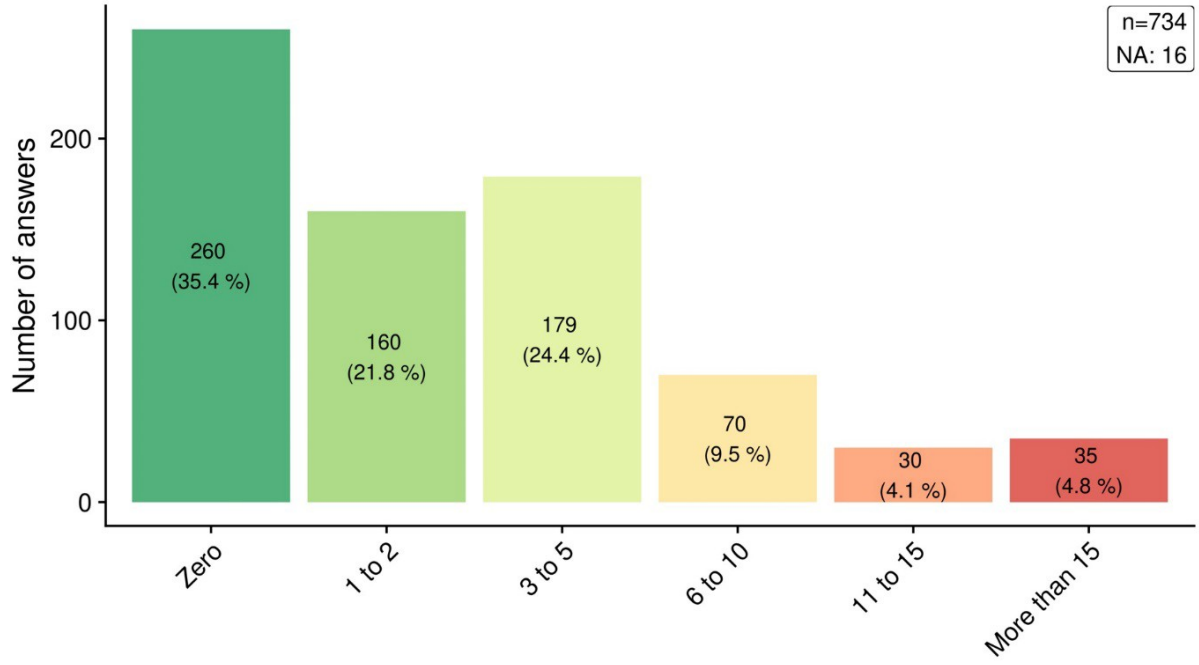
Of the 750 respondents in Part B, 299 (41%) were women and 435 (59%) were men (no answer n=16). Their age ranged from 18 to 80 years with a median age of 43 years (IQR 38-50) (Figure 3).

Figure 3 – Age range (B30)



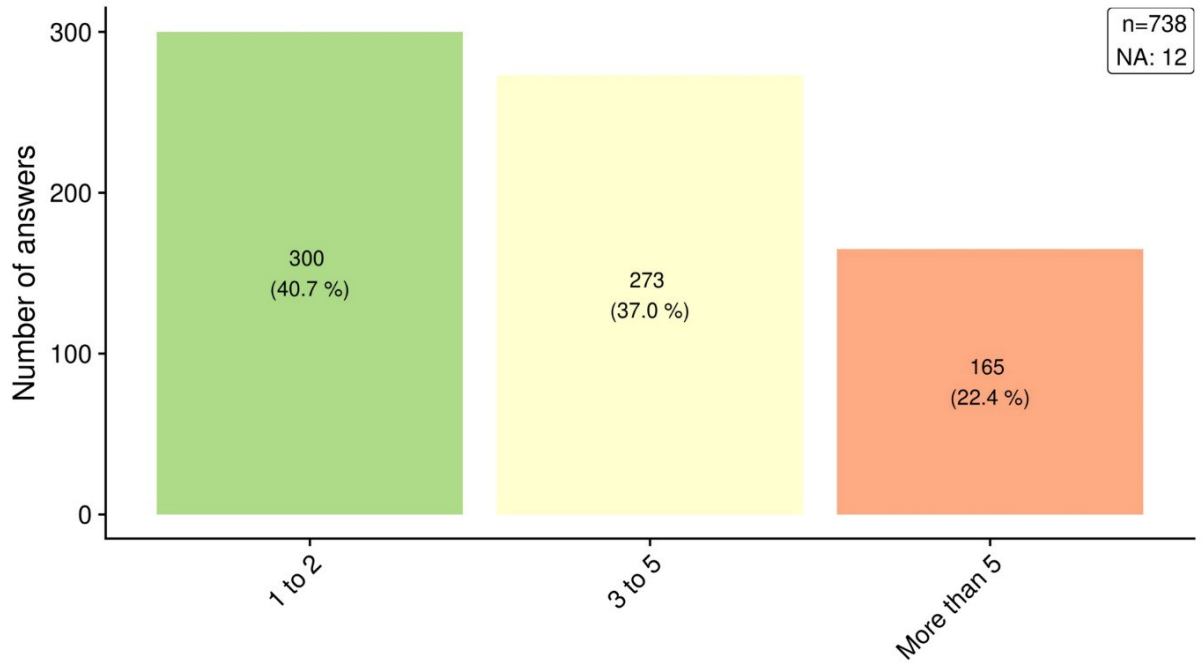
Before 1st January 2014, most researchers had submitted either no or up to two research projects to ECs in Switzerland in any role (Figure 4).

Figure 4 – Number of submitted projects before 2014 (B32)



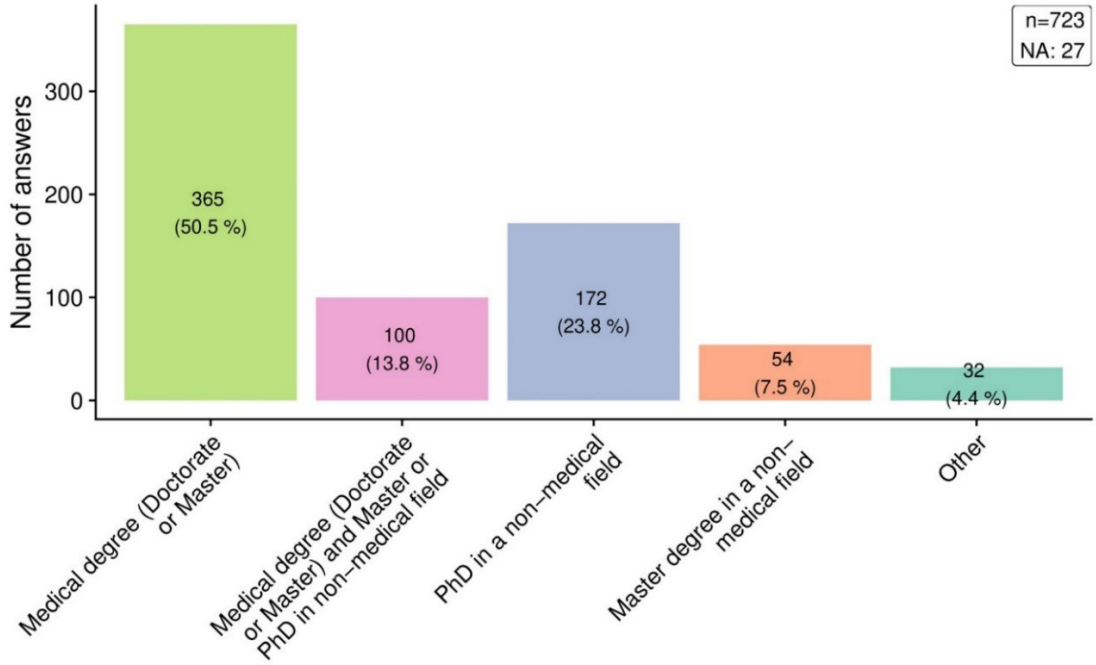
After 1st January 2014, 41% of researchers had submitted either one or two research projects, 37% three to five projects and 22% more than five projects to ECs in Switzerland in any role (Figure 5).

Figure 5 – Number of submitted projects after 2014 (B33)



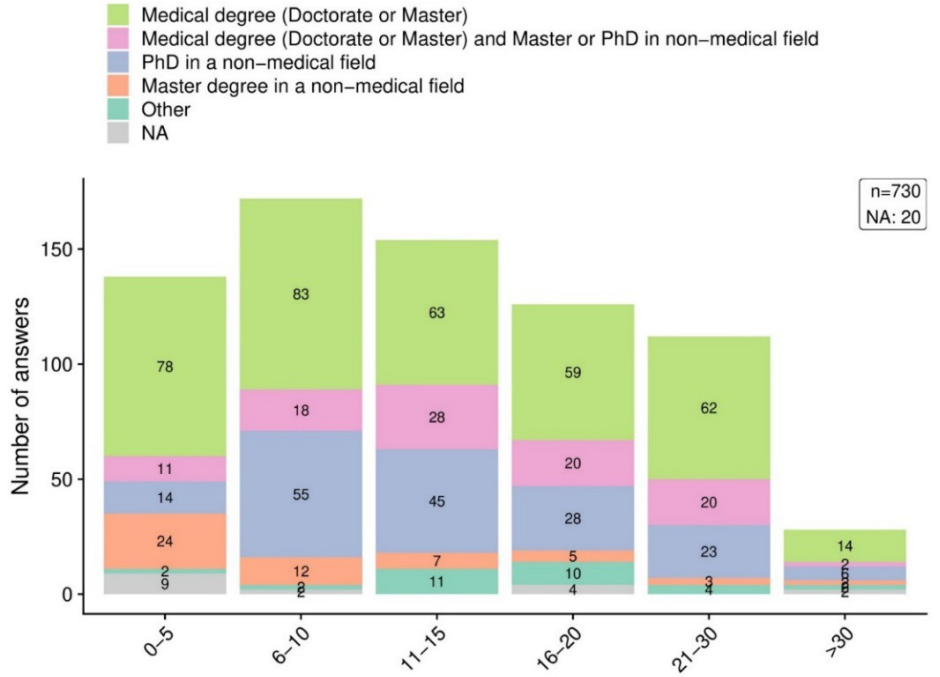
The highest professional qualification of about half of the researchers was a medical degree (Doctorate or Master) and another 14% had a medical degree combined with a Master or PhD degree in a non-medical field (Figure 6).

Figure 6 – Highest professional qualification (B34)



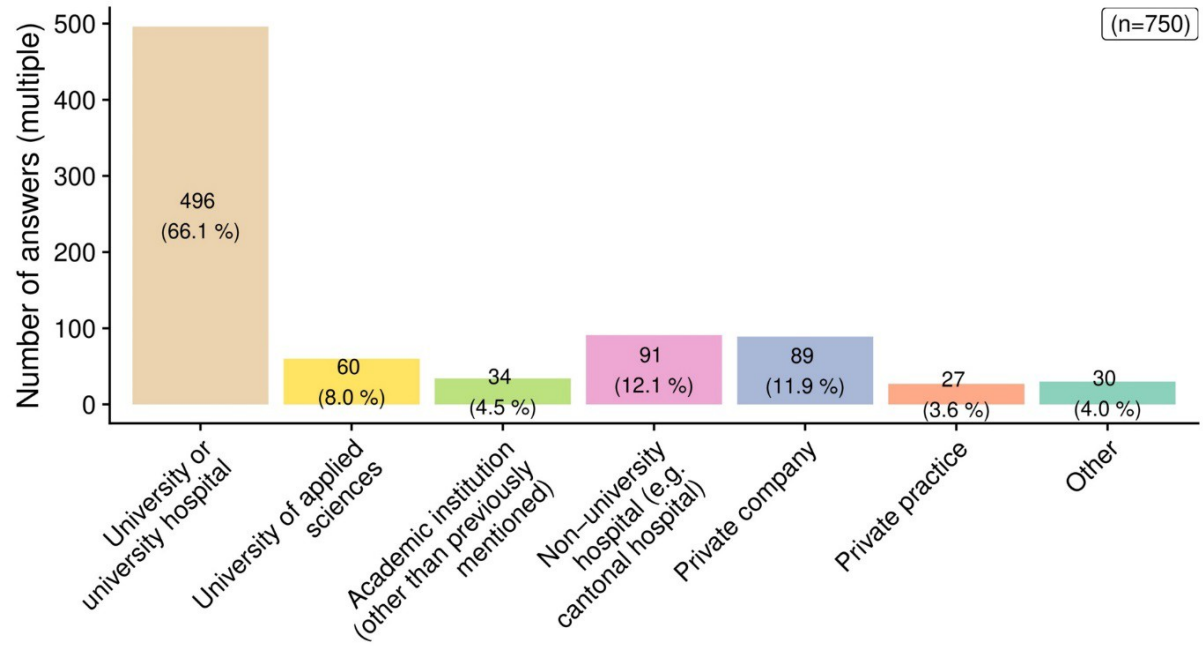
Research working experience was categorised into 5-year intervals. Except for the group with >30 years of experience, all groups had more than 100 respondents, reflecting a balanced distribution (Figure 7).

Figure 7 – Working experience (in years) (B35)



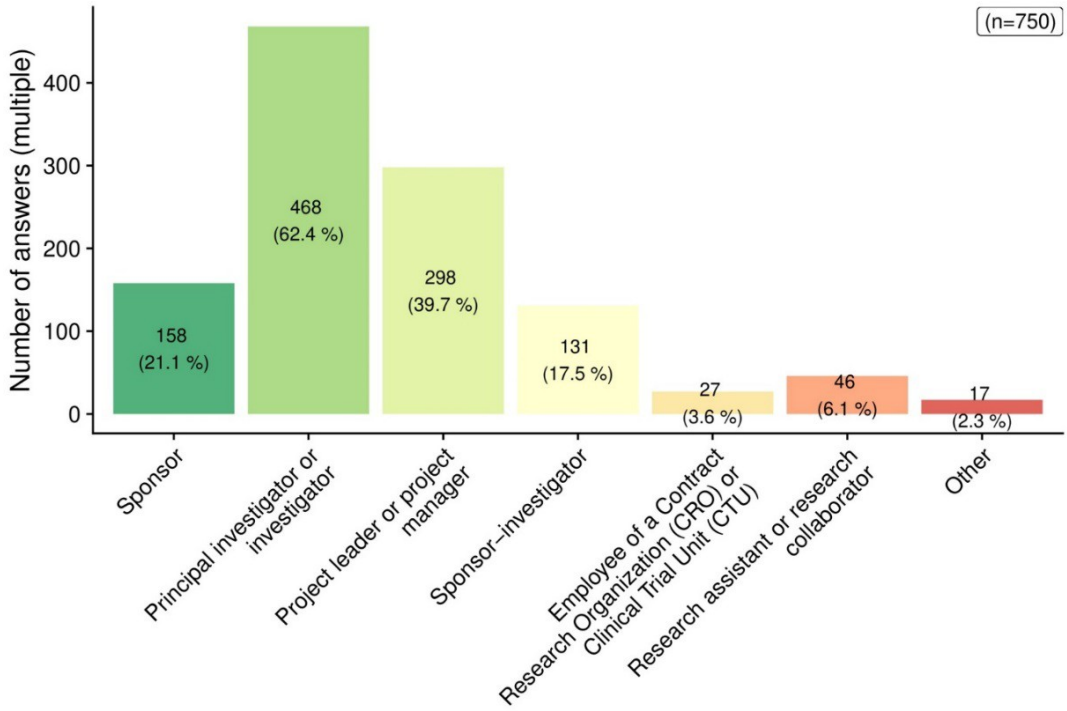
With regard to their current work environment, two thirds of the researchers indicated that they were employed at a university or in a university hospital (Figure 8).

Figure 8 – Work environment (B37), multiple answers possible



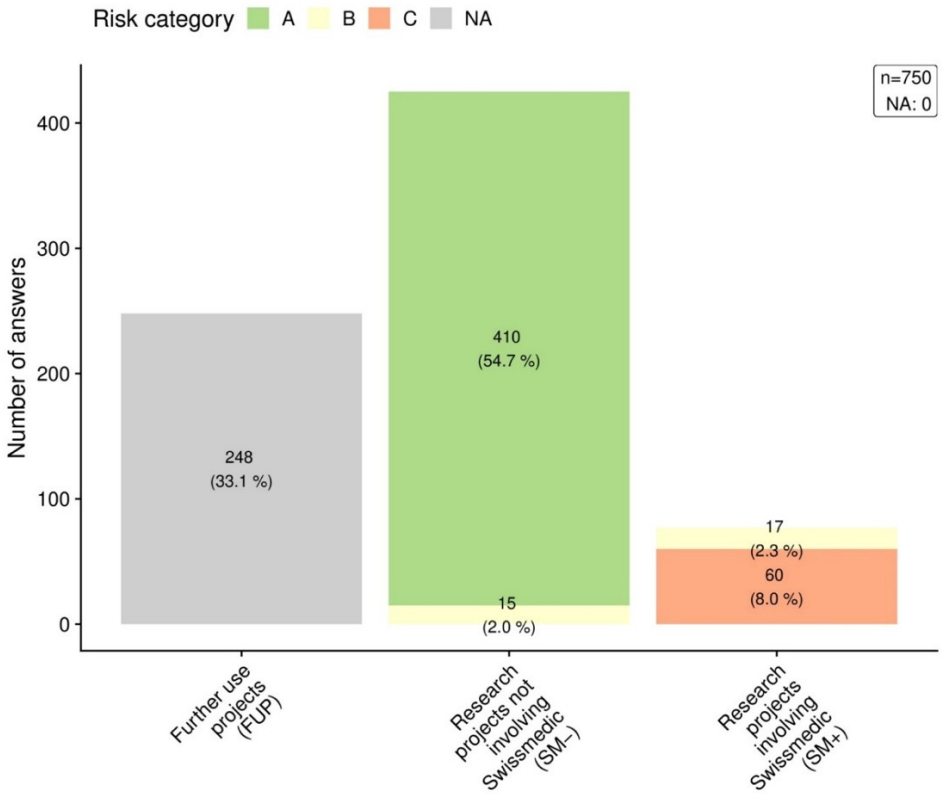
Respondents were asked about their actual role in the research project: most were either principal investigator or investigator (Figure 9).

Figure 9 – Role in research project (B1), multiple answers possible



With regard to the type of studies, almost 55% of research projects were in group SM- (Figure 10). This was followed by projects in group FUP (33%) and group SM+ (for definitions of groups, see the box on p.7 and Appendix 2).

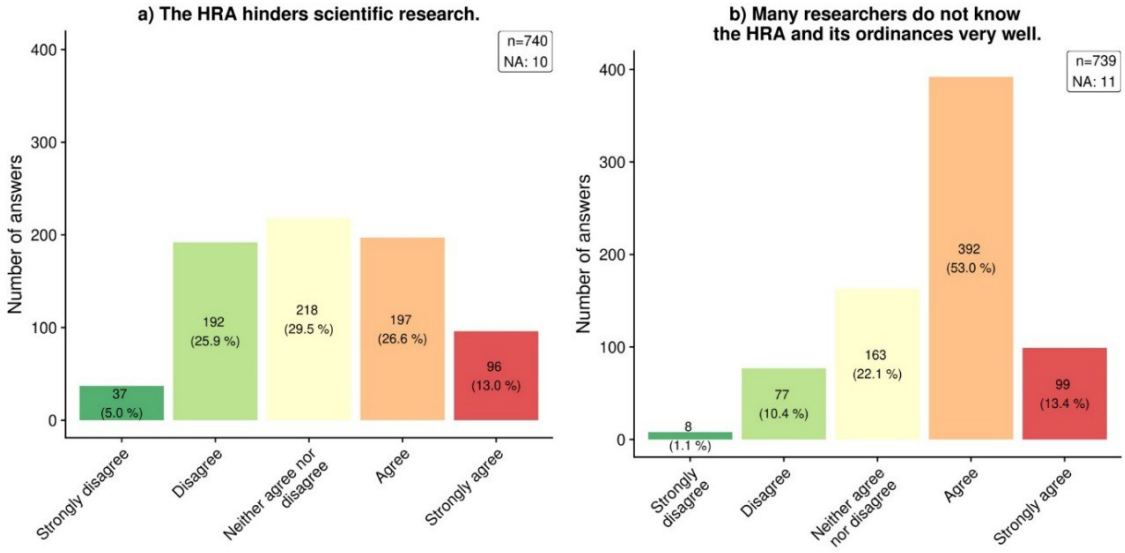
Figure 10 – Type of study by risk category (Full report, p. 31)



4.3. General attitude towards human research legislation

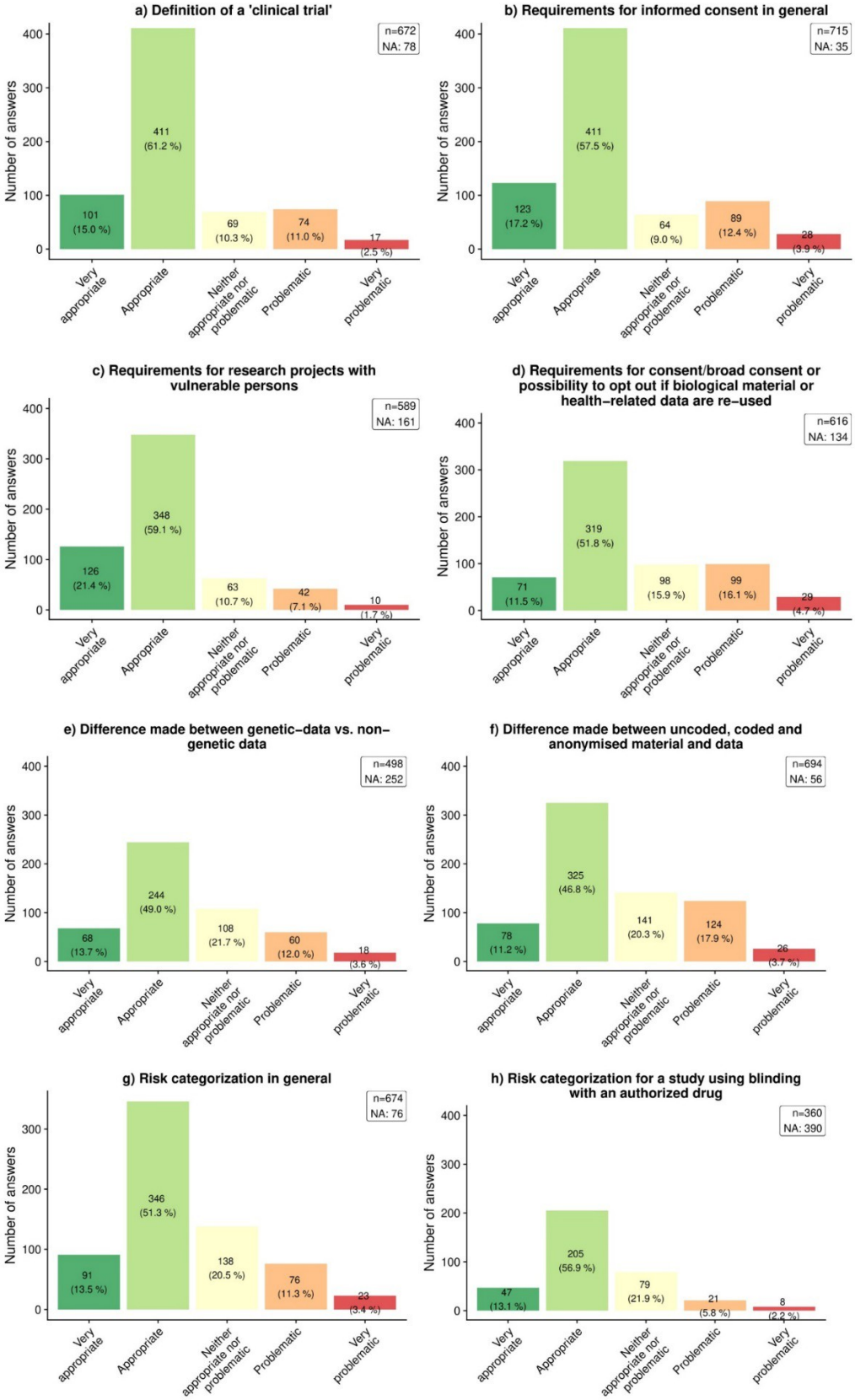
The researchers were asked about their level of agreement with two general statements. While a majority of researchers did not agree or were undecided whether the HRA hinders scientific research, about 40% agreed or even strongly agreed with this statement (Figure 11a). About two thirds agreed or strongly agreed with the statement that many researchers do not know the HRA and its ordinances very well (Figure 11b).

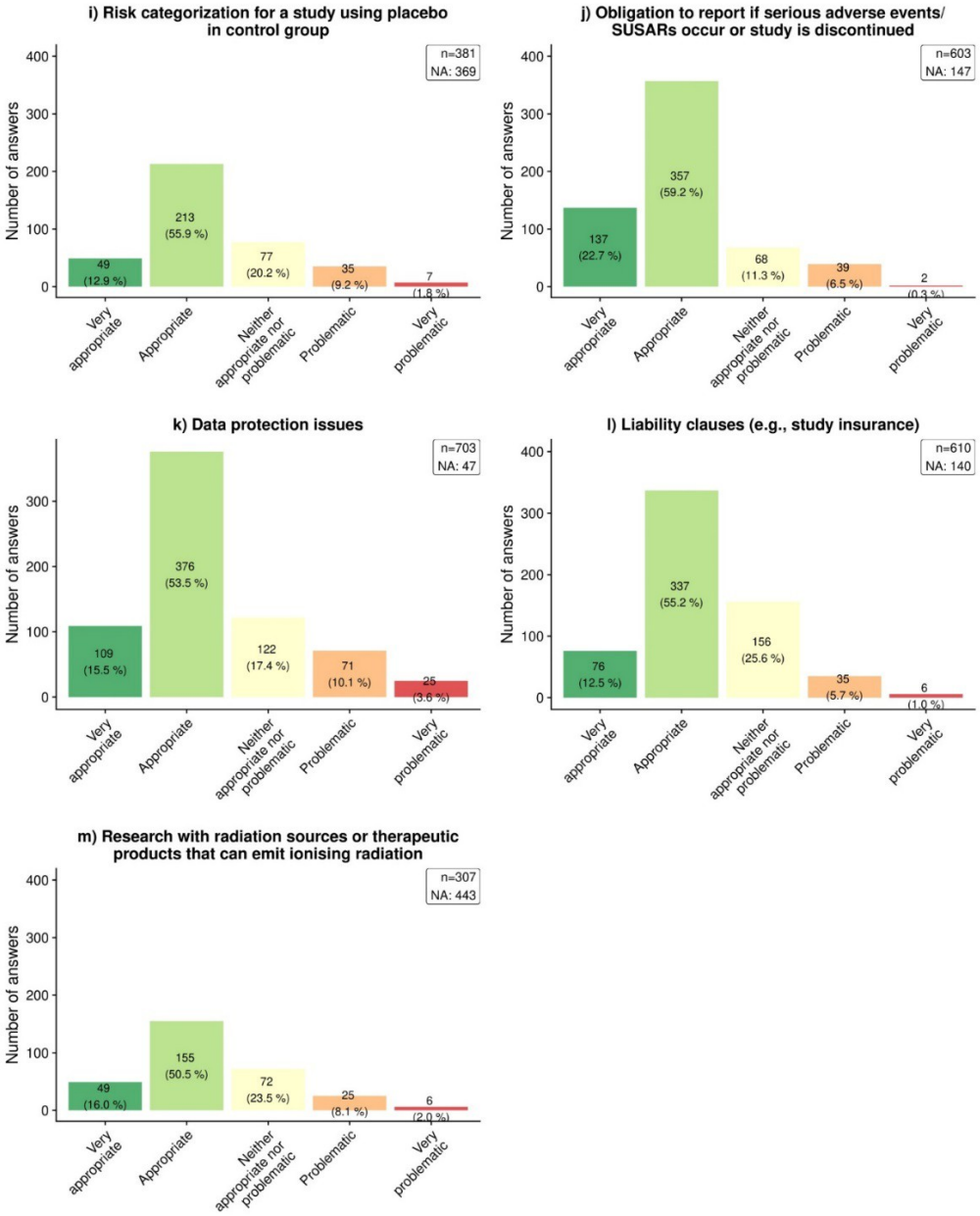
Figure 11 – General attitude towards human research legislation (B21)



We displayed a list of thirteen different aspects that are usually covered by human research regulations and asked the researchers whether these aspects are appropriately regulated in the HRA and related ordinances in their view. For all aspects the most frequently chosen answer was that regulation was appropriate (Figure 12).

Figure 12 – Appropriateness of specific regulatory aspects (B22)

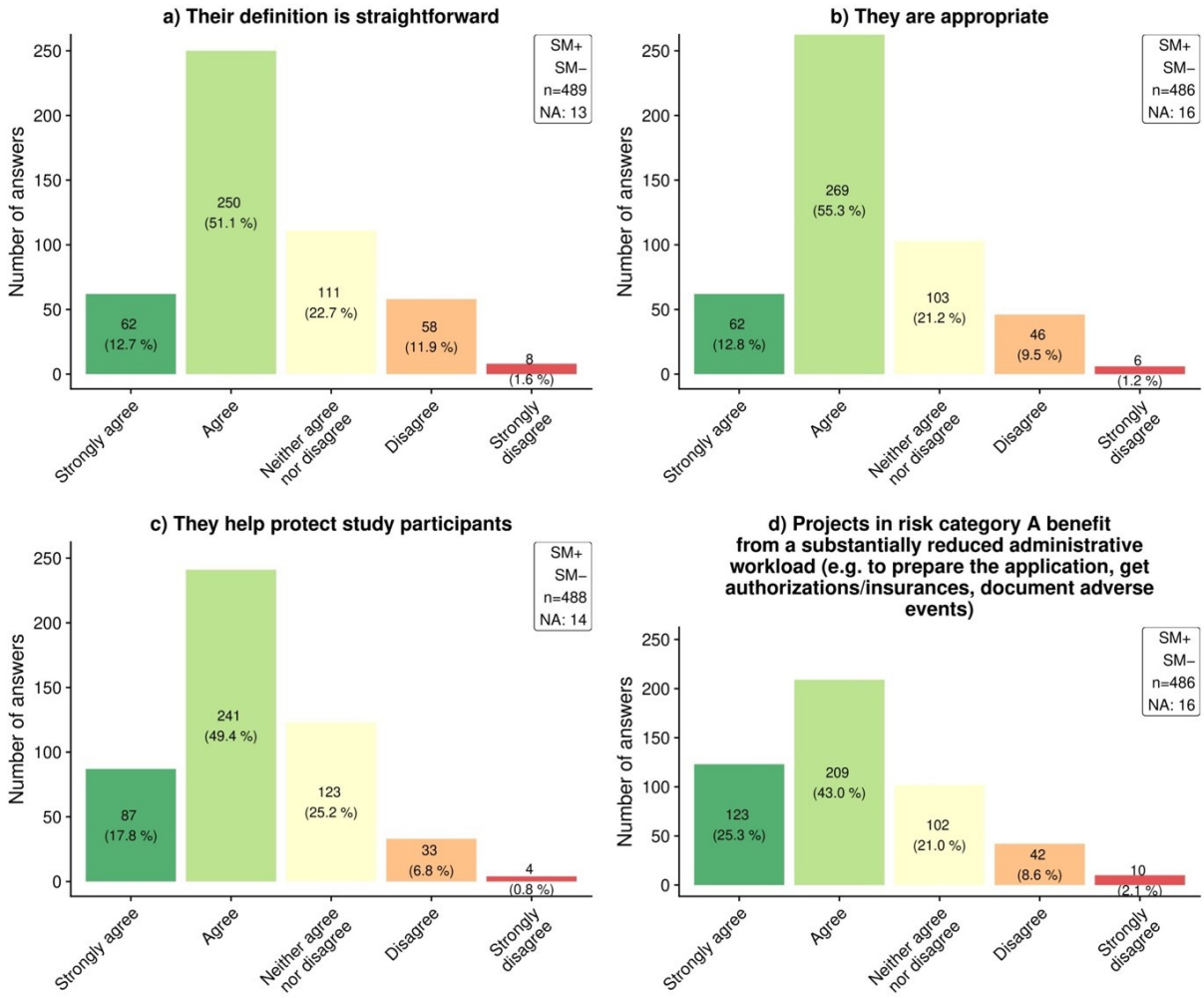




Graph i: This refers to practical implementation of the ClinO by Swissmedic requiring classification of clinical trials using a new placebo formulation (not authorised by Swissmedic) in risk category B.

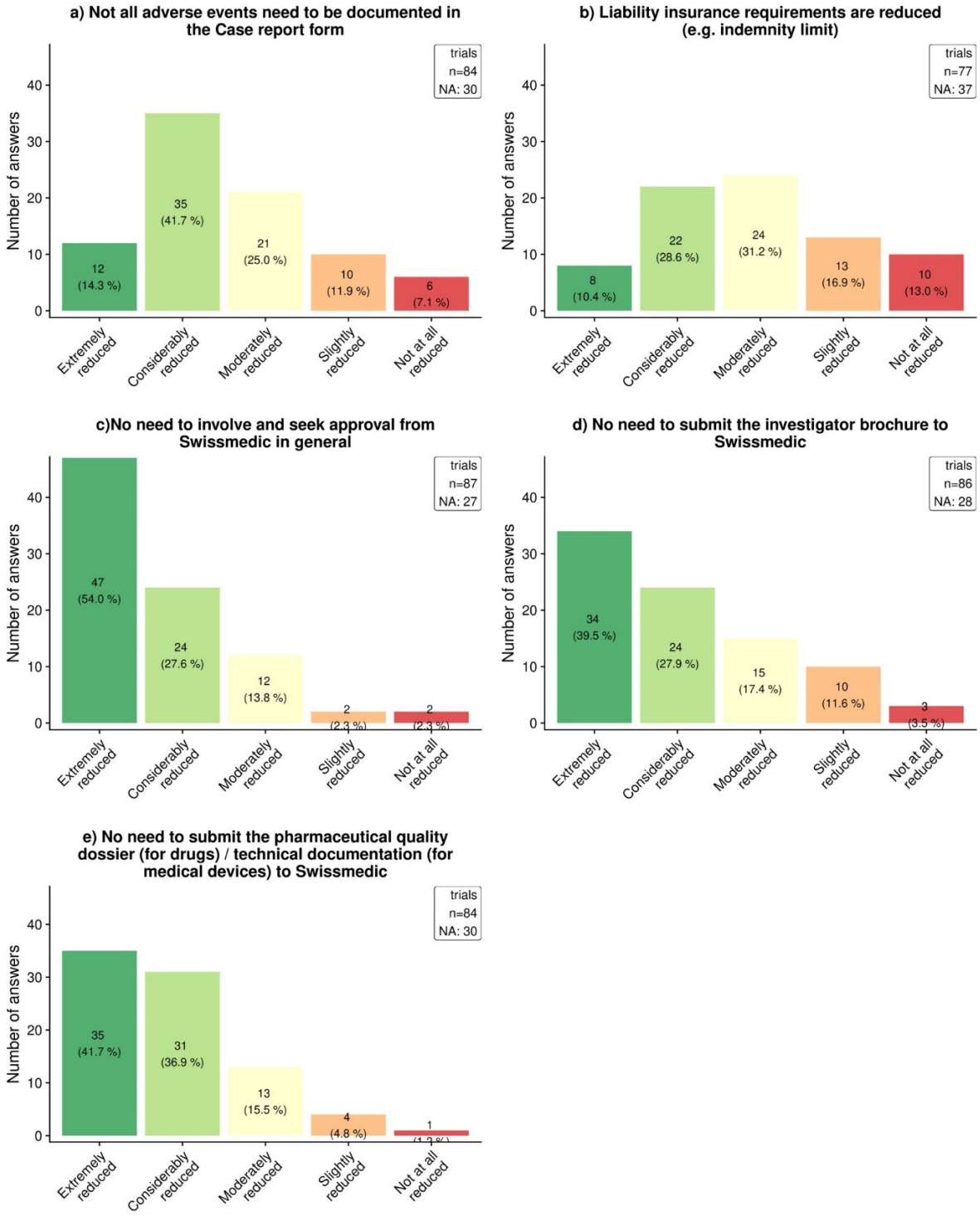
We also asked researchers with projects that are subject to risk classification (groups SM+ and SM-) about their level of agreement with four statements regarding the risk classification according to current legislation. For each statement, a majority indicated that they agreed or strongly agreed (Figure 13).

Figure 13 – Agreement with risk classification according to current legislation (B23)



We asked the 114 researchers seeking approval for a clinical trial involving medicinal products or medical devices about the reduced legal requirements in risk category A as compared to B or C. The focus was on their opinion on whether five selected aspects help reduce the administrative workload. Most respondents agreed for four of the five aspects (Figure 14a, c, d, e) that they considerably or extremely reduced the workload. This was not the case for requirements for liability insurance; 30% of respondents answered that the legal requirements were only slightly reduced or not at all (Figure 14b).

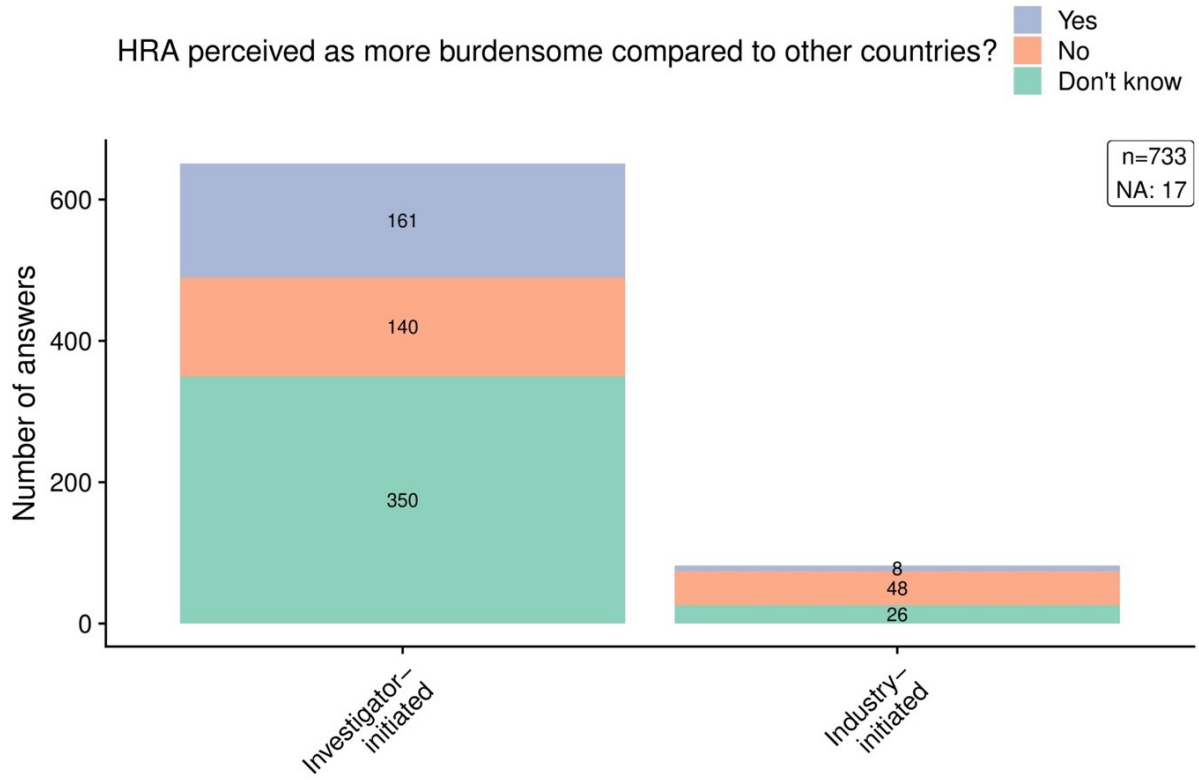
Figure 14 – Administrative workload of clinical trials to comply with HRA (B24)



4.3.1. Comparison with other countries

Of 733 respondents, 169 (23%) thought that the current Swiss legislation was more burdensome than comparable laws in other countries, while 188 (26%) rejected this notion (Figure 15). More than half (n=376, 51%) answered with "Don't know" (no answer n=17). Researchers with investigator- initiated studies regarded the Swiss legislation as burdensome more frequently (25%) than those with industry-initiated projects (10%) (Figure 15). The same was true for researchers with "further use" studies (28%) as compared to clinical trials (21%) or research projects with persons (20%) (Figure B25.1 in Full Report).

Figure 15 – Is Swiss legislation more burdensome than in other countries? (B25)



Ninety-four respondents (13%) provided a comment when asked if the regulations of the HRA and its ordinances were perceived as more burdensome than comparable laws in other countries. The HRA was perceived recurrently as burdensome regarding informed consent, particularly the obligation of informed consent for retrospective studies (Table 1).

"Difficulties to opt-out from obtaining informed consent even for retrospective studies"

Generally, researchers thought that the submission process for ethical approval is stricter than in other countries.

"The application process and the formal requirements appear much stricter and less flexible than, e.g., in Germany"

They frequently commented that the information requested was too exhaustive.

"General comment: It requires more paperwork than, for instance in Germany, for the same project."

For all verbatim answers see Full Report C Appendix v p.158 (Question 25a) and for additional stratifications see Full Report p. 68 – 70.

Table 1 – Reasons why the HRA and its ordinances were perceived as more burdensome (B25a)

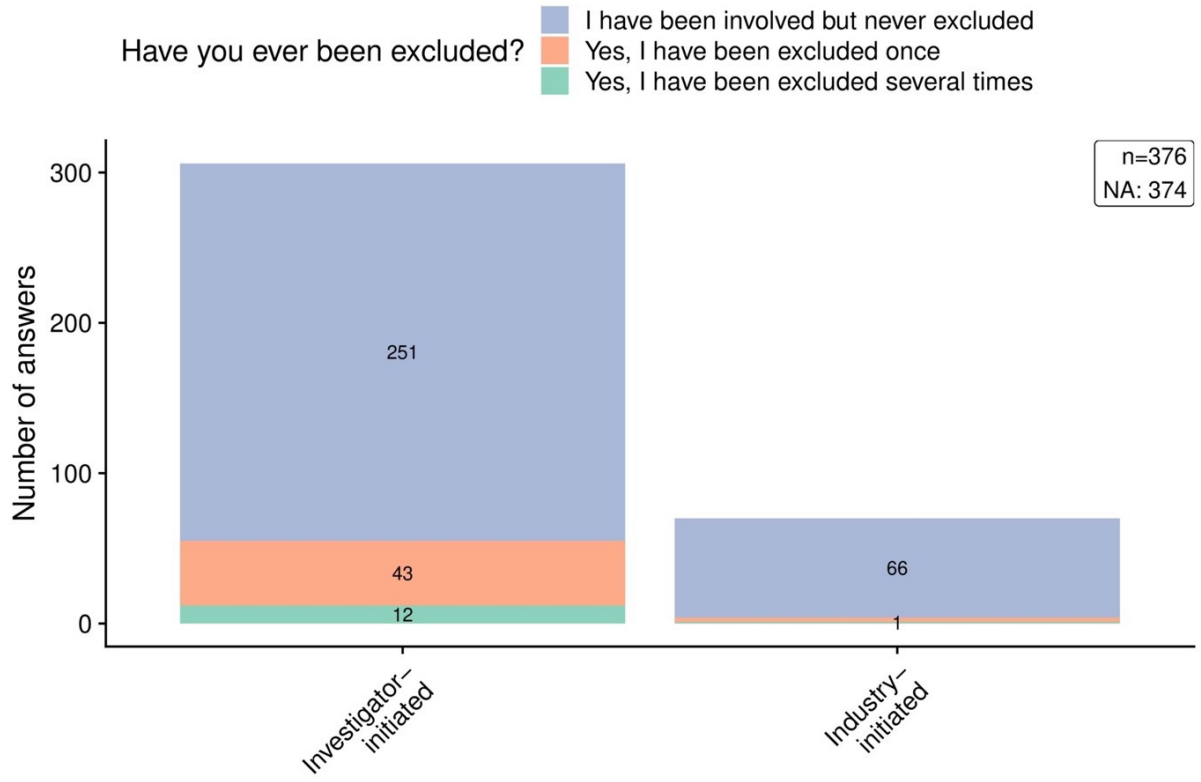
A	**Aspects related to the legal framework:**	**Number of comments**
A.1.	Informed consent (and patient information), including obligation to obtain informed consent for retrospective studies	17
A.2.	Use of already collected data or biological material for research is more burdensome	7
A.3.	Law too focused on medical interventional studies, other study types are overregulated and/or templates / BASEC do not match non-medical studies (especially if low risk)	4
A.4.	Research in vulnerable persons	3
A.5.	Law too strict if low risk for participants	3
A.6.	Too strict in general, too many regulations	3
A.7.	Risk classification	2
A.8.	Differences with EU law	2
A.9.	Law favours research by industry (amount of paper work and costs which industry can afford but not academic investigators)	2
A.10.	Data transfer is more burdensome	2
A.11.	Working with genetic data	2
A.12.	Submission for ethical approval is project based as opposed to data collection method based	1
A.13.	Unclear what kind of studies fall outside the scope of the HRA	1
A.14.	Definition of what is a clinical trial	1
A.15.	Studies using medication/ placebo	1
A.16.	Laws too strict for "simple" or “educational” research (e.g. Master thesis)	1
A.17.	Difficulty when adapting the design of an ongoing clinical trial	1
B	**Aspects related to the submission process at the EC:**	
B.1.	Exhaustive information requested / too much paper work	21
B.2.	Submission process for ethical approval stricter than in other countries	12
B.3.	Lack of communication and efficient work among EC in case of international studies	2
B.4.	Multiple ECs in Switzerland; request for only one EC for Switzerland	1
B.5.	Formal things more important than content / patients	1
B.6.	Not the HRA itself but its interpretation by the EC is burdensome	1
B.7.	Obligation of annual safety reports	1
C	**Other aspects:**	
C.1.	Explicitly commented “All aspects”/ “All”	2
	Total	**94***

***** 4 answers excluded: 2 for unclear meaning of the free-text answer; 2 without applicable category (“harder”, “see comment below”)

We further asked researchers whether they had been excluded from any international multi-site study because of the perceived hurdles caused by legislation in Switzerland. Of 376 researchers answering this question, 317 (84%) had been involved in international multi-site studies but never excluded. A minority had been excluded once (n=46; 12%) or several times (n=13; 3%); these were

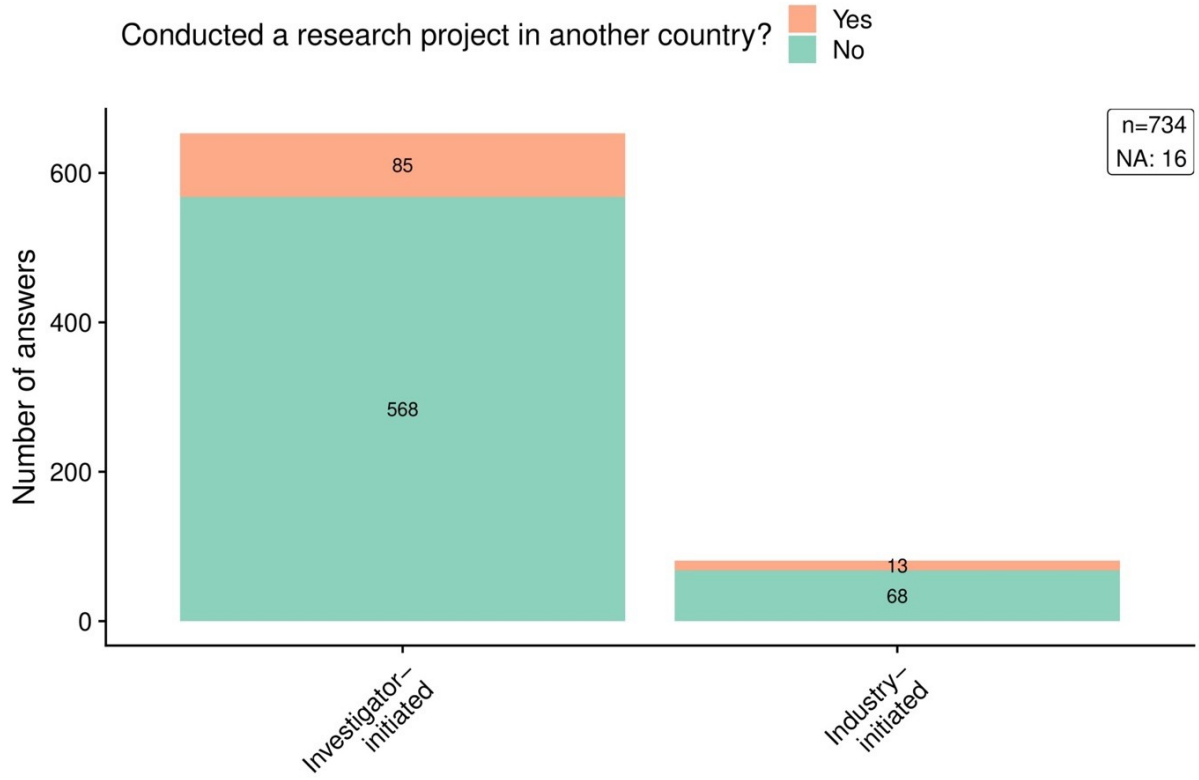
predominantly researchers with investigator-initiated studies (Figure 16). About half of them (n=28, 47%) had submitted a "further use" study in 2017 (Figure B26.2 in Full Report).

Figure 16 – Exclusion from international multi-site studies (B26)



Of the 736 researchers who responded, 98 (13%) affirmed that they had at least once decided to conduct a research project in another country and specifically not in Switzerland in the past (due to any possible reason). 638 (87%) did not affirm this and 14 rendered no answer. Stratification by industry or academic type of research project did not show differences (Figure 17); neither did stratification by type of study (clinical trial, research with persons, "further use" studies (Figure B27.2 in Full Report). In both analyses, the respective proportions of researchers affirming conduct of research abroad ranged between 13% and 16%.

Figure 17 – Researchers' decisions to conduct research project abroad (B27)



Those 98 researchers who affirmed the question were asked to choose from several reasons and to provide additional information when choosing "Other reasons". The displayed results are stratified by project initiator (Figure 18) and by project type (Figure 19).

Figure 18 – Reasons to conduct research project abroad (B27a), stratified by project initiator, multiple answers possible

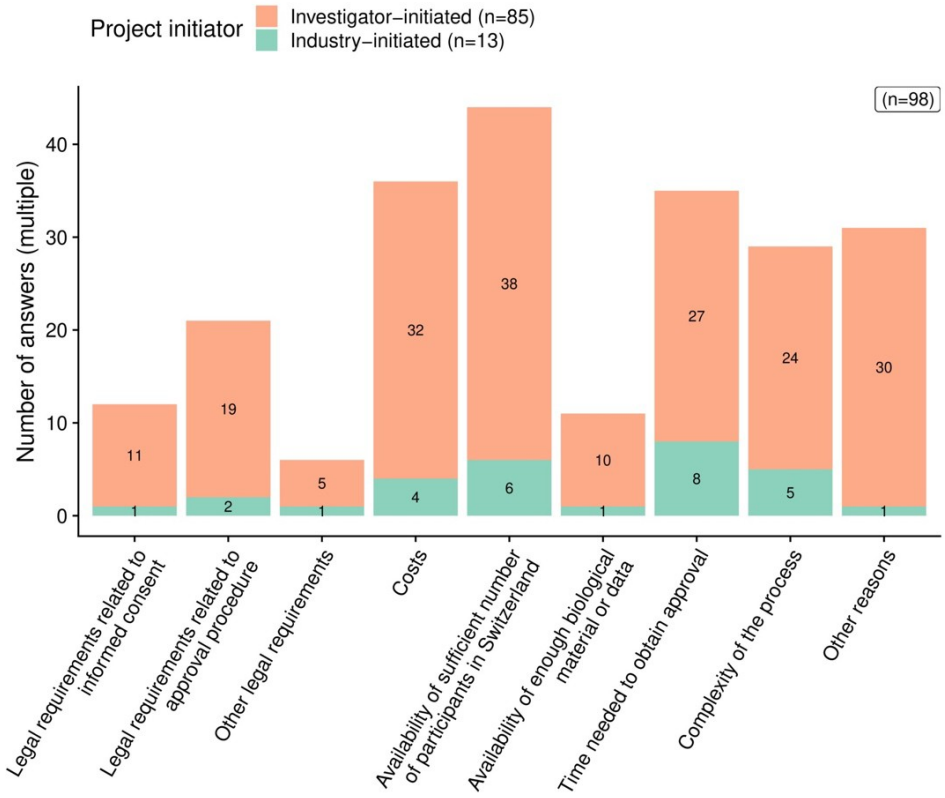
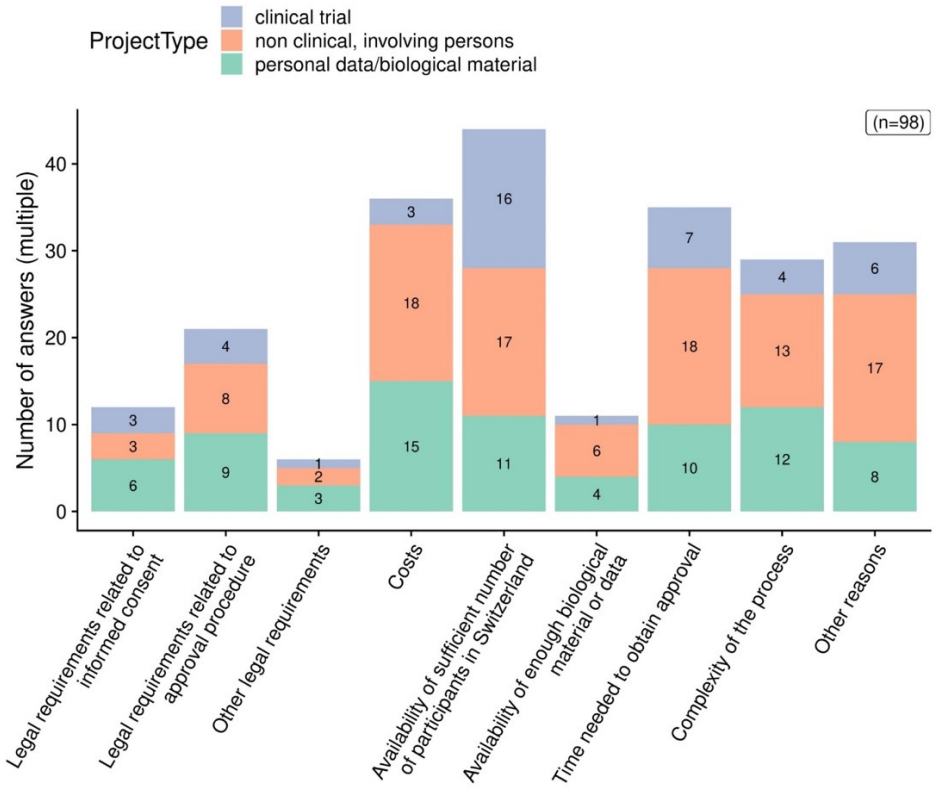


Figure 19 – Reasons to conduct research project abroad (B27a), stratified by project type, multiple answers possible



Of the 31 researchers who indicated other reasons, 22 provided more detail: nine mentioned reasons related to their career (e.g. fellowship abroad) or personal reasons (e.g. moving back to home country). The decision of seven respondents was motivated by an international collaboration or by EU funding. In five projects the target population, study settings or costs were reasons to conduct the study elsewhere. For one project, the requirements by the EC were perceived as too burdensome and a lack of consensus in Switzerland about the specific type of research was mentioned.

4.3.2. Research projects with further use of biological material or health-related data

For the 248 projects with further use of biological material or health-related data (group FUP) more than four out of five researchers either used biological material or health-related data from their own previous projects or from someone else in their institution; only 15% received such material or data from other institutions (Figure 20). The latter were mostly university institutions or hospitals (Figure 21).

Figure 20 – Origin of biological material or health-related data (B18), multiple answers possible

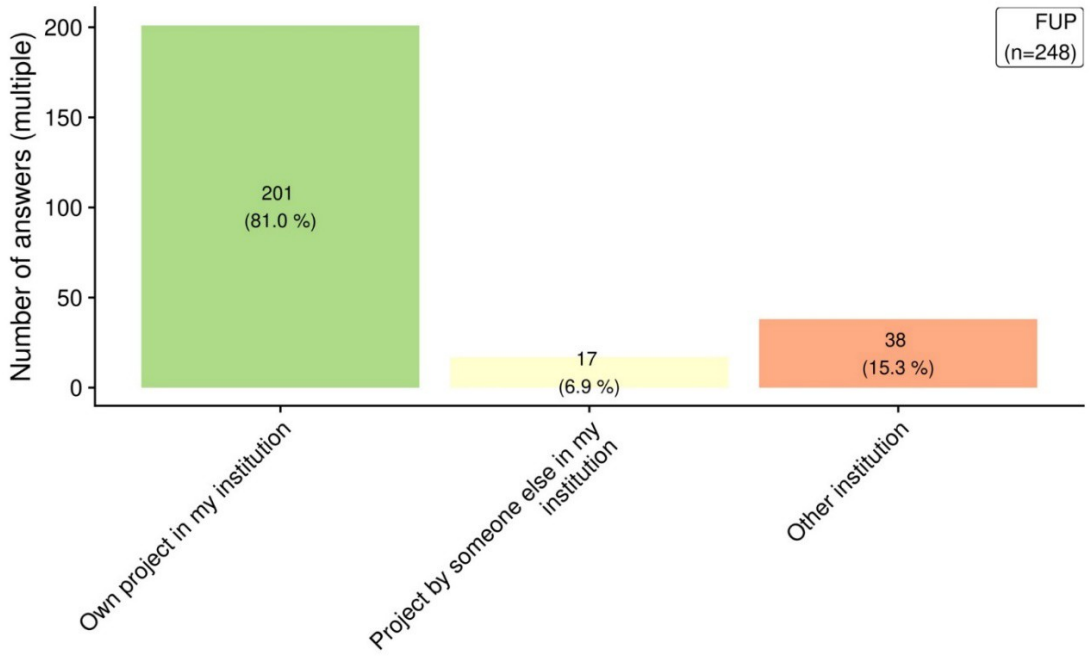
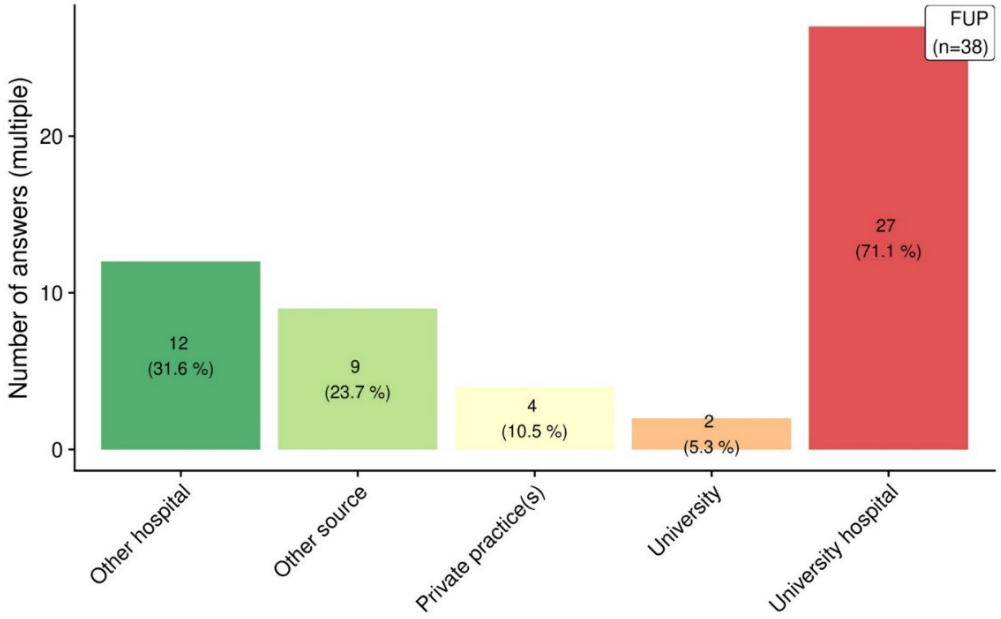


Figure 21 – Origin of biological material or health-related data if from other institution (B18), multiple answers possible



Most researchers involved in "further use" projects (FUP) had not used biological material or data from other countries for this or another project since 1st January 2014 (Figure 22). Seventeen (53%) of the 32 researchers who once or several times used foreign material or data, responded that it was coded, and fourteen (44%) that it was anonymised (Figure 23). Four of them affirmed that the use of biological material or data from other countries had caused problems with the authorisation of at least one research project in Switzerland, while 25 did not affirm this (no answer n=3).

Figure 22 – Use of biological material or health-related data from other countries (B19)

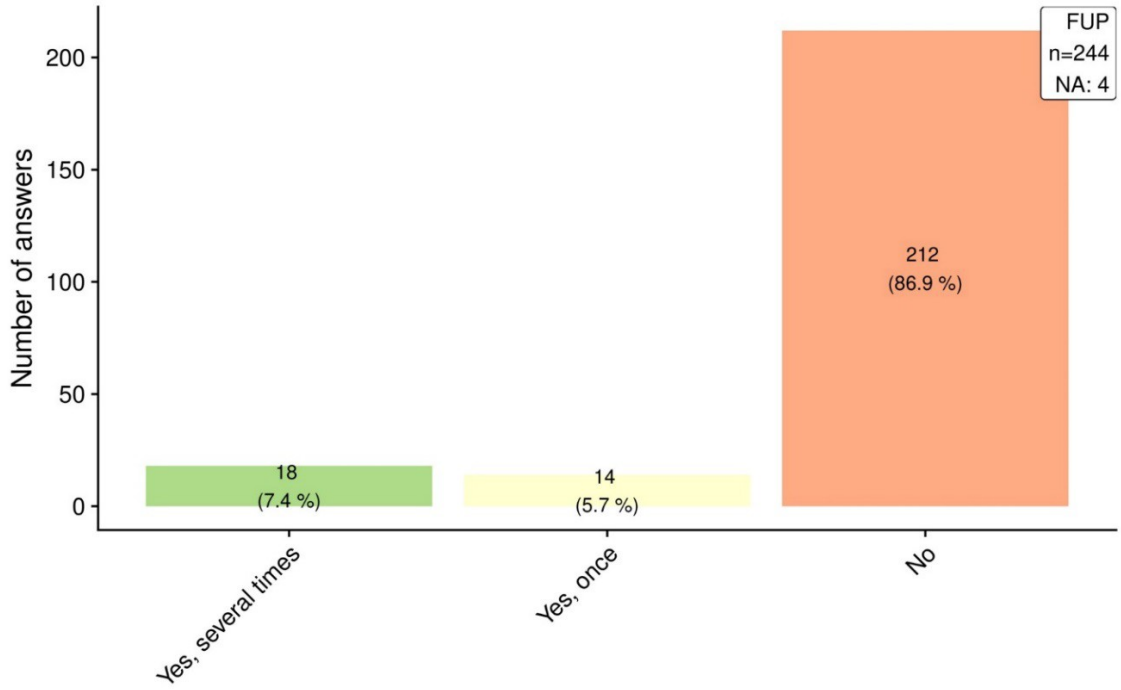
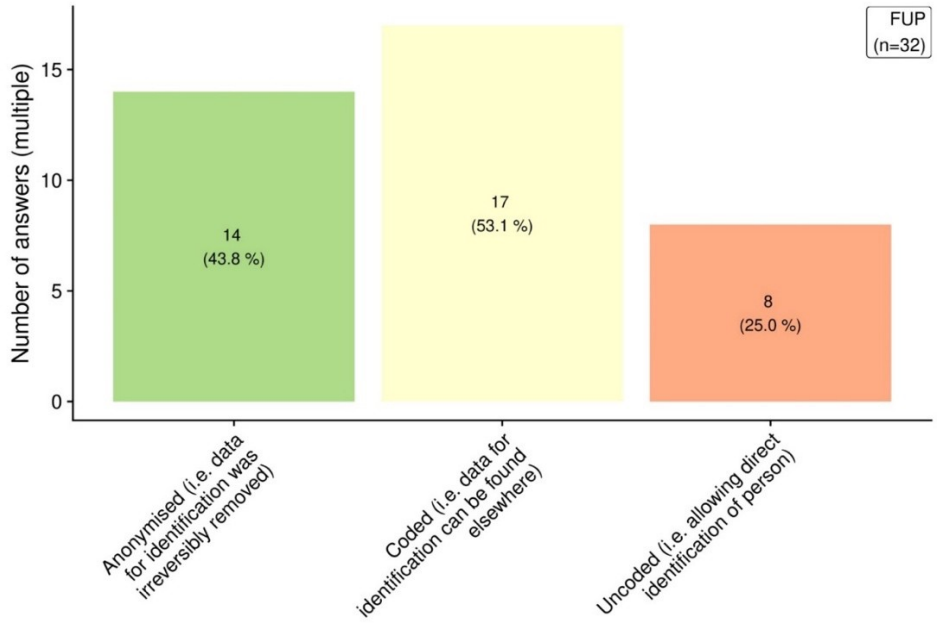
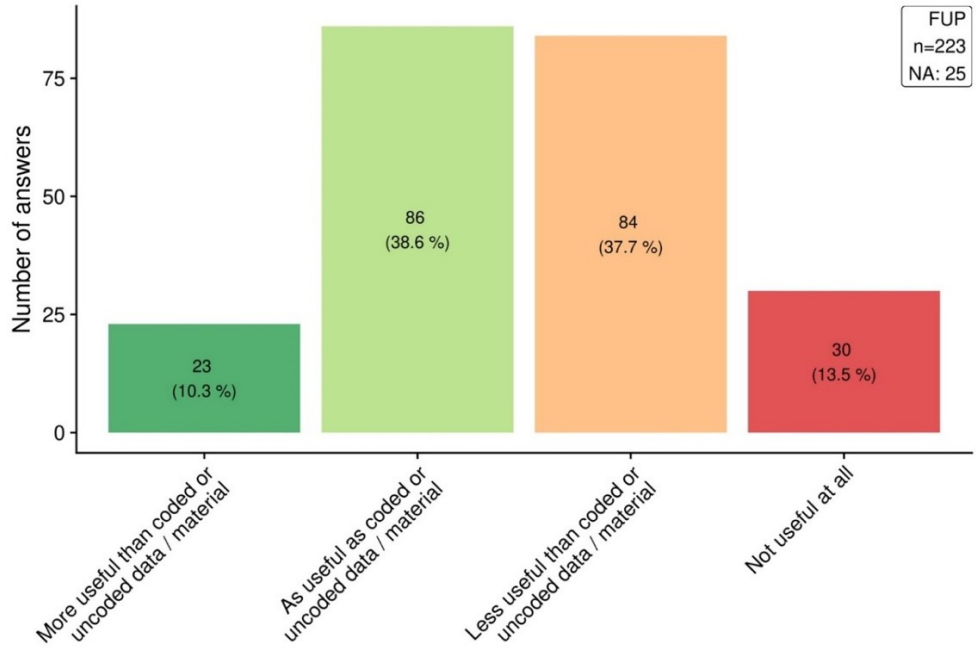


Figure 23 – Coding or anonymisation of material / data received from other countries (B19a), multiple answers possible



One survey question to the 248 researchers with “further use” projects focused on the issue that for the handling of anonymised data or material, the current legal requirements are less strict than for uncoded or coded data or material. About half of the respondents deemed anonymised data or material "more" or "equally useful", and the other half "less useful" or "not at all useful" compared to uncoded or coded data or material (Figure 24).

Figure 24 – Usefulness of anonymised material / data (B20)



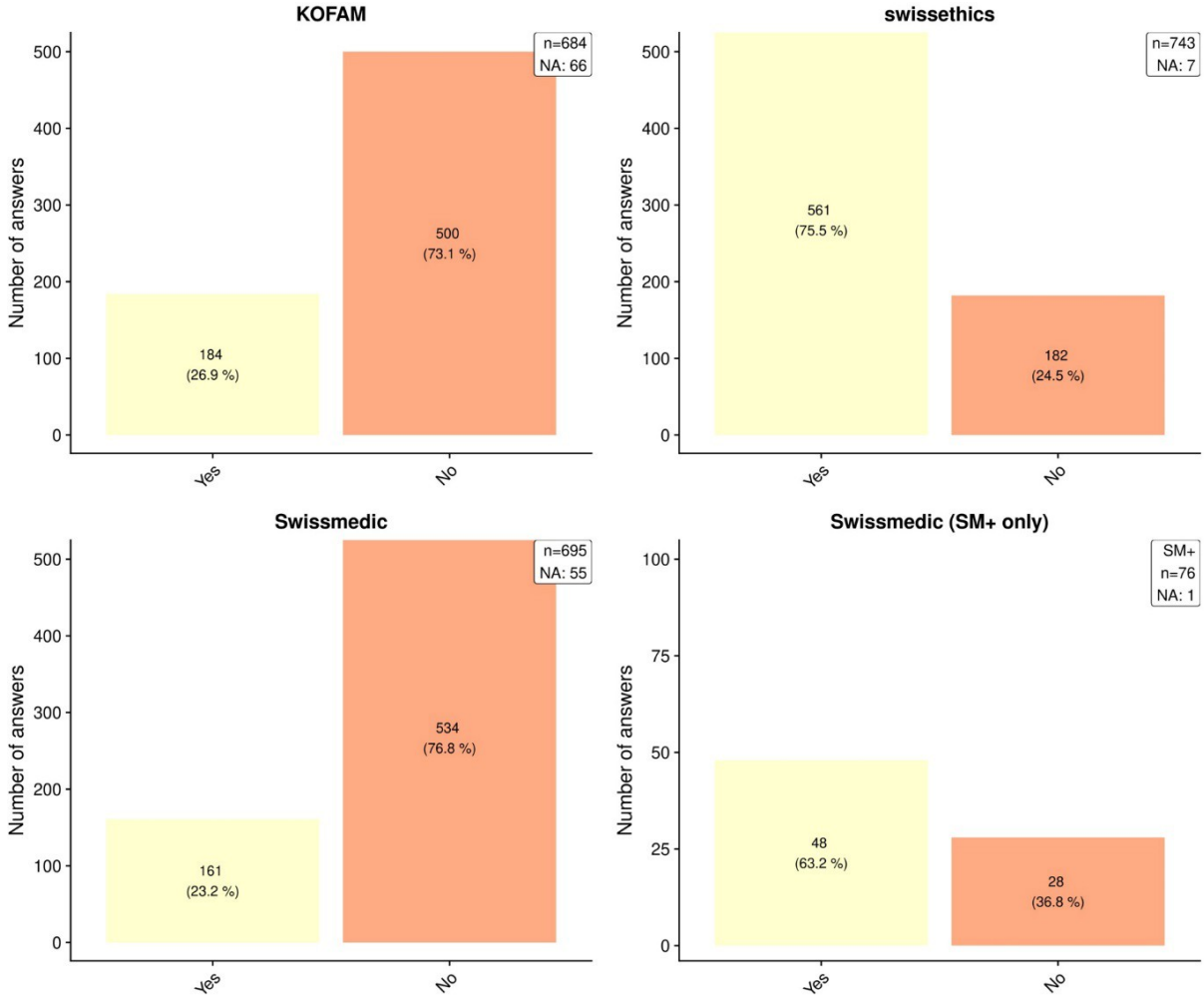
4.4. Compliance with HRA and related ordinances

4.4.1. Interaction with competent authorities

Respondents who were not employees of either a CTU or Contract Research Organisation (CRO) were asked whether they received support from a CTU or a CRO for the design and planning of their project. Of 728 eligible researchers who answered questionnaire Part B, 130 (18%) affirmed such support and 585 (82%) did not (no answer n=13). Respondents in Part A (project managers) responded in a similar way (Full Report, question A8).

Researchers were asked whether they visited the websites of the three entities KOFAM ("Koordinationsstelle Forschung am Menschen", maintained by FOPH), swissethics, or Swissmedic before and during the design and planning of their project. A large majority accessed the swissethics website but those of KOFAM and Swissmedic were used less (Figure 25). In the group of projects subject to approval by Swissmedic (SM+) about 63% of respondents had visited the Swissmedic website (Figure 25 bottom right).

Figure 25 – Visit of relevant websites (B3)



When asked whether they contacted the EC for questions or advice about the design or planning of their project, about two thirds of respondents in Part B (investigators) responded no (Figure 26). When asked the same question in Part A (project managers), most of them affirmed one or more contacts with the EC (Figure 27).

Figure 26 – Questionnaire Part B: Contact of researchers with Ethics Committee (B4)

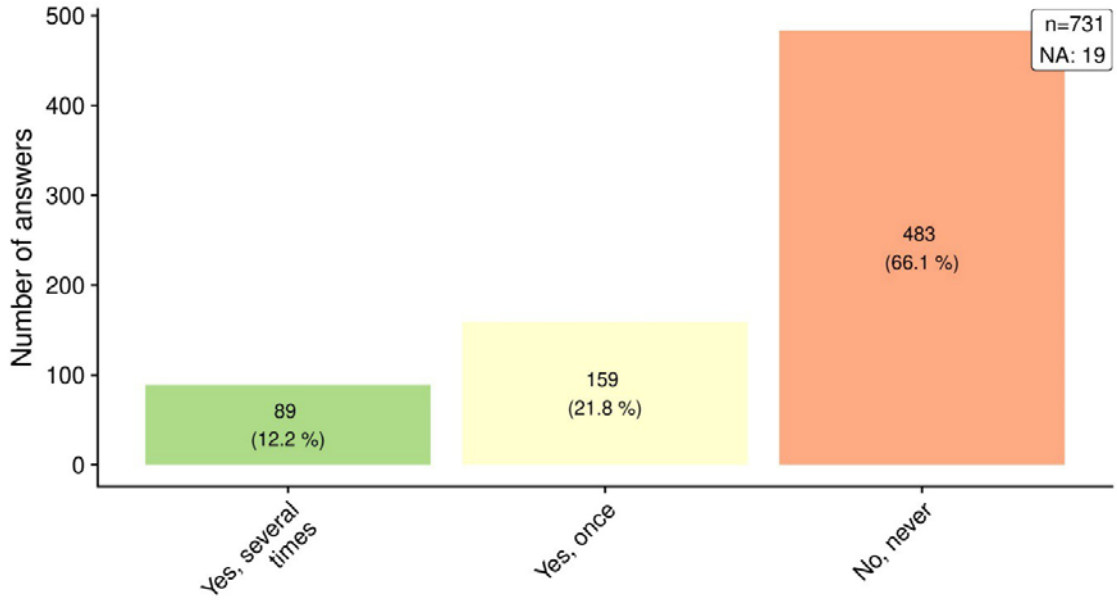
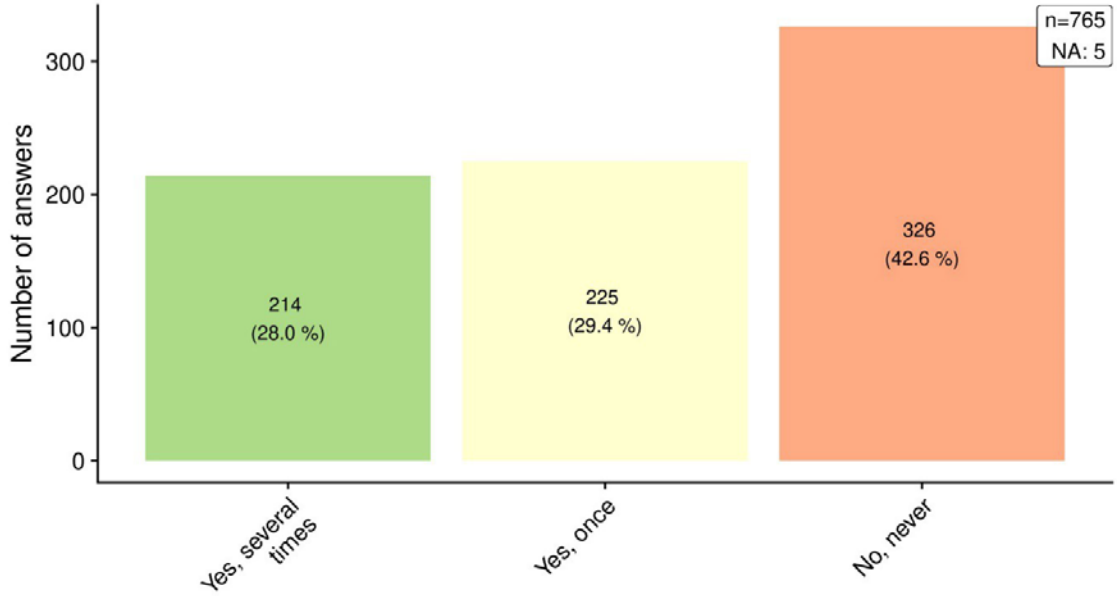


Figure 27 – Questionnaire Part A: Contact of researchers with Ethics Committee (A10)



Of the 248 researchers who confirmed one or more contacts with the EC, a large majority was in contact already before the initial submission to the EC (Figure 28) and about four out of five always received an answer (Figure 29).

Figure 28 – Timing of contact with Ethics Committee (B4a), multiple answers possible

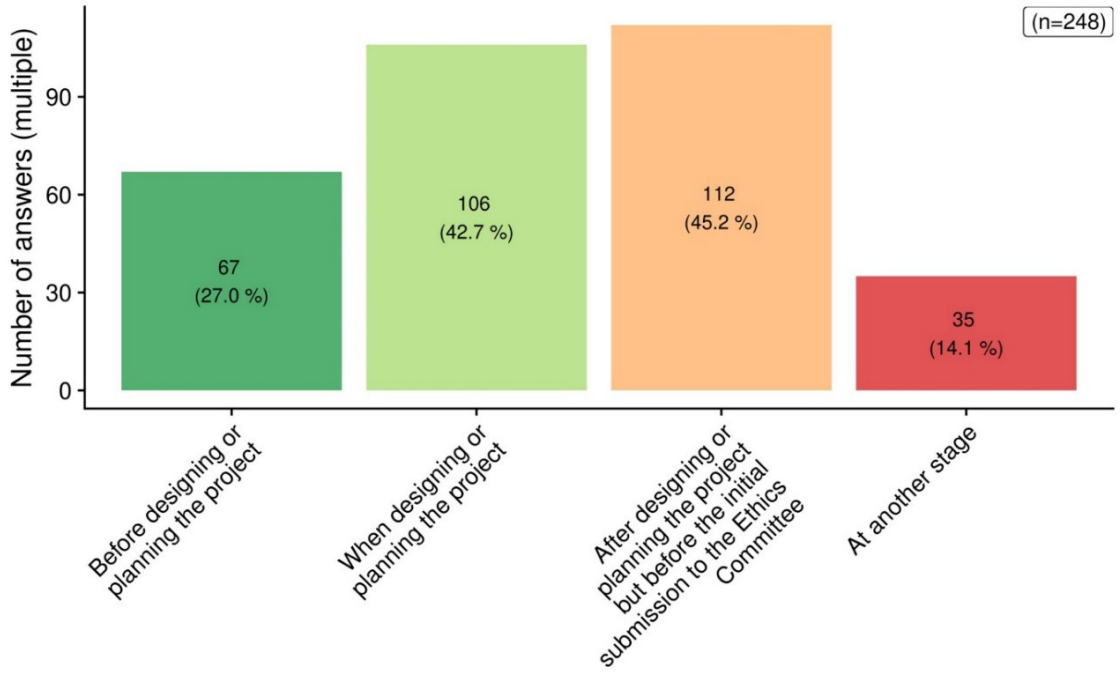
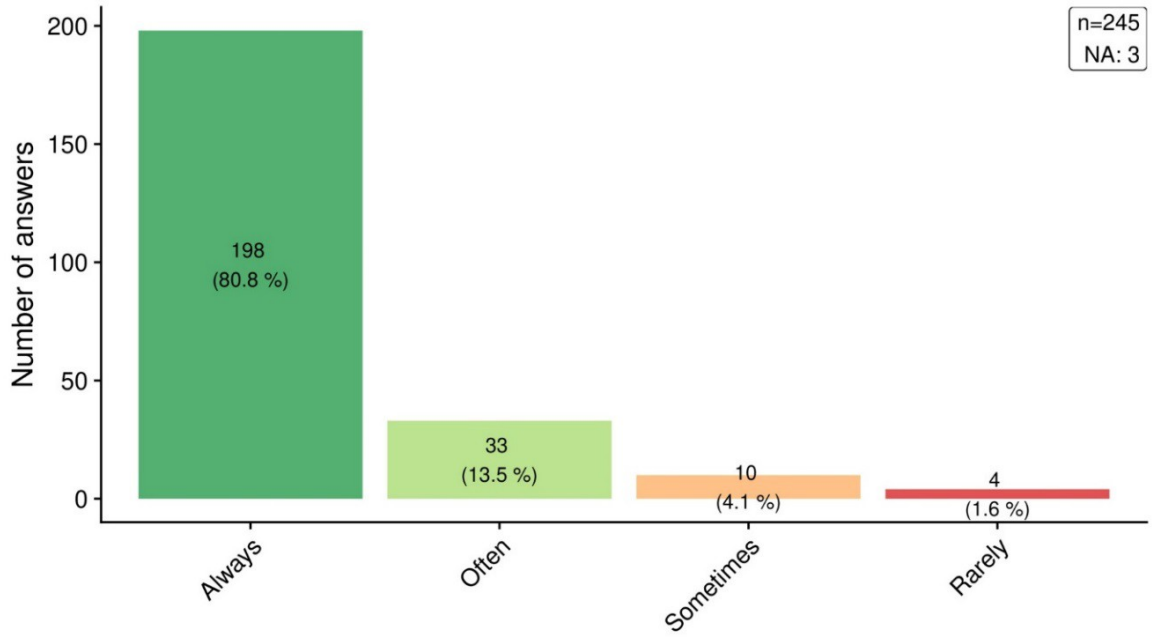
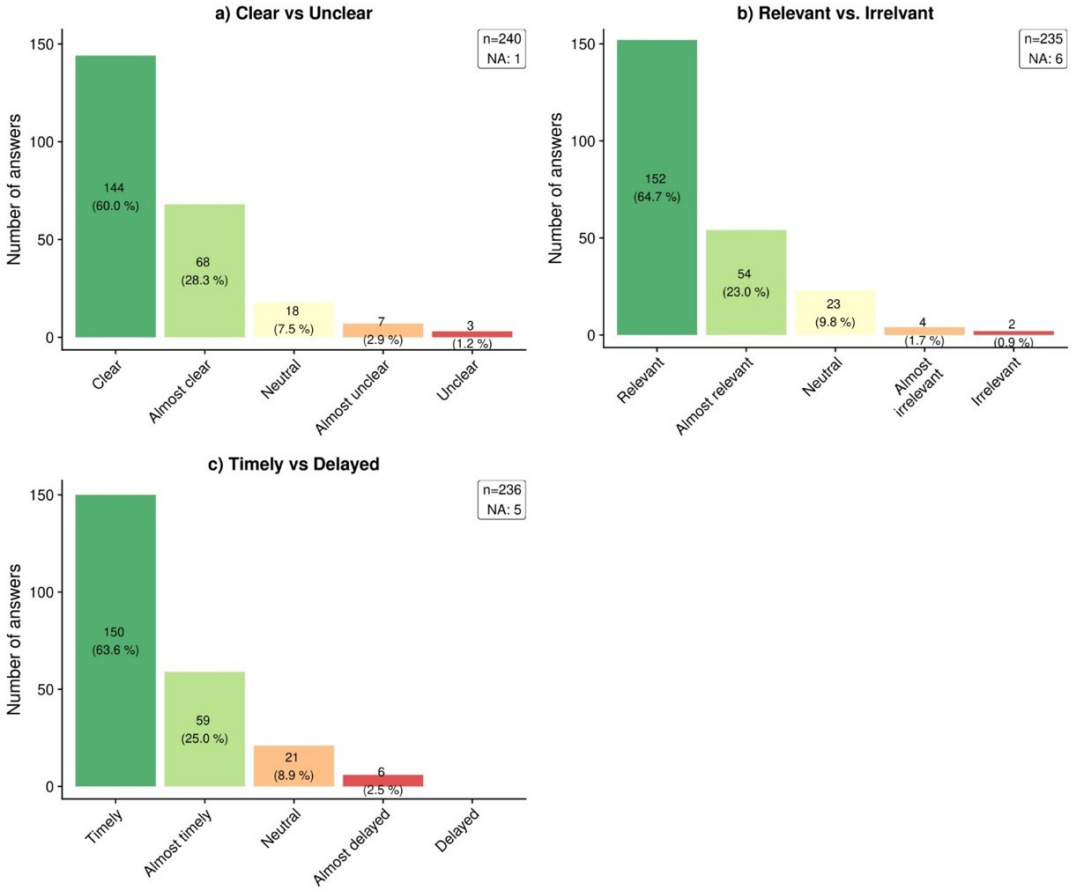


Figure 29 –Responsiveness of Ethics Committee ("Did you get answers to your requests?") (B4b)



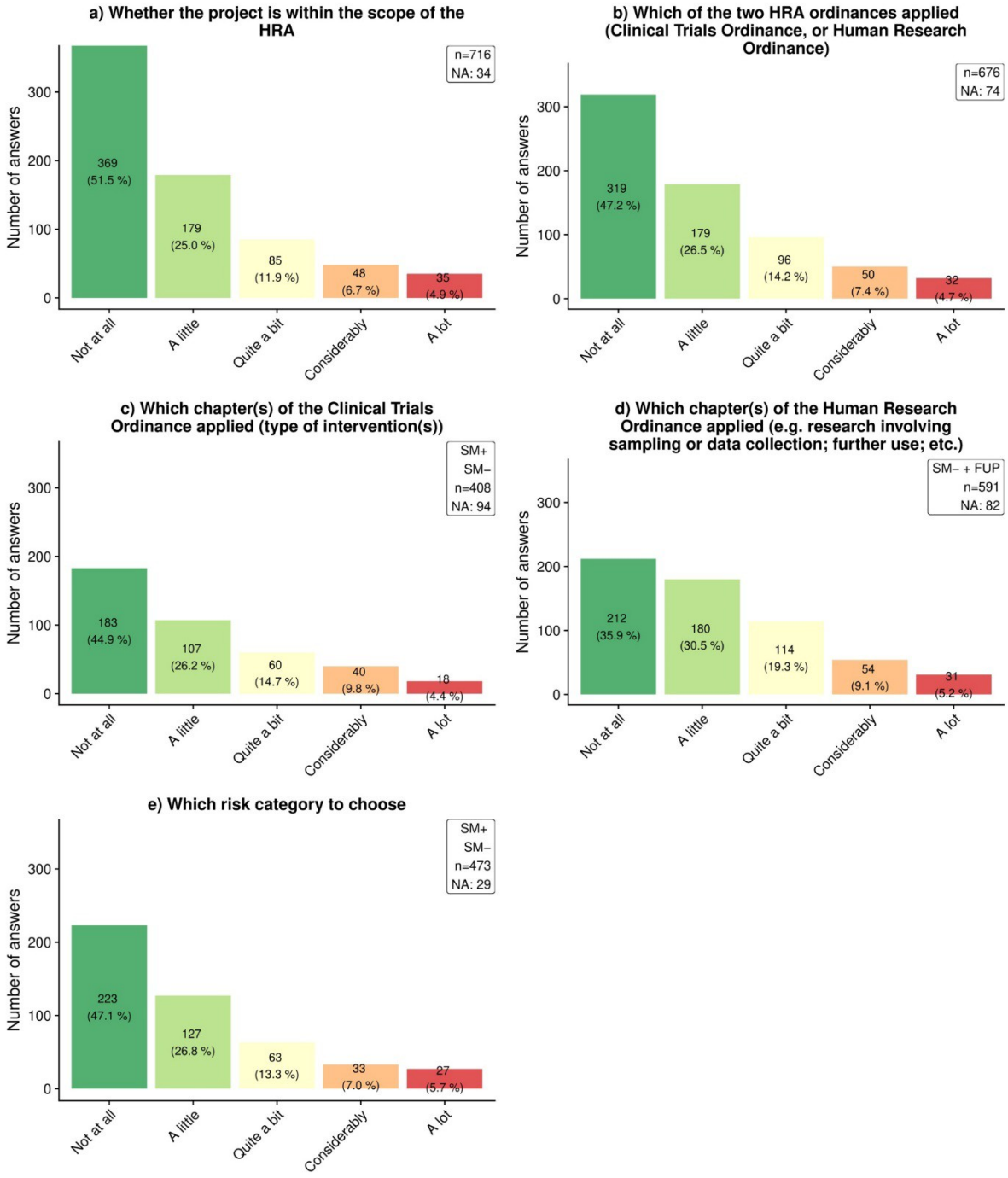
We asked researchers with regard to three selected pairs of attributes describing the quality of the responses received by the EC. For each of these pairs, 60% or more of the researchers deemed that the responses were respectively clear, relevant and timely (Figure 30).

Figure 30 – Quality of responses received by Ethics Committee (B4c)



Researchers were asked whether it was difficult to determine five selected project aspects when designing or planning their work. Three of these aspects were only applicable in certain groups of projects. For all five aspects, the most frequently chosen answer was that this was not at all a difficulty, while for each aspect 4% to 6% responded that they had a lot of difficulty with them (Figure 31).

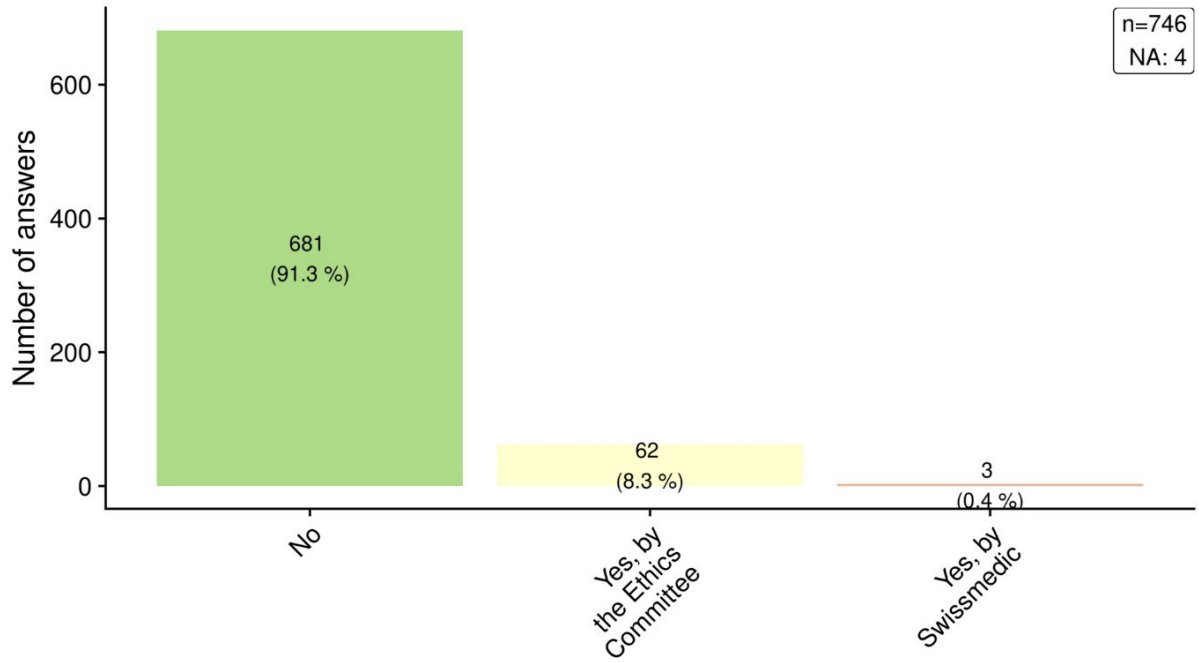
Figure 31 – Difficulty with certain aspects of HRA (B9)



4.4.2. Change of type of study

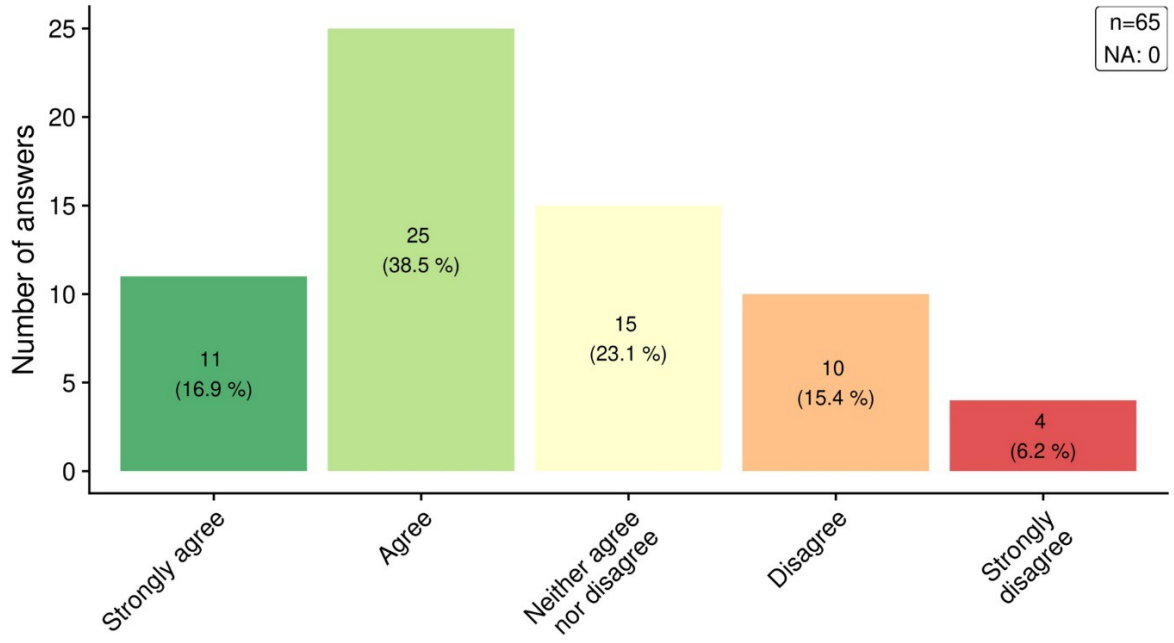
For 91% of projects the type of study was not changed after submission to the EC. In 9% it was changed by the EC or (to a much lesser extent) by Swissmedic (Figure 32).

Figure 32 – Change of type of study by Ethics Committee or Swissmedic (B10)



When the 65 researchers whose projects underwent reclassification of the type of study were asked about their agreement with this change, the opinions were mixed (Figure 33). Fourteen of them (22%) disagreed or strongly disagreed.

Figure 33 – Agreement with reclassification of type of study (B10a)



Of these, 12 gave reasons (Table 2). Five mentioned that they disagreed with the EC about the definition of a clinical trial.

"Study was a simple follow-up of healthy population with minimal intervention and yet had to be considered a clinical trial."

"A telephone interview doesn't make the study prospective in my opinion. We had some discussions."

"The EC does seem to apply too strict interpretations of terms, different from common sense/legislator intent."

Otherwise, researchers generally related that their understanding of legal terms was different and that they regarded the EC's interpretation of the law as too strict.

Table 2 - Reasons for disagreement if study type changed after submission (B10a)

Reason for disagreement	**Number of comments**
Definition of a clinical trial	5
Definition of a prospective study	1
What falls outside scope of the HRA (comment by researcher: "*I was surprised that the committee decided that the project is not a HRA project")*	1
EC being only authority to interpret the HRA was felt to be problematic, EC's interpretation of HRA was too strict	1
Disagreement between Swissmedic and EC about study type and risk classification	1
Study type was changed after submission although it was asked about the correct study type before submission	1
"Harmless" projects generate too much paper work	1
Communication problem (lack of explanation)	1
Total	**12***

* No statement/ missing free-text answer, n=1; Unclear meaning of the free-text answer, n=1

When changes to the type of study were made by the EC, all but four researchers received a partial or full explanation by them (Figure 34). Of those 58 researchers, most responded that changes by the EC were clear or even extremely clear to them (Figure 35).

Figure 34 – Explanation of change by Ethics Committee (B10b)

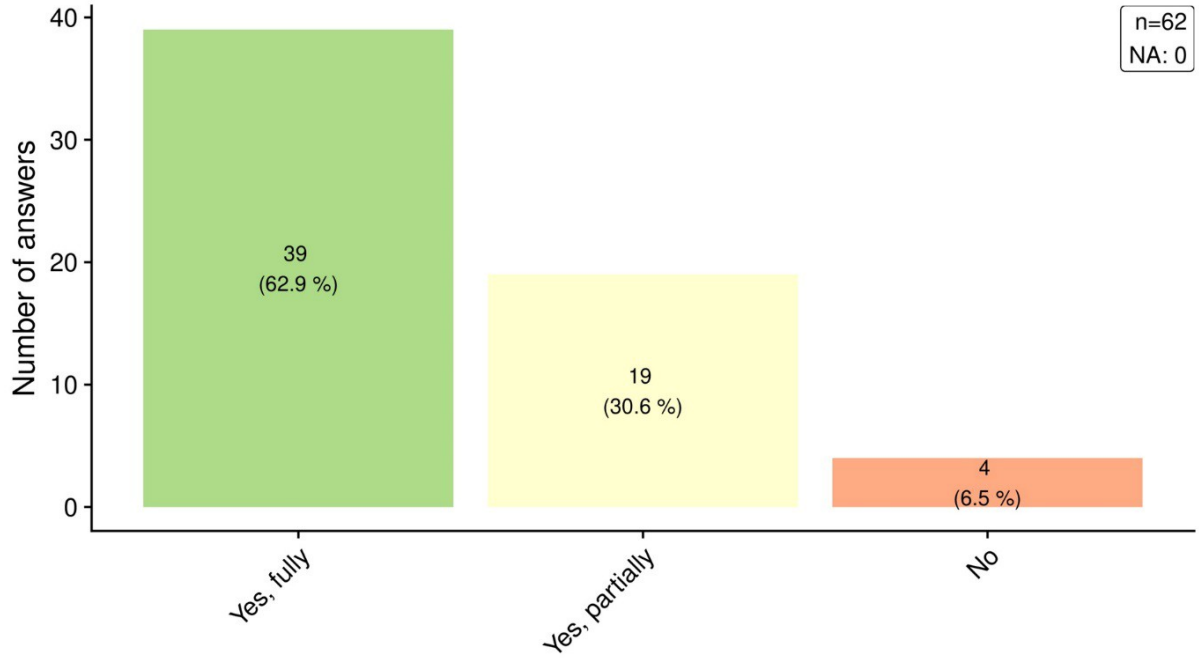
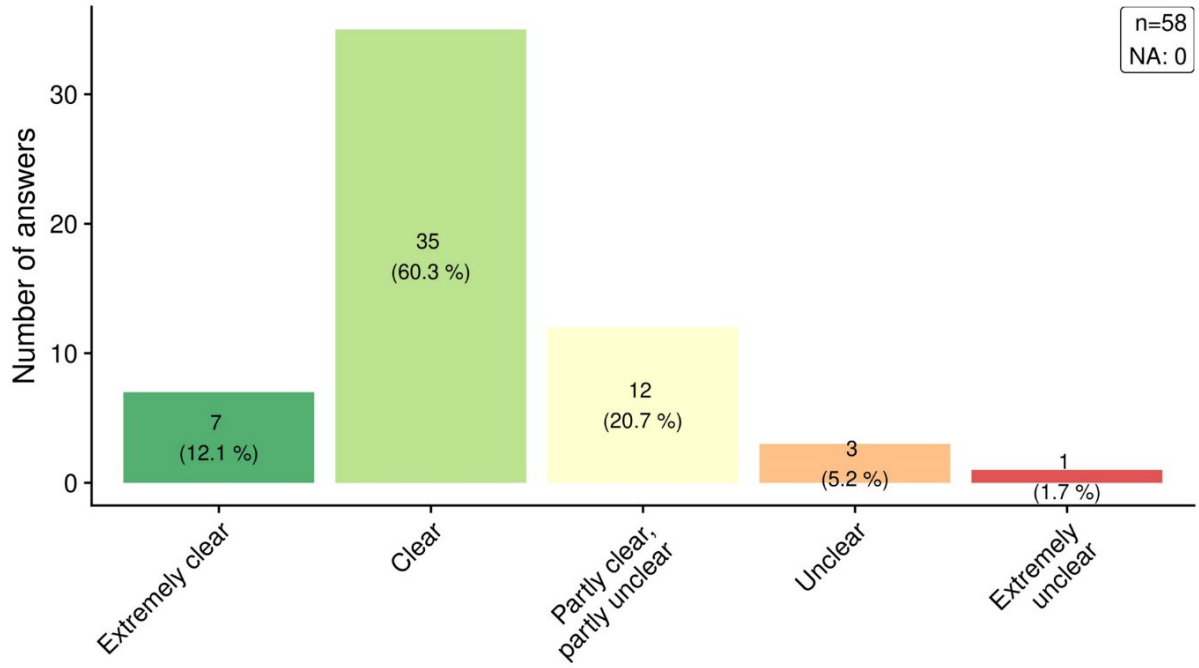


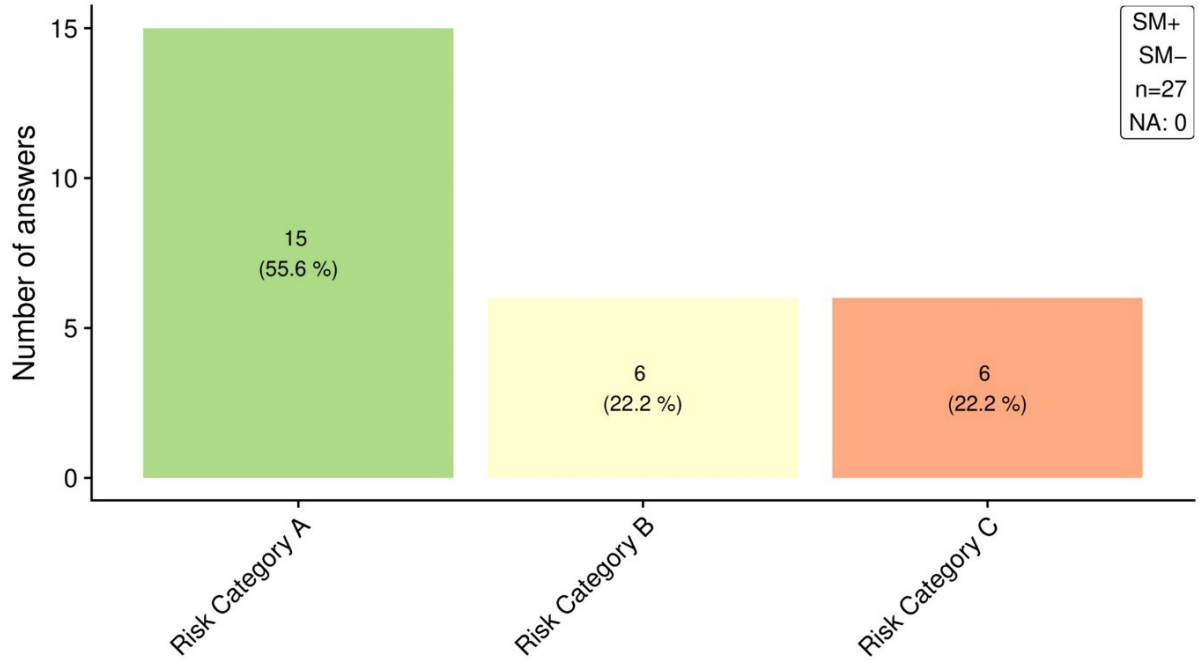
Figure 35 – Clarity of explanation by Ethics Committee (B10b)



4.4.3. Change of risk category

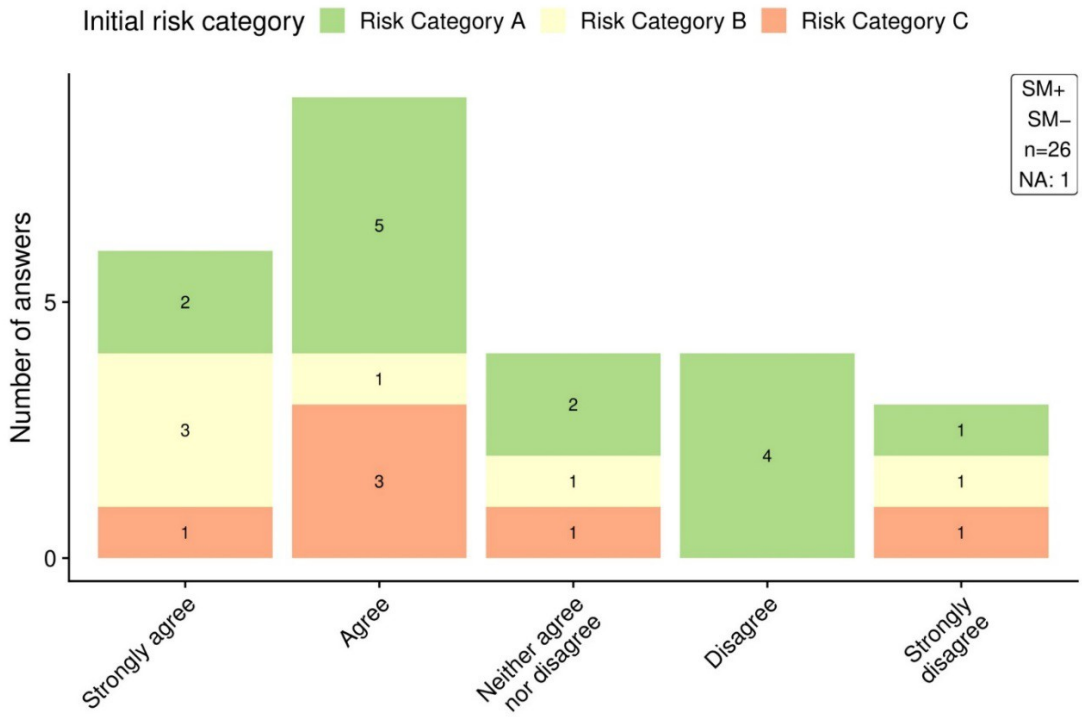
For the 502 projects that implied selection of a risk category A, B or C (groups SM+ and SM-) we asked whether the EC accepted the one chosen by the researchers. This was confirmed for 470 (95%) projects and rejected for 27 (5%) projects (no answer n=5). For the 27 projects in which the initially chosen risk category was not accepted, the initial choice was Risk Category A in more than half (Figure 36).

Figure 36 – Initial choice of risk category (B11a)



Regarding agreement with the decision of the EC to change the risk category, the opinions of the researchers were again mixed (Figure 37). Of the seven persons who disagreed or strongly disagreed with the EC, five had chosen Risk Category A initially.

Figure 37 – Agreement with change of risk category by Ethics Committee (B11b)



Of seven researchers who disagreed, six gave reasons (Table 3). They generally expected another (lower) risk category for their projects and had problems accepting the EC's classification.

"I think that our project, even if it involves minors, doesn't entail more than only minimal risks."

Other reasons mentioned suggest that there was a lack of communication and perceived transparency of the decisions made by the ECs.

"Even after asking the ethics committee and getting a response, the decision for re-classification seems arbitrary."

"They did not understand the purpose of our project."

Table 3 - Reasons for disagreements with final risk classification (B11b)

Reason for disagreement	**Number of comments**
Expecting a lower risk category	3
Classification by EC seemed arbitrary	1
Category was changed to one with lower risk by EC and then changed to category with higher risk by Swissmedic	1
Purpose of the project was not understood by EC	1
Total	**6***

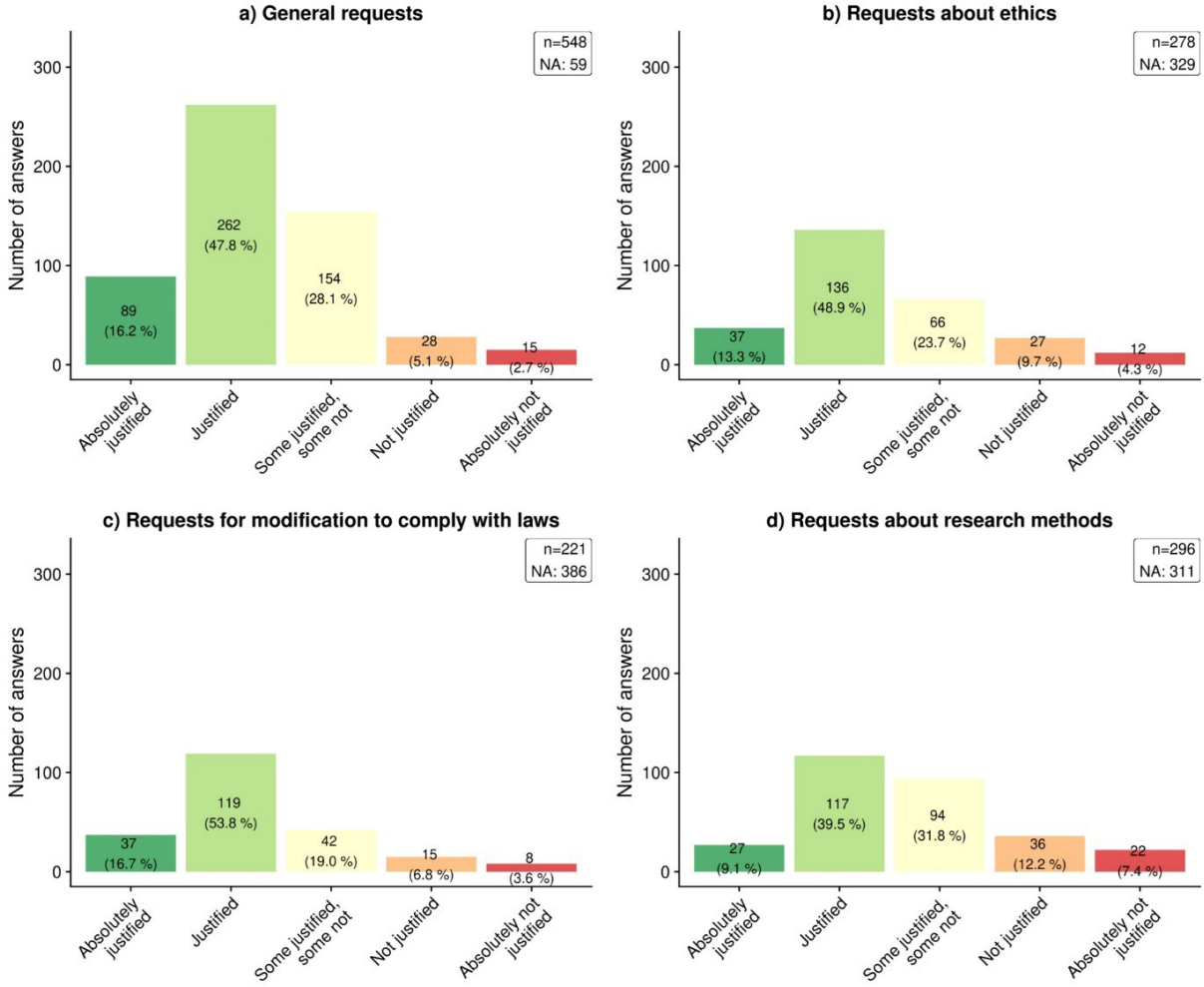
* No statement/ missing free-text answer, n=1

In the 66 projects for which the EC accepted the risk classification and that were also submitted to Swissmedic (subset of group SM+) we also asked whether Swissmedic accepted the initially chosen risk category. This was confirmed for 61 (95%) projects and rejected for 3 (5%) projects (no answer n=2). Of these three, one was in Risk Category B and one in Risk Category C (no answer n=1) and all three researchers agreed or strongly agreed with the change.

4.4.4. Charges, conditions or requests by the Ethics Committee

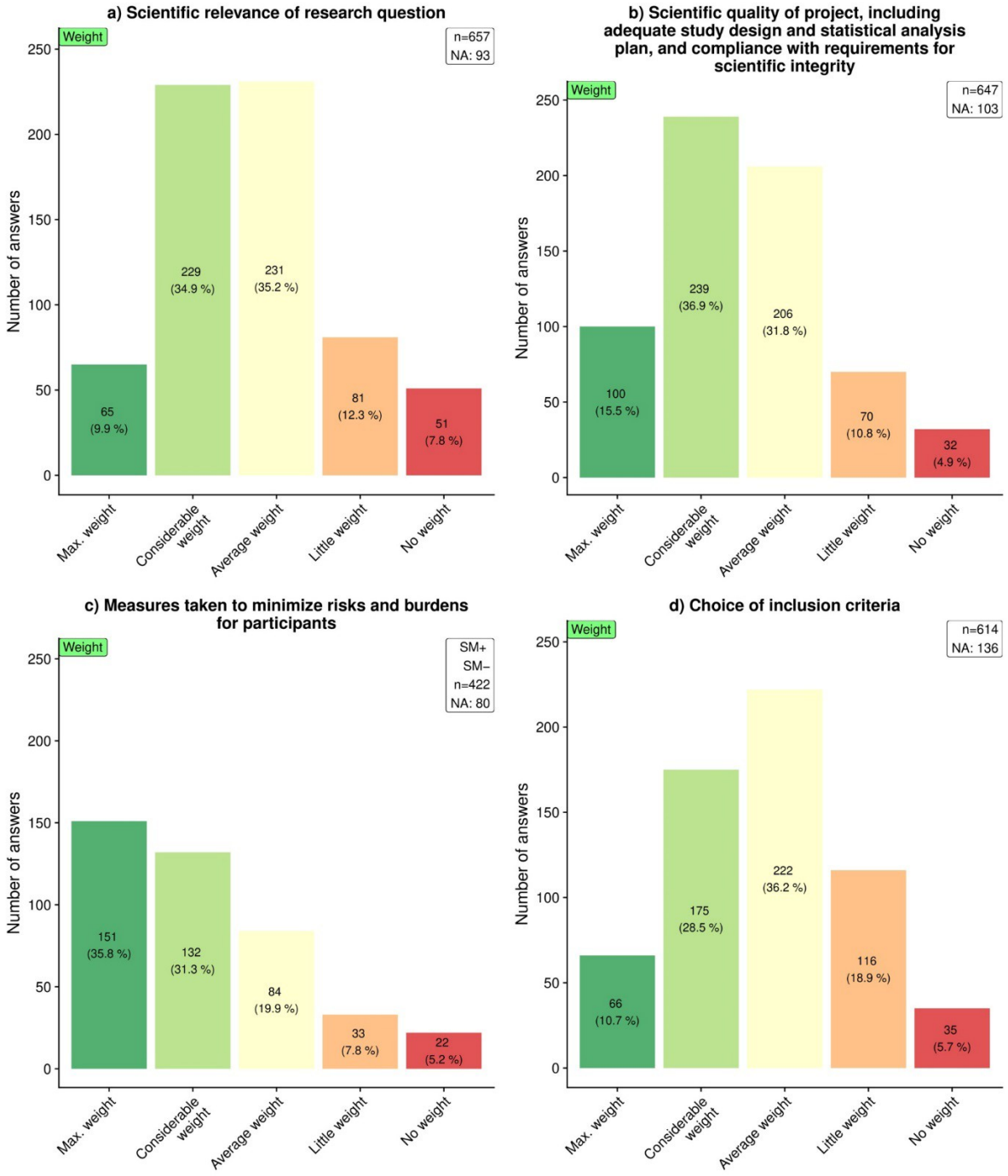
In the large majority of projects the EC made charges or conditions, or requested modifications in their first decision letter (i.e. before approval). This was the case in 607 (81%) projects and not in 138 (19%) projects (no answer n=5). We asked the researchers whether they perceived such additional requests by the EC as justified or not, while focussing on four different areas. The most frequent answer in all four areas was that such requests were justified (Figure 38). Agreement with such requests was less when they were about research methods; about 20% of researchers deemed that such requests were not or absolutely not justified. A limitation is that only less than half of the researchers responded to three of the specific questions (or they were not applicable because there was no such request by the EC).

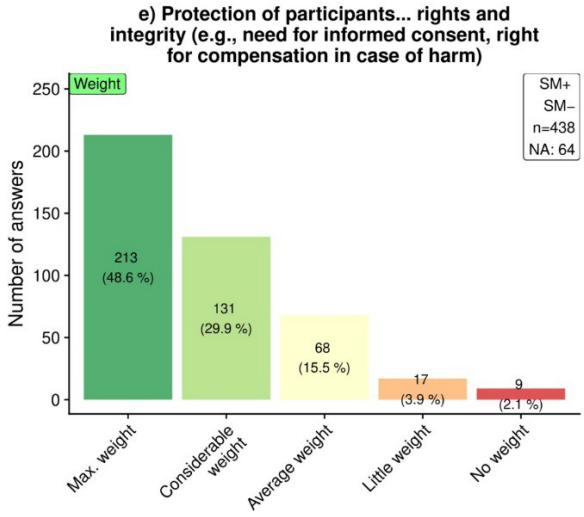
Figure 38 – Agreement with requests by Ethics Committee (B13)

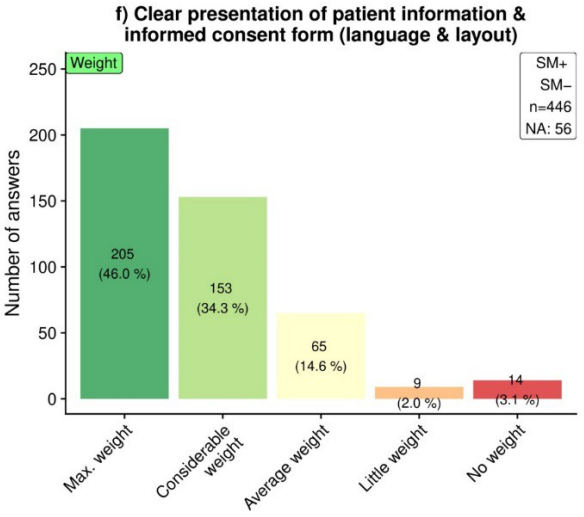


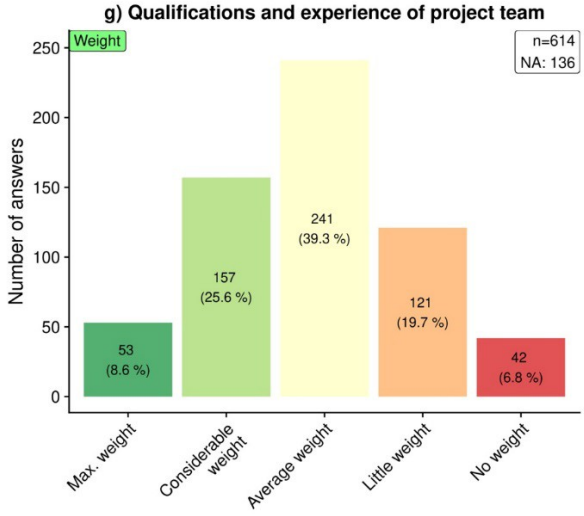
With regard to thirteen domains concerning the HRA or the related ordinances that could have been considered by the EC when assessing the project, we asked the researchers' opinion on how much weight the EC would have given to each domain (Figure 39). More than half of them thought that the EC had given maximum, considerable or average weight to them. Sizeable subgroups of 20% or more deemed that it had given little or no weight to scientific relevance, choice of inclusion criteria, sufficient funding, suitability of research infrastructure, qualification and experience of project team, and feasibility.

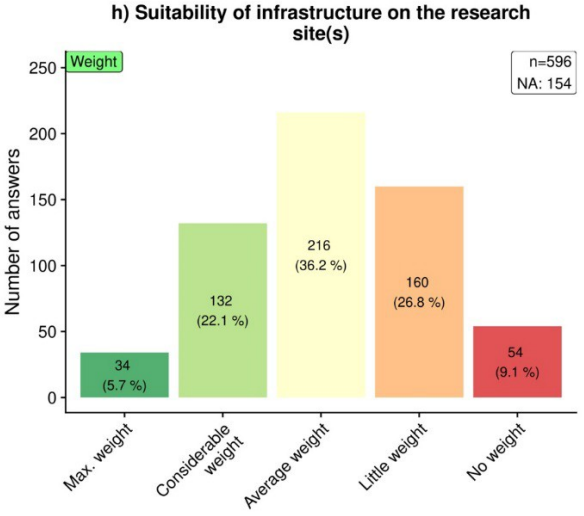
Figure 39 – Weight attributed by Ethics Committee (B14)

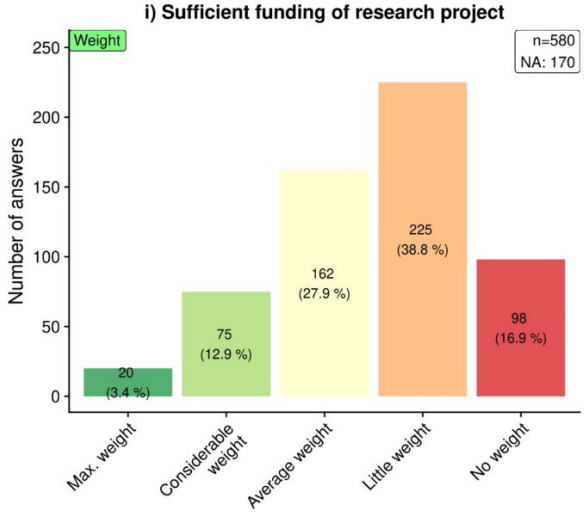


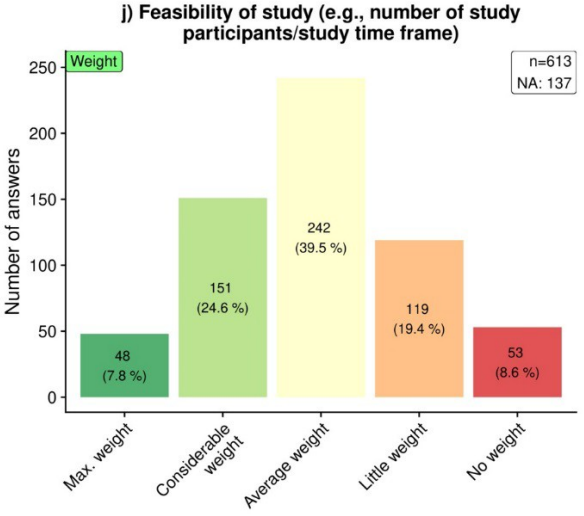

e) Protection of participants... rights and integrity (e.g., need for informed consent, right for compensation in case of harm)
Weight
SM+
SM−
n=438
NA: 64
Number of answers
213 (48.6 %)
131 (29.9 %)
68 (15.5 %)
17 (3.9 %)
9 (2.1 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

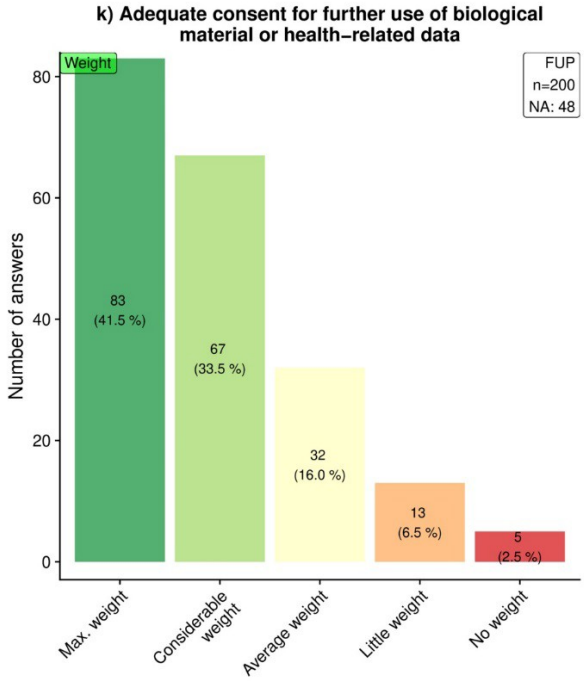

f) Clear presentation of patient information & informed consent form (language & layout)
Weight
SM+
SM−
n=446
NA: 56
Number of answers
205 (46.0 %)
153 (34.3 %)
65 (14.6 %)
9 (2.0 %)
14 (3.1 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

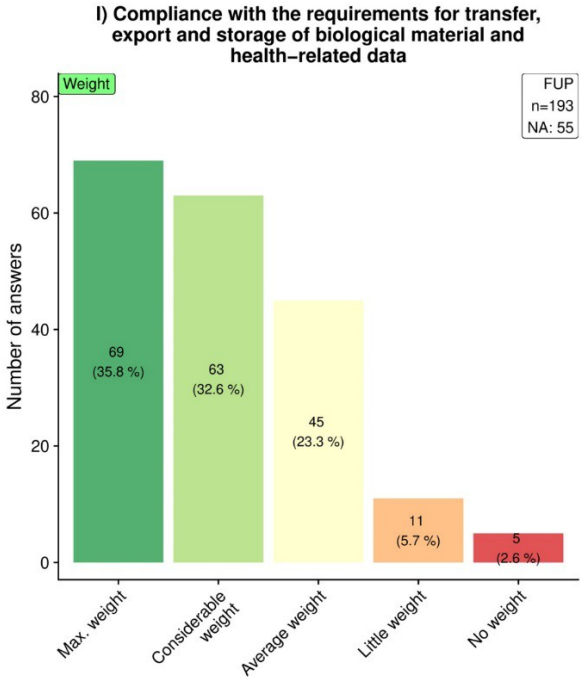

g) Qualifications and experience of project team
Weight
n=614
NA: 136
Number of answers
53 (8.6 %)
157 (25.6 %)
241 (39.3 %)
121 (19.7 %)
42 (6.8 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

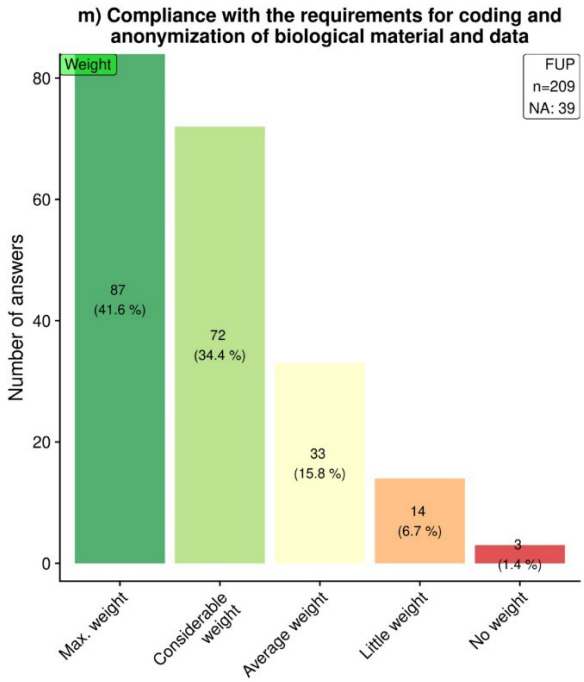

h) Suitability of infrastructure on the research site(s)
Weight
n=596
NA: 154
Number of answers
34 (5.7 %)
132 (22.1 %)
216 (36.2 %)
160 (26.8 %)
54 (9.1 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight


i) Sufficient funding of research project
Weight
n=580
NA: 170
Number of answers
20 (3.4 %)
75 (12.9 %)
162 (27.9 %)
225 (38.8 %)
98 (16.9 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight


j) Feasibility of study (e.g., number of study participants/study time frame)
Weight
n=613
NA: 137
Number of answers
48 (7.8 %)
151 (24.6 %)
242 (39.5 %)
119 (19.4 %)
53 (8.6 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

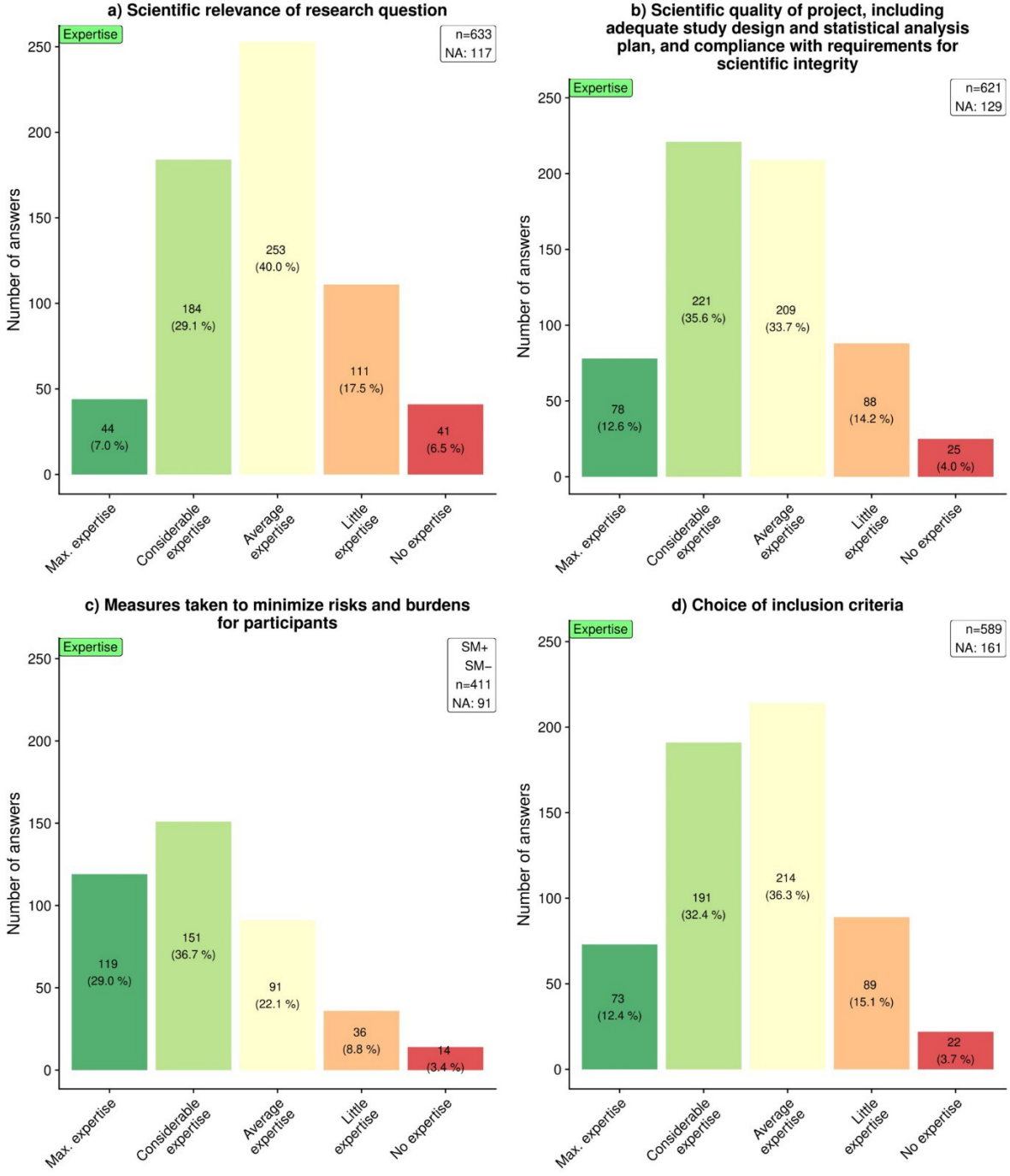

k) Adequate consent for further use of biological material or health−related data
Weight
FUP
n=200
NA: 48
Number of answers
0
20
40
60
80
83
(41.5 %)
67
(33.5 %)
32
(16.0 %)
13
(6.5 %)
5
(2.5 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

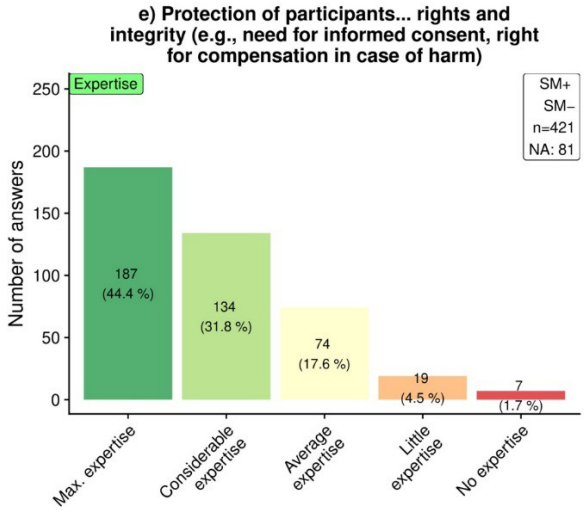

l) Compliance with the requirements for transfer, export and storage of biological material and health−related data
Weight
FUP
n=193
NA: 55
Number of answers
0
20
40
60
80
69
(35.8 %)
63
(32.6 %)
45
(23.3 %)
11
(5.7 %)
5
(2.6 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

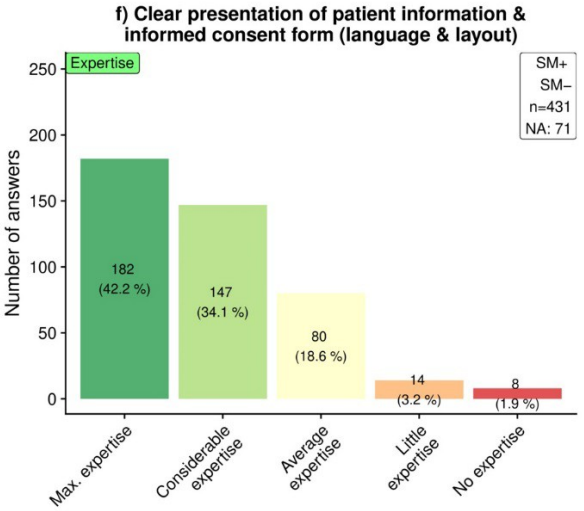

m) Compliance with the requirements for coding and anonymization of biological material and data
Weight
FUP
n=209
NA: 39
Number of answers
0
20
40
60
80
87
(41.6 %)
72
(34.4 %)
33
(15.8 %)
14
(6.7 %)
3
(1.4 %)
Max. weight
Considerable weight
Average weight
Little weight
No weight

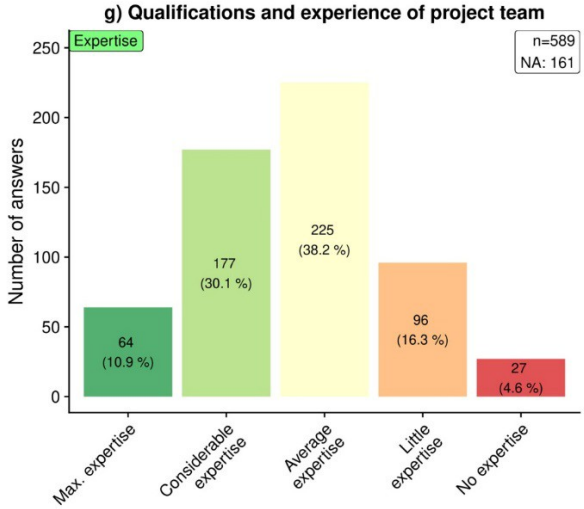
For the same thirteen domains we also asked the researchers' opinion about how much expertise the EC had to assess each of these domains (Figure 40).

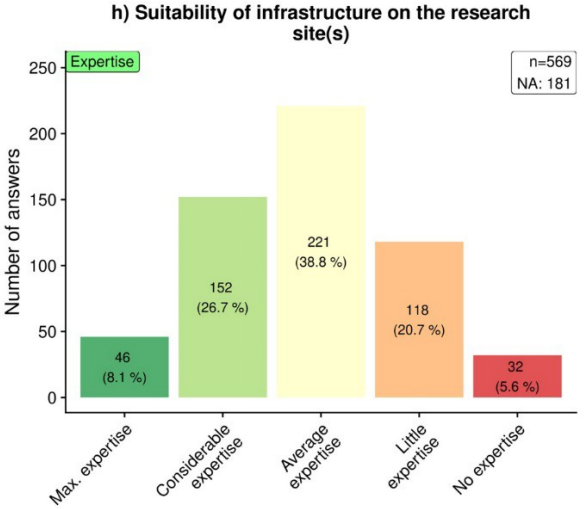
Figure 40 – Expertise of Ethics Committee (B14)

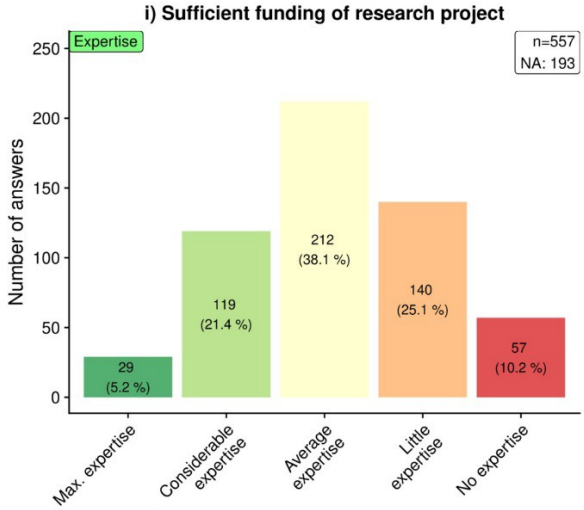


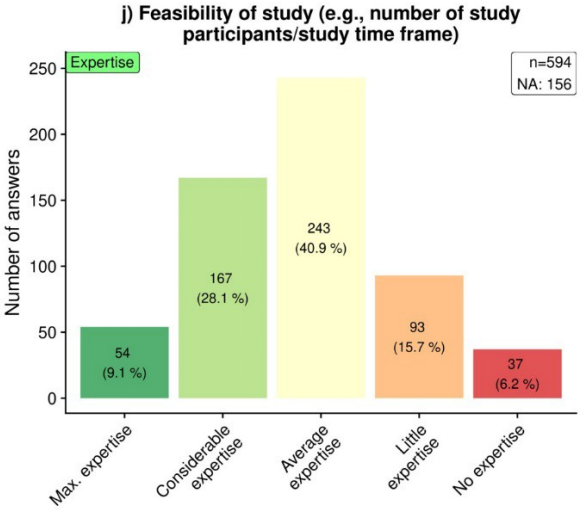

e) Protection of participants... rights and integrity (e.g., need for informed consent, right for compensation in case of harm)
Expertise
SM+
SM−
n=421
NA: 81
Number of answers
187 (44.4 %)
134 (31.8 %)
74 (17.6 %)
19 (4.5 %)
7 (1.7 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise

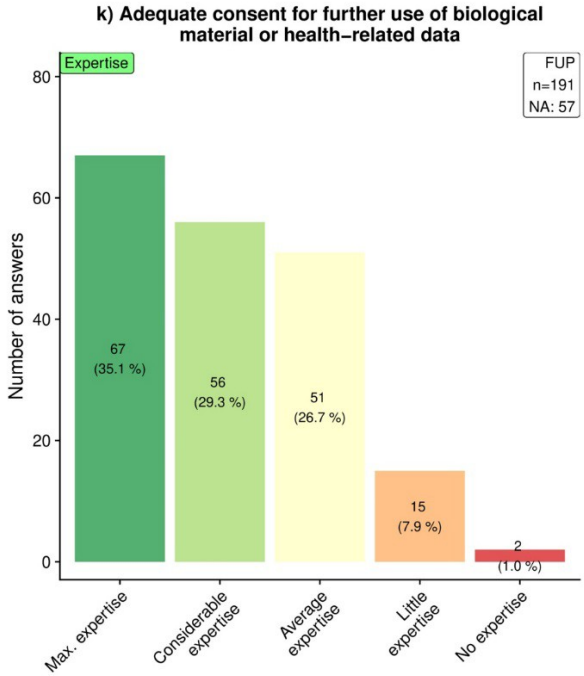

f) Clear presentation of patient information & informed consent form (language & layout)
Expertise
SM+
SM−
n=431
NA: 71
Number of answers
182 (42.2 %)
147 (34.1 %)
80 (18.6 %)
14 (3.2 %)
8 (1.9 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise

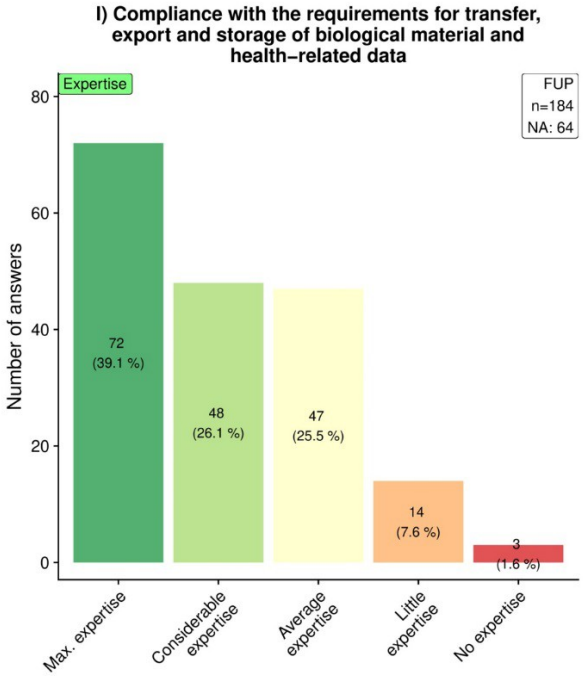

g) Qualifications and experience of project team
Expertise
n=589
NA: 161
Number of answers
64 (10.9 %)
177 (30.1 %)
225 (38.2 %)
96 (16.3 %)
27 (4.6 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise

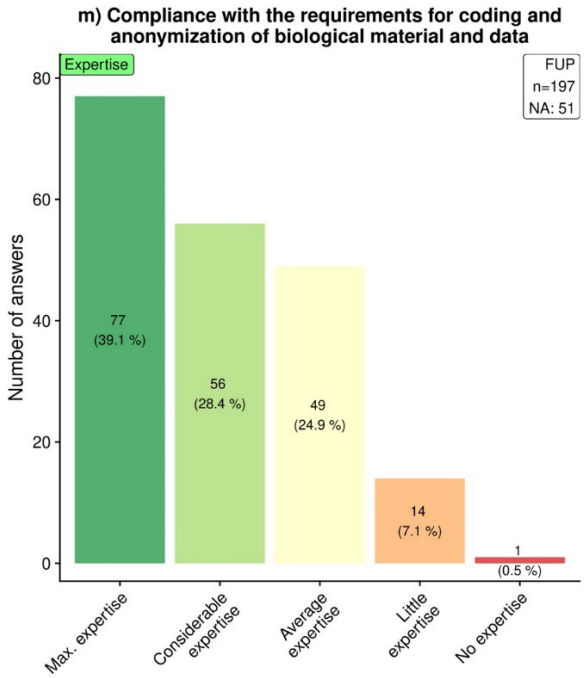

h) Suitability of infrastructure on the research site(s)
Expertise
n=569
NA: 181
Number of answers
46 (8.1 %)
152 (26.7 %)
221 (38.8 %)
118 (20.7 %)
32 (5.6 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise


i) Sufficient funding of research project
Expertise
n=557
NA: 193
Number of answers
29 (5.2 %)
119 (21.4 %)
212 (38.1 %)
140 (25.1 %)
57 (10.2 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise


j) Feasibility of study (e.g., number of study participants/study time frame)
Expertise
n=594
NA: 156
Number of answers
54 (9.1 %)
167 (28.1 %)
243 (40.9 %)
93 (15.7 %)
37 (6.2 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise


k) Adequate consent for further use of biological material or health−related data
Expertise
FUP
n=191
NA: 57
Number of answers
0
20
40
60
80
67
(35.1 %)
56
(29.3 %)
51
(26.7 %)
15
(7.9 %)
2
(1.0 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise

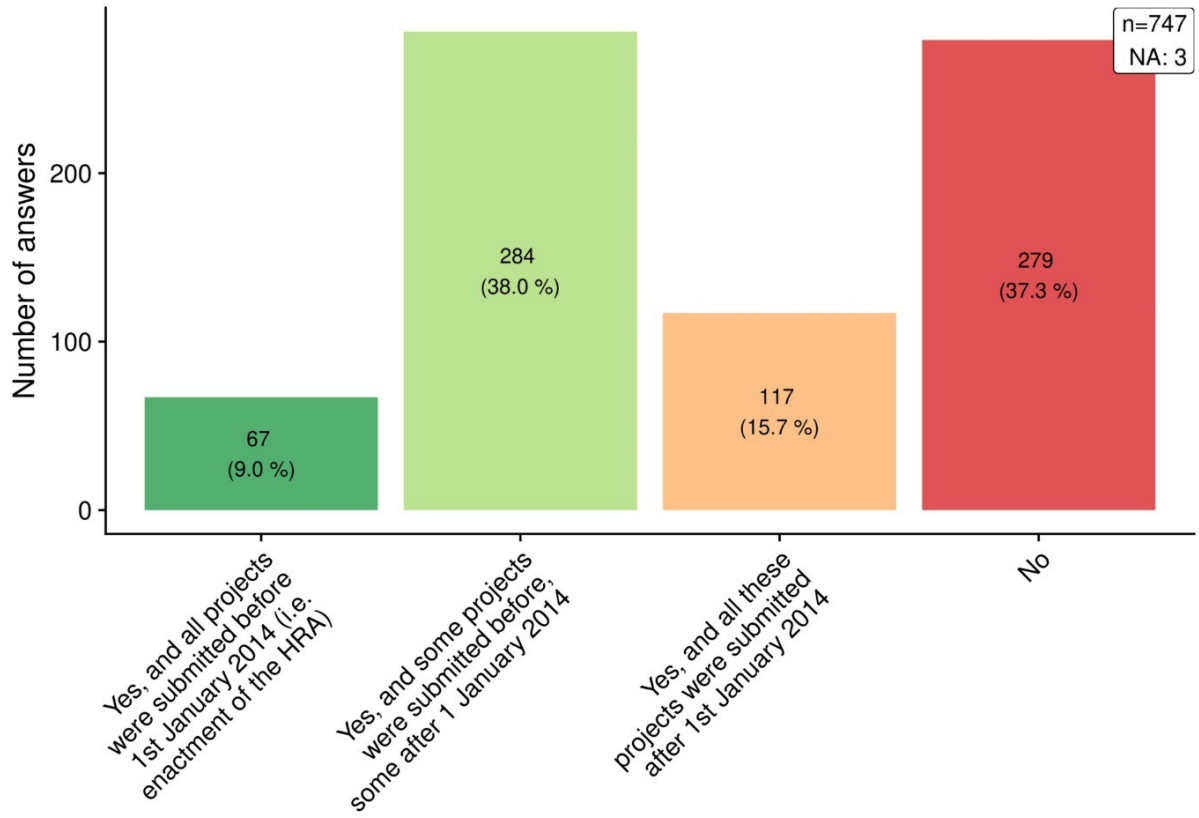

l) Compliance with the requirements for transfer, export and storage of biological material and health−related data
Expertise
FUP
n=184
NA: 64
Number of answers
0
20
40
60
80
72
(39.1 %)
48
(26.1 %)
47
(25.5 %)
14
(7.6 %)
3
(1.6 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise


m) Compliance with the requirements for coding and anonymization of biological material and data
Expertise
FUP
n=197
NA: 51
Number of answers
0
20
40
60
80
77
(39.1 %)
56
(28.4 %)
49
(24.9 %)
14
(7.1 %)
1
(0.5 %)
Max. expertise
Considerable expertise
Average expertise
Little expertise
No expertise

4.4.5. General experience with ethical approval in Switzerland

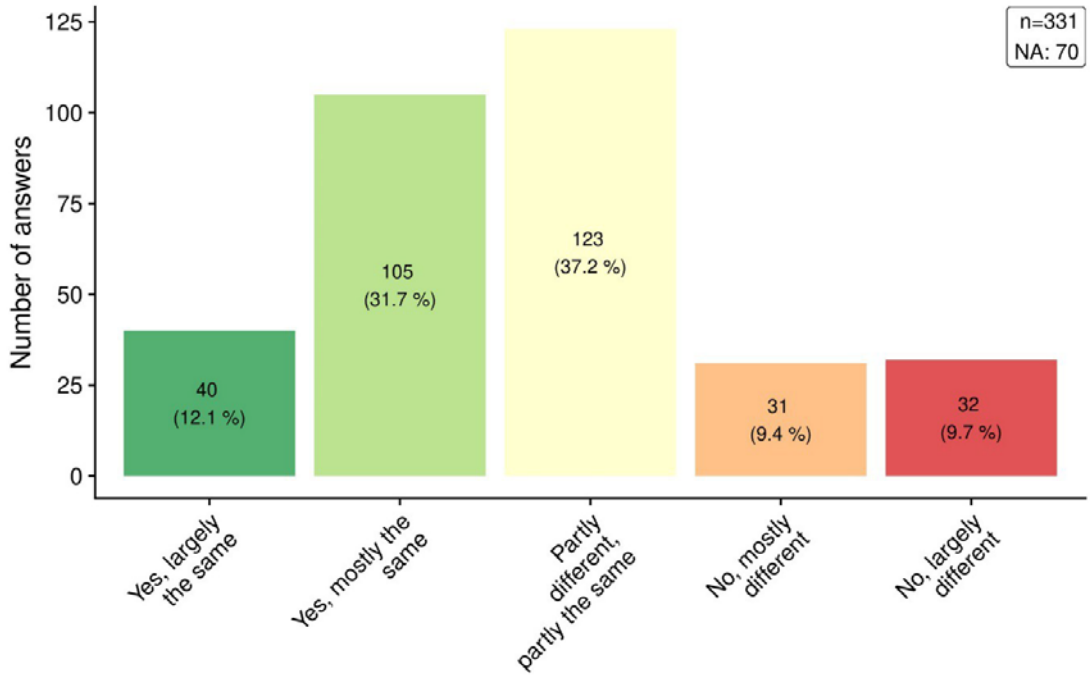
About two thirds of respondents had submitted research projects to an EC in Switzerland that was different from the one that had decided on the submitted project in 2017 (Figure 41).

Figure 41 – Submission to other Ethics Committees in Switzerland (B15)



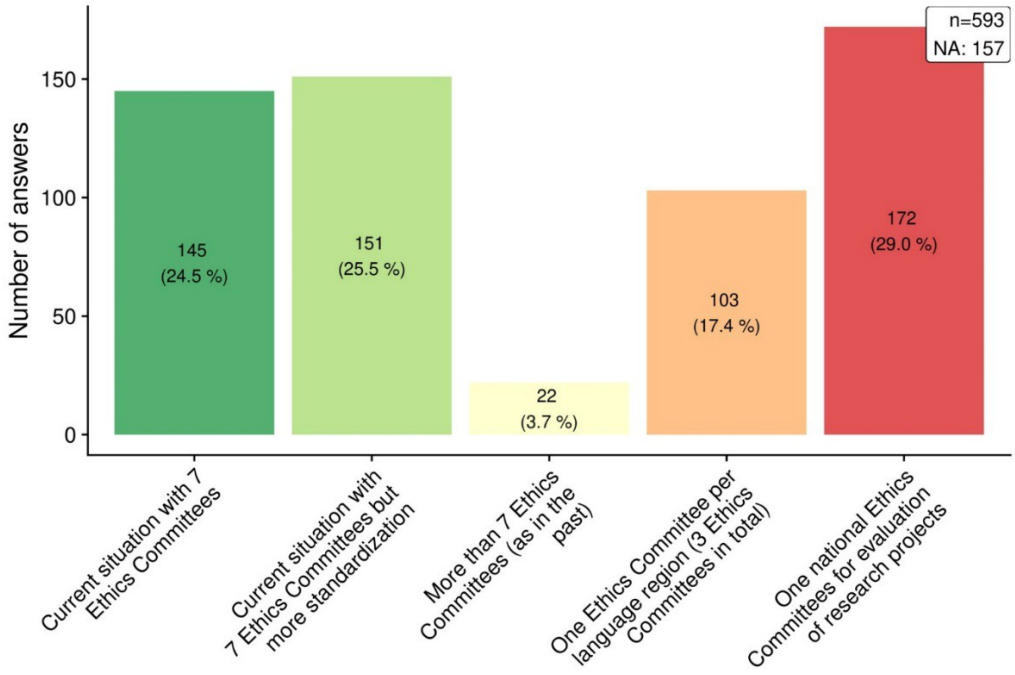
The 401 respondents with some or all projects submitted after 1st January 2014 (i.e. under the current legislation) were asked about their opinion on whether the seven cantonal ECs in Switzerland evaluate research projects according to a common standard. This was partly or fully confirmed by 44% of respondents, while 19% thought that evaluations were mostly or largely different (Figure 42).

Figure 42 – Common standards of Ethics Committees in evaluating research projects (B16)



When we asked about preferences among several options for the organisation of ECs on the national level, more than 70% of respondents opted for more standardisation across ECs. Only few preferred more than seven committees (as in the past), and almost half opted for one EC by language region or one single national EC (Figure 43).

Figure 43 – Preference for standardisation / number of Ethics Committees in Switzerland (B17)



4.4.6. Aspects specific to projects submitted to Swissmedic

The 77 researchers whose projects required submission to Swissmedic (group SM+) were asked in more detail about their contact with this authority for questions or advice about the design or planning of their project. Importantly, interpretation of survey data for this group is limited by the small number of respondents.

Eight (10%) researchers confirmed one or more of such contacts (Figure 44). Of these, three always received an answer, three often and two sometimes. Opinions about the quality of the communication varied (Figure 45).

Figure 44 – Contact of researchers with Swissmedic (B5)

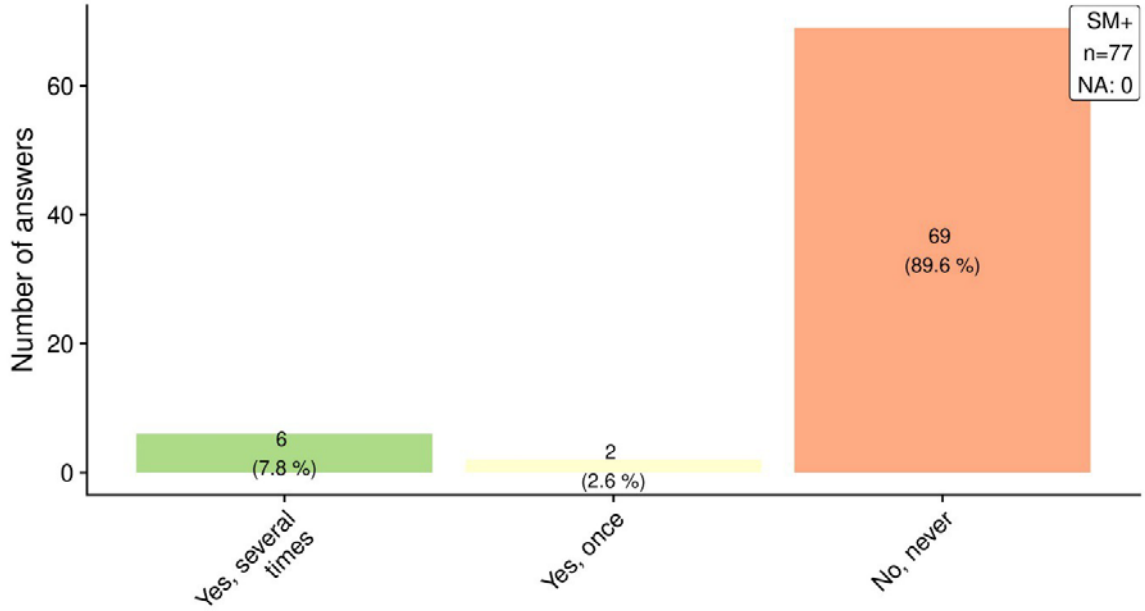
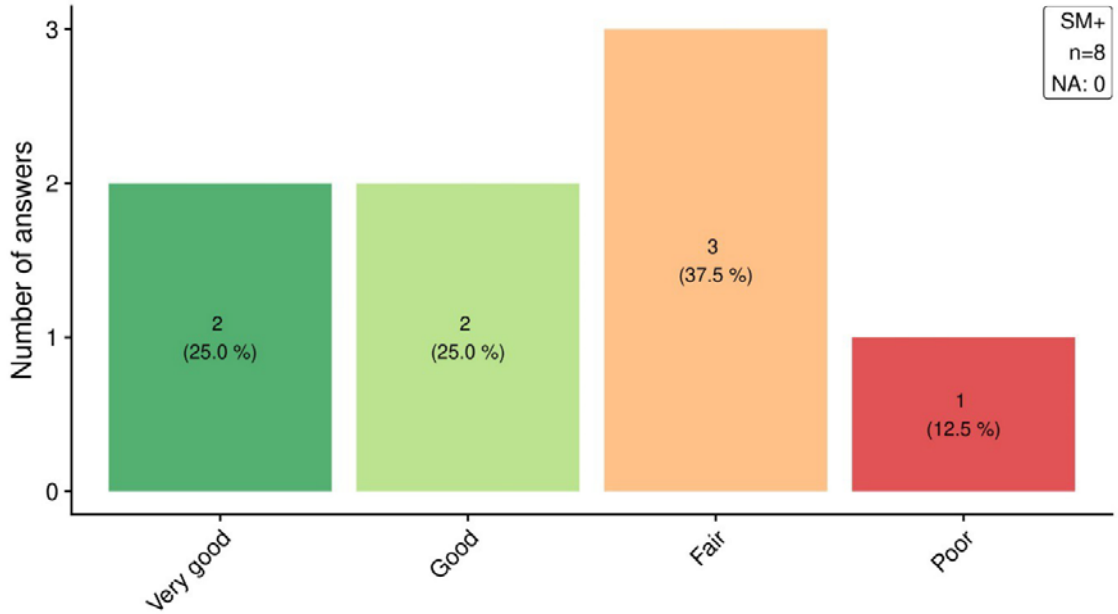


Figure 45 – Quality of communication with Swissmedic (B5b)



Researchers of 14 (18%) of SM+ projects observed inconsistencies between the EC and Swissmedic once or several times (Figure 46) and twelve described them in further detail (Table 4). When asked about the nature of these inconsistencies, five mentioned that the risk category was judged differently by the EC and Swissmedic.

Figure 46 – Observed inconsistencies between Ethics Committee and Swissmedic (B6)

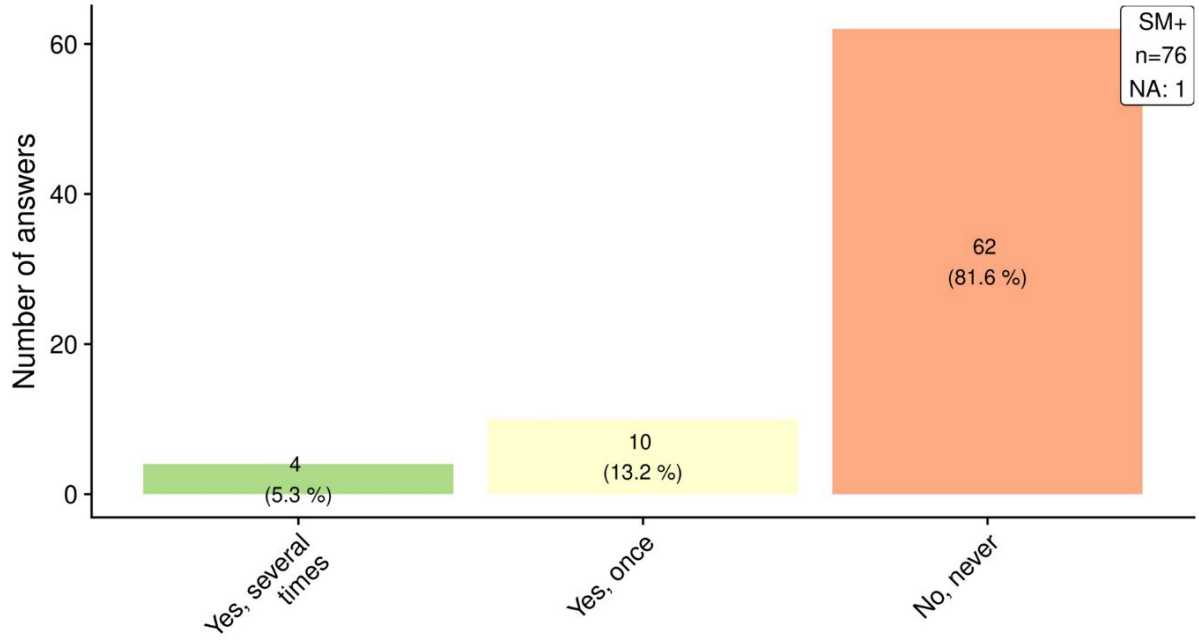
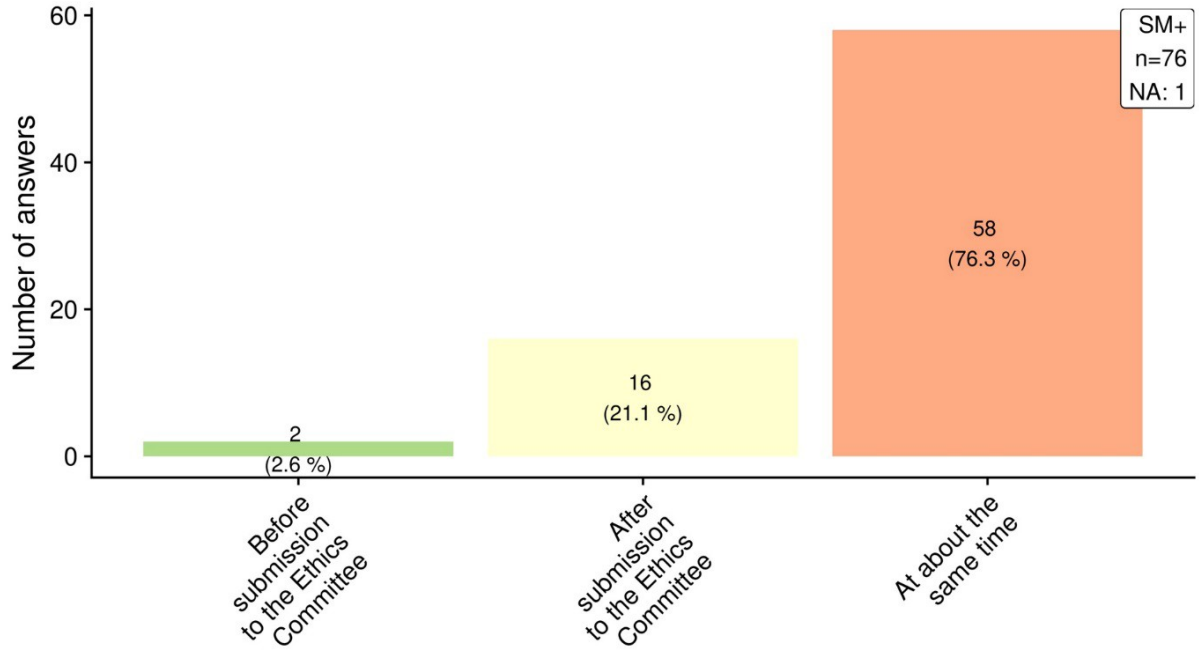


Table 4 - Inconsistencies between Ethics Committee and Swissmedic (B6a)

Inconsistencies with regard to:	**Number of comments**
Risk category	5
Formal requirements, including protocol layout, GCP (good clinical practice) certificates	3
Exclusion criteria for patients	2
Sample size calculation	1
Requests for changes of documents not relevant for approval	1
Total	**12**

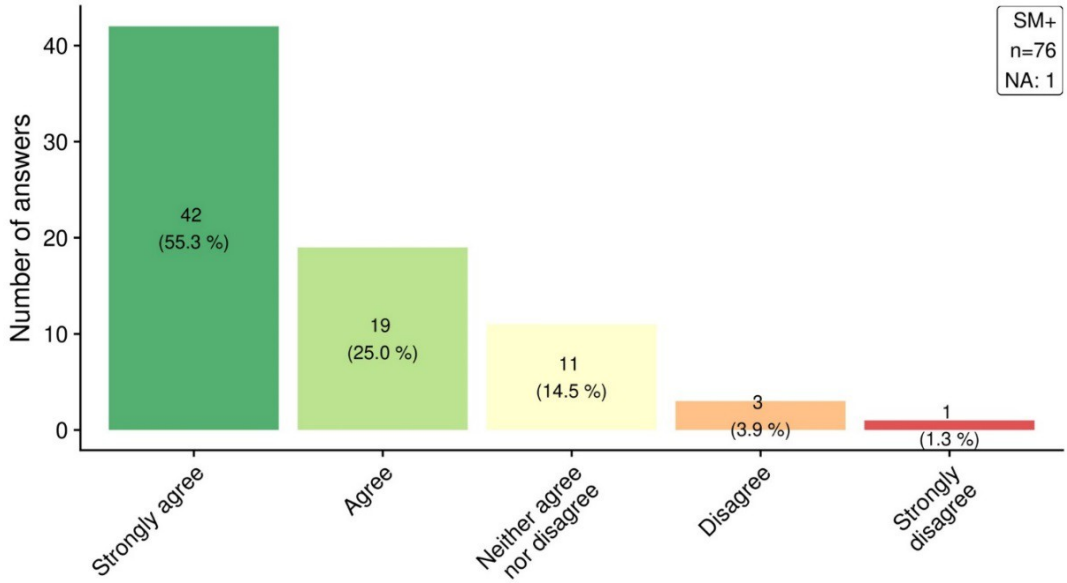
When asked about their timing of submission of the application to Swissmedic (in relation to the submission to the EC), 76% of respondents answered that it was submitted at about the same time (Figure 47).

Figure 47 – Timing of submission to Swissmedic (B7)



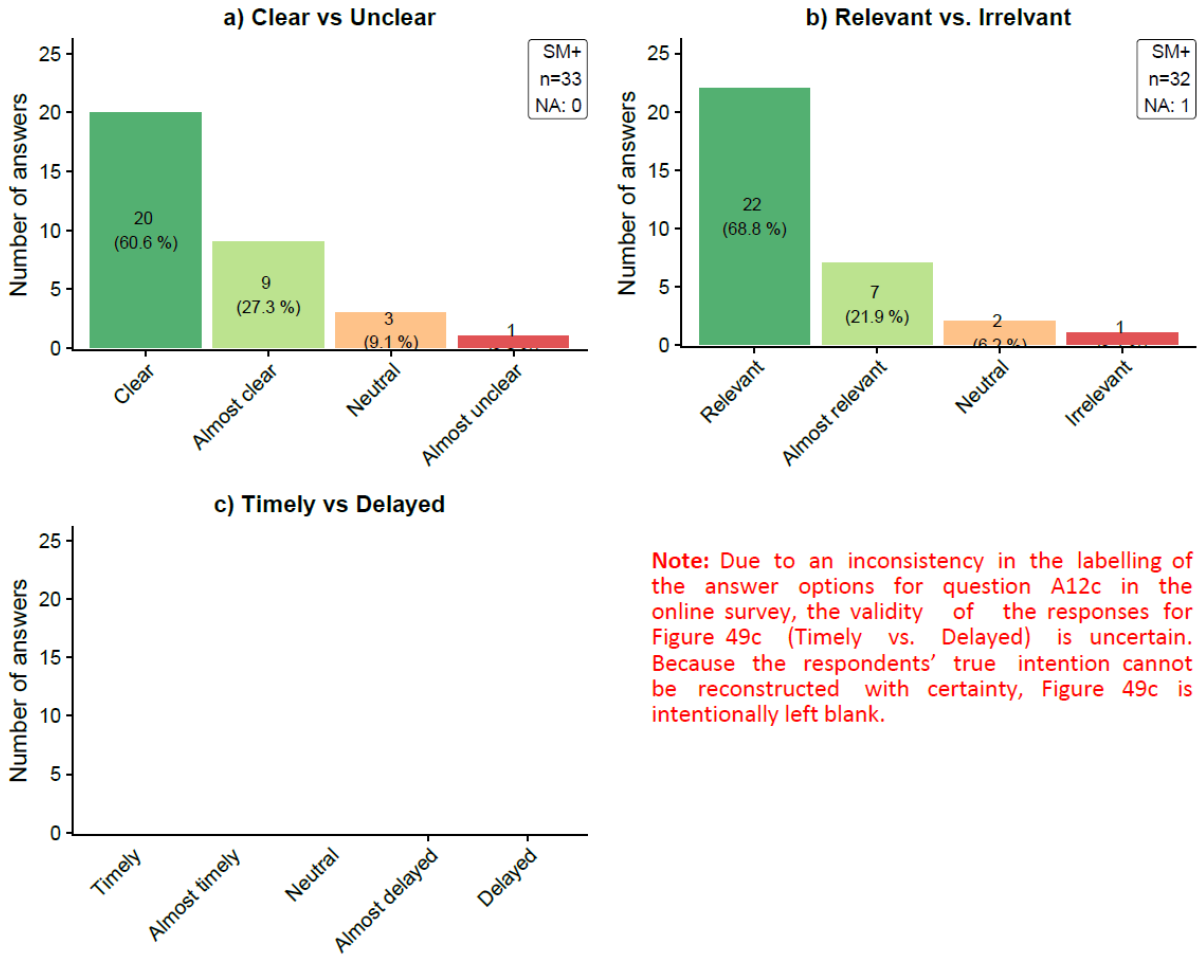
We specifically asked whether researchers thought that parallel submission of applications to both EC and Swissmedic was an advantage. This was agreed or strongly agreed by 80% of respondents (Figure 48).

Figure 48 – Agreement with statement that parallel submission of applications to Ethics Committee and Swissmedic is an advantage (B8)



In Part A of the questionnaire, researchers were asked with regard to three pairs of attributes describing the quality of the responses received by Swissmedic. For two of these pairs, 60% or more deemed that the responses were clear or relevant, respectively (Figure 49a and 49b).

Figure 49 – Quality of responses received by Swissmedic (A12c)

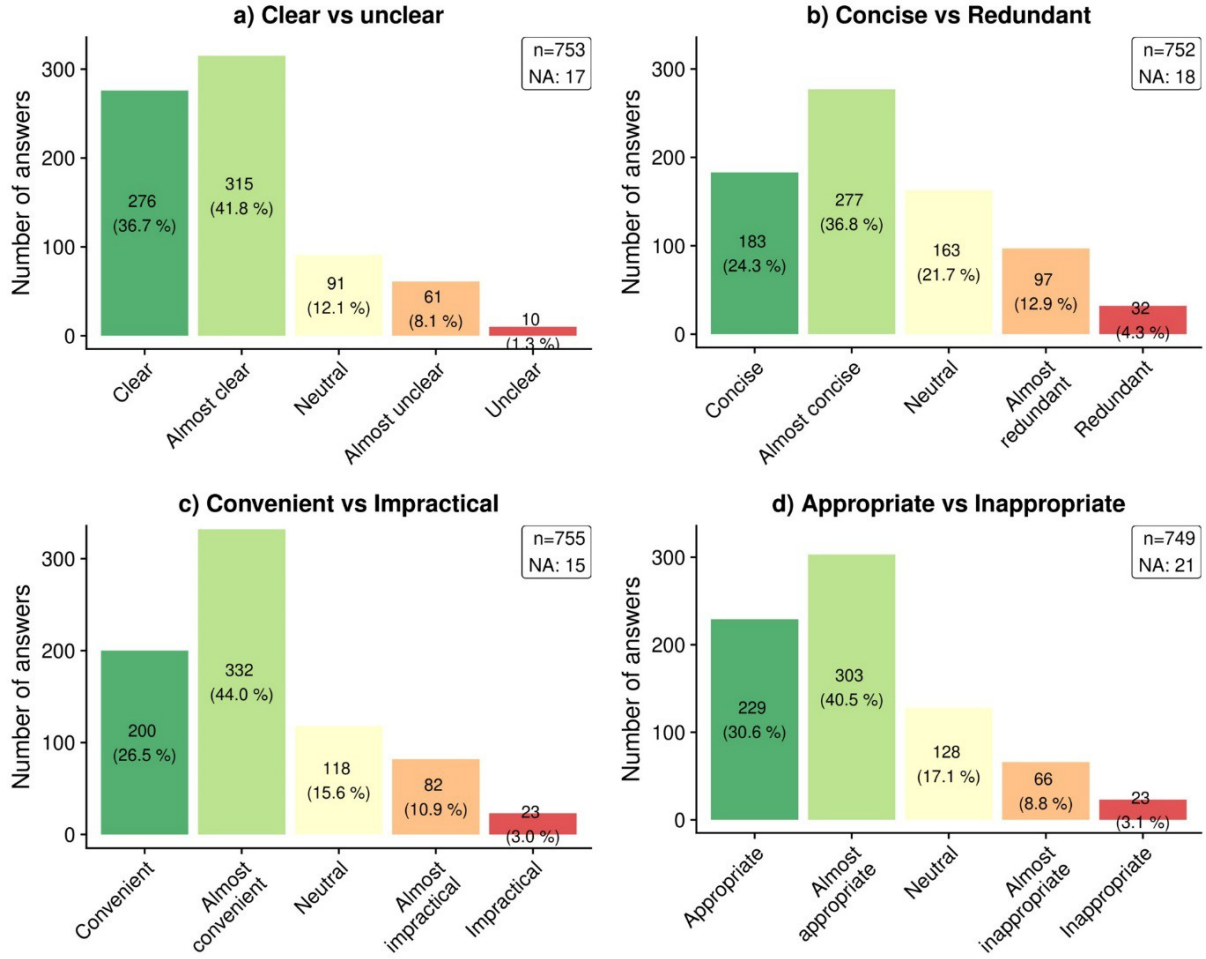


Note: Due to an inconsistency in the labelling of the answer options for question A12c in the online survey, the validity of the responses for Figure 49c (Timely vs. Delayed) is uncertain. Because the respondents' true intention cannot be reconstructed with certainty, Figure 49c is intentionally left blank.

4.5. Experience of researchers with BASEC submission and contact with authorities

We asked researchers to rate four pairs of adjectives that describe the way one may perceive the overall submission process of the project. For each pair, respondents chose one of five adjectives that best described the process (Figure 50).

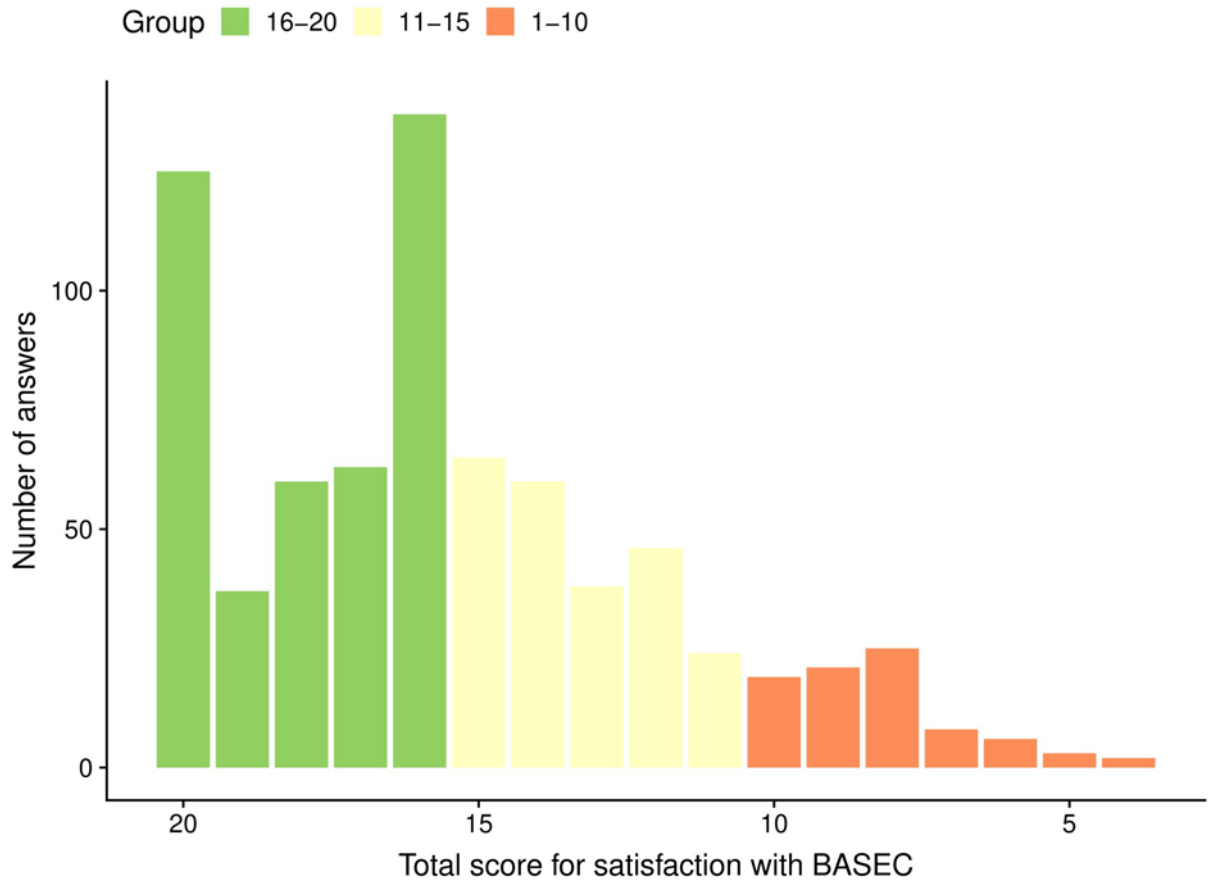
Figure 50 – Overall perception of submission process (A2)



We then constructed a total score as a measure of satisfaction with the BASEC submission process as the sum of scores in response to these four pairs of adjectives. The individual answers were scored from positive to negative attributes (left to right in Figure 50) using values from 5 to 1.

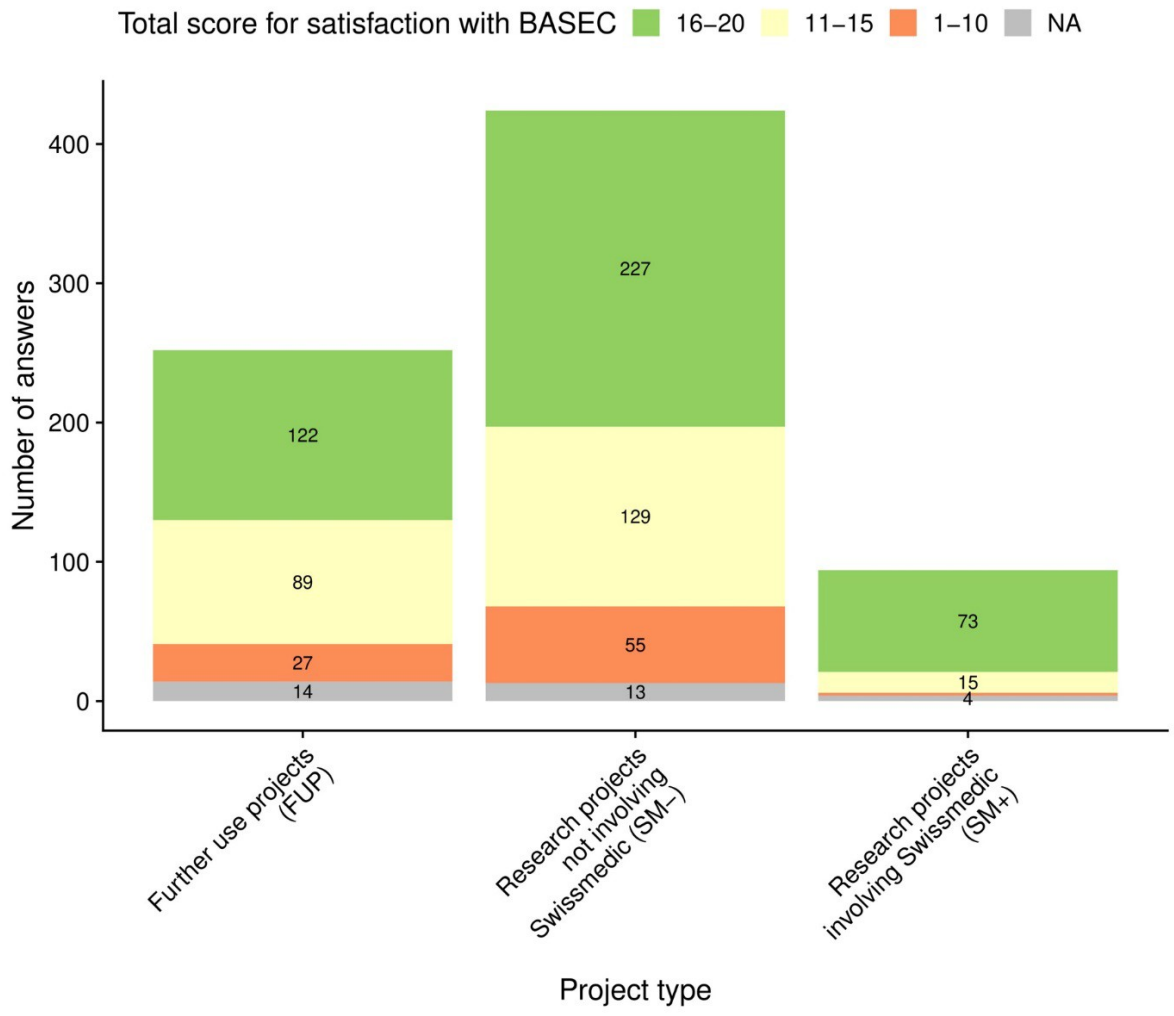
The distribution of sum of scores was left-skewed, which is consistent with a good to medium level of satisfaction (Figure 51). Total score values 16 and 20 were overrepresented, which can be explained by a preference to select score value 4 or 5 for all four pairs of adjectives.

Figure 51 – Summary score of satisfaction with BASEC submission process (A2)



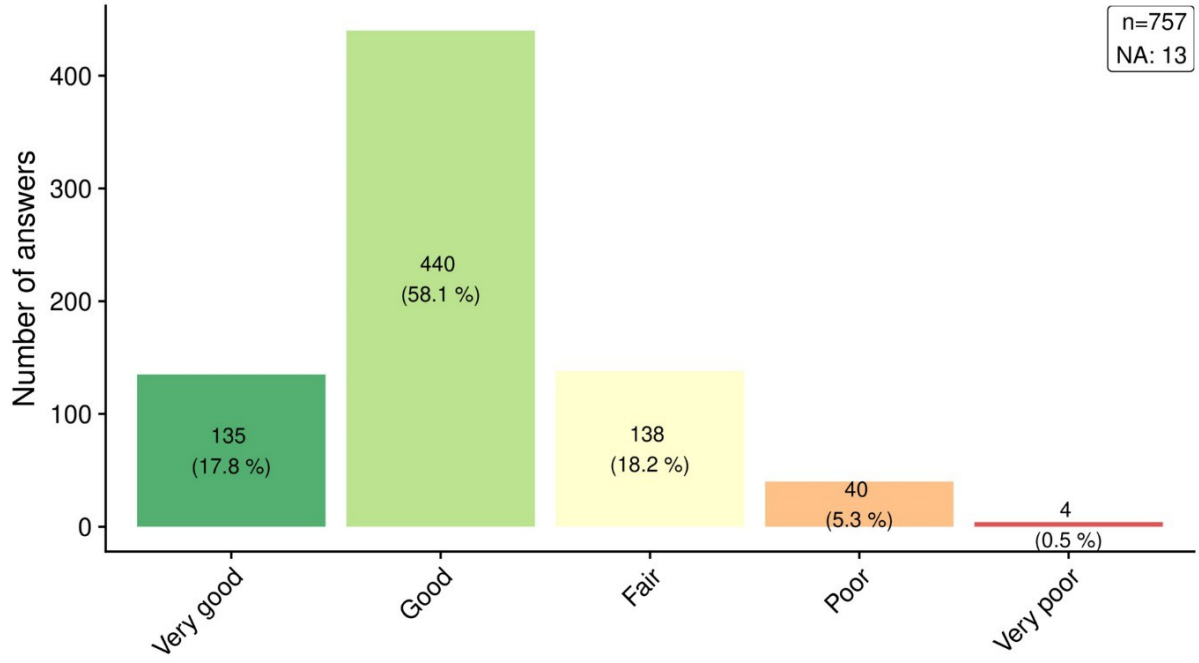
Across the three groups of projects SM+, SM- and FUP the distribution of total score values was slightly different with a larger proportion of scores 16 to 20 for SM+ projects (Figure 52).

Figure 52 – Overall satisfaction by type of study (Full report, p.85)



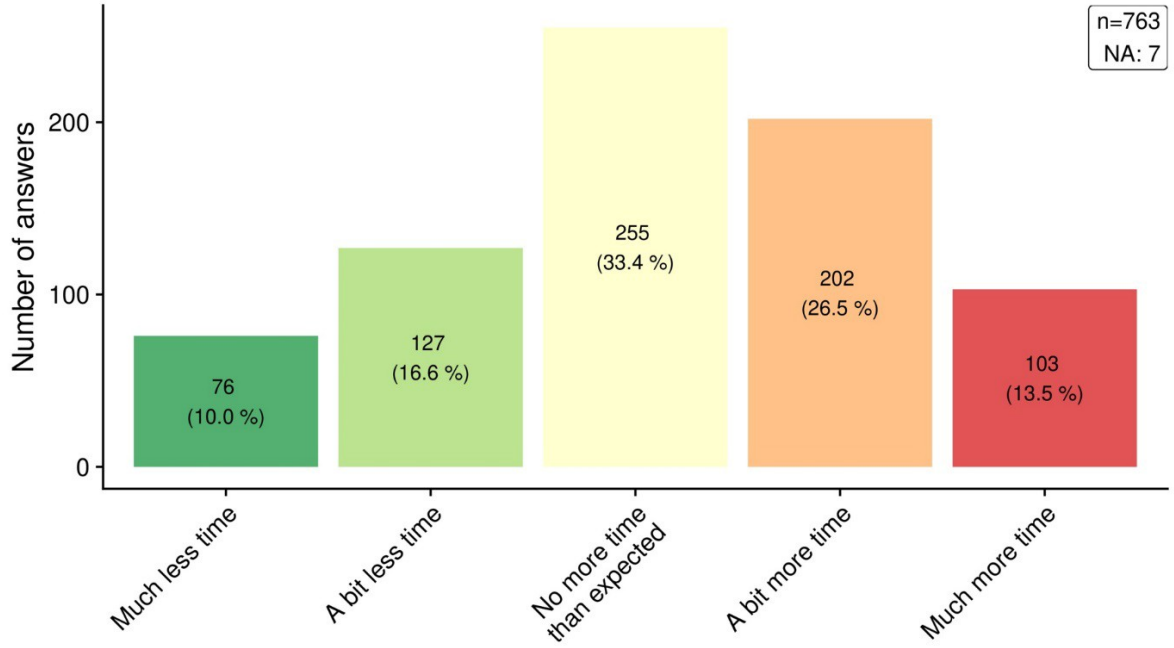
When asked in a single question, 76% of researchers perceived the overall submission process as good or very good (Figure 53).

Figure 53 – Overall quality of submission process (A5)



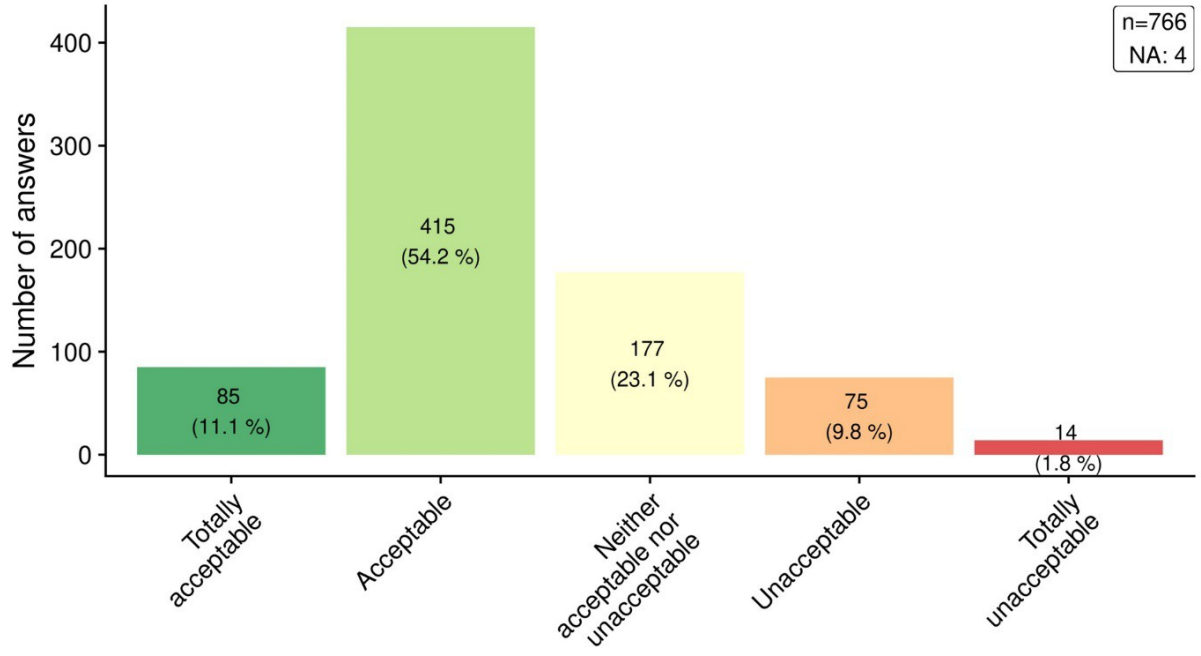
When comparing the expected and actual time to submit study information and documents, 40% of researchers answered that it took them a bit or much more time to complete this task than expected, while 27% responded that it took them a bit or much less time than expected (Figure 54).

Figure 54 – Time needed for submission vs. time expected (A6)



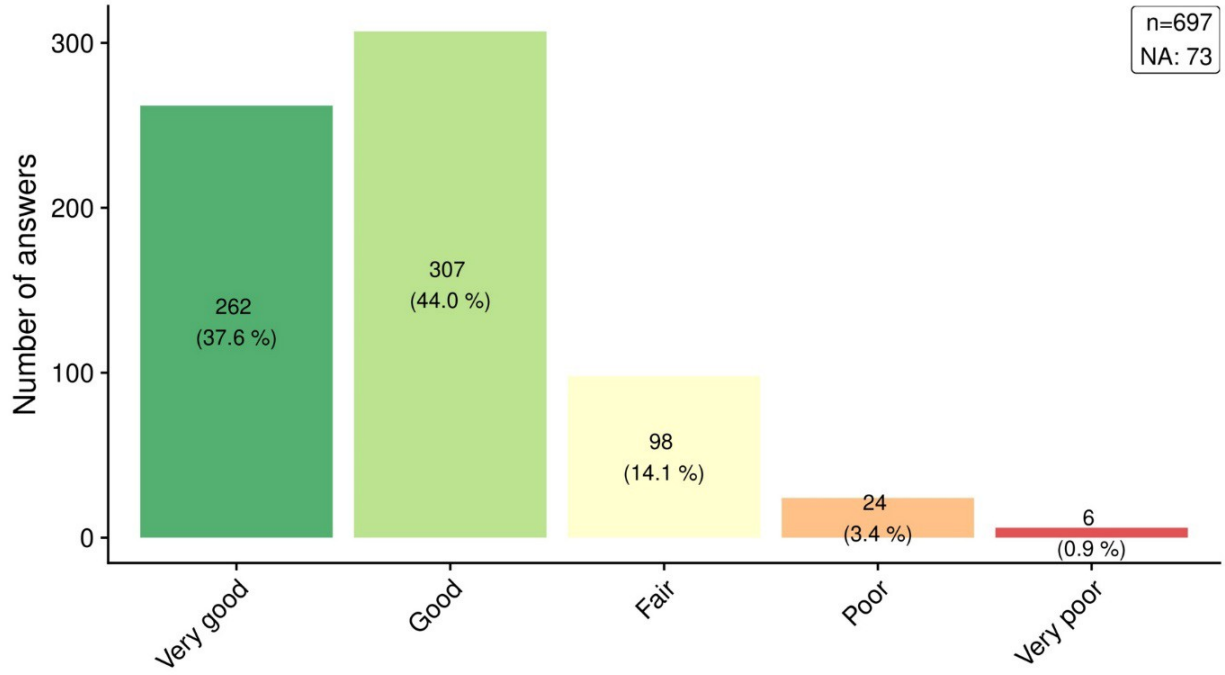
The number of documents that needed to be uploaded was acceptable or totally acceptable for about two thirds of the respondents (Figure 55).

Figure 55 – Number of documents to be submitted (A7)



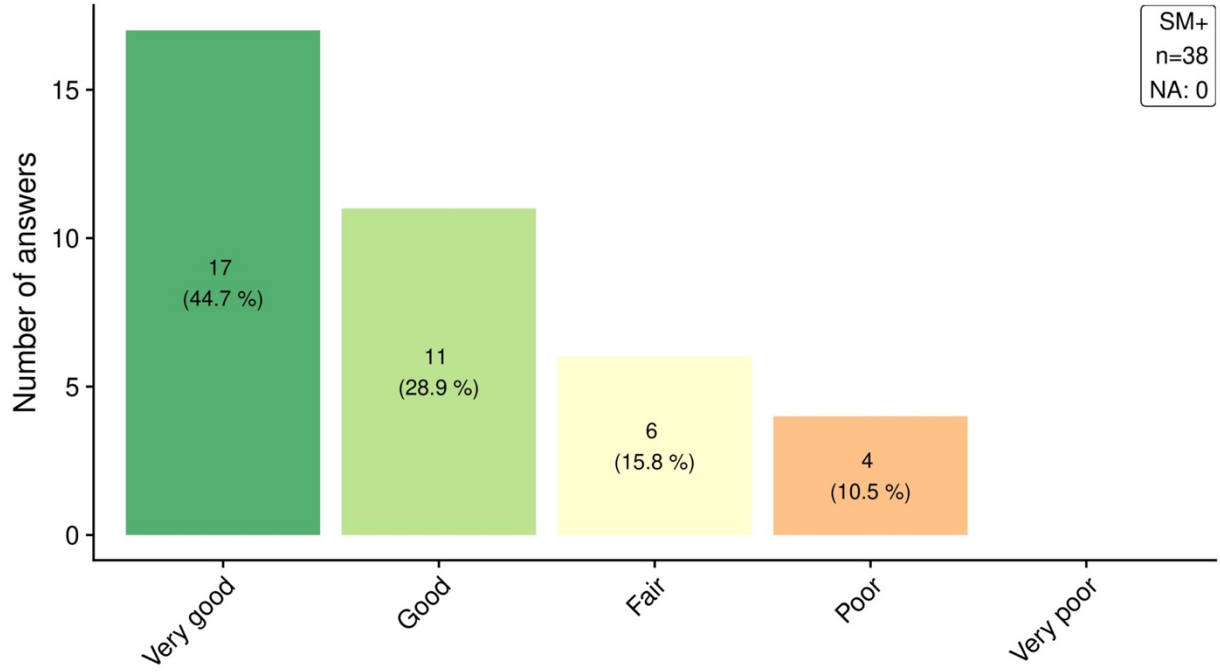
Four out of five researchers rated their contact with the EC as good or very good overall (Figure 56).

Figure 56 –Quality of contact with Ethics Committee (A11)



Also with regard to Swissmedic, most researchers rated their contact as good or very good (Figure 57).

Figure 57 –Quality of contact with Swissmedic (A13)



We asked what aspects were particularly positive or negative with the submission process. Generally, researchers described negative aspects in more detail than positive aspects. One or more positive aspect was mentioned by 457 (59%) of the 770 researchers (Table 5). Four researchers explicitly stated that they had no positive aspect to mention.

Among positive aspects regarding the submission process at the ECs, researchers mentioned the fast and helpful written feedback, as well as the personal contact with the EC. Among positive technical aspects of BASEC, they emphasised the convenience of electronic online submission (including auto-saving, electronic uploading of documents, easy tracking or editing of submitted documents).

"All is in a central place and electronically, no need for paper. System is very convenient."

Respondents mentioned the clear and helpful instructions and templates as well as the user-friendly navigation (including the feature that only applicable questions are shown, that only required templates appear, and that the submission process is step by step).

"Clearly guided through the process of what has to be entered."

"You could save all information on BASEC until submission and editing was easy."

Table 5 - Positive aspects of BASEC submission process (A3)

A	Aspects related to the submission process at the EC:	Number of comments
A.1.	Fast feedback/ review by EC	35
A.2.	Personal contact to EC	29
A.3.	Helpful feedback/ review by EC	11
A.4.	Final approval by EC	3
B	**Technical aspects of BASEC:**	
B.1.	Convenience of electronic/online submission (including autosaving, electronic uploading of documents, easy tracking or editing of submitted documents)	170
B.2.	Clear and helpful instructions and templates	151
B.3.	User-friendly navigation (including that only applicable questions are shown, required templates appear, submission step by step)	94
B.4.	Complete submission through BASEC (e.g. safeguards so that required files or information in fields is not forgotten, only one channel for entire submission)	26
B.5.	"Open box" for comments	8
B.6.	Overall positive (unspecific comment)	4
B.7.	Relevant information in English / multiple language	2
C	**Other aspects:**	
C.1.	None reported	0
	Total	**533***

*461 researchers entered text; of those 457 mentioned positive aspects. 76 mentioned more than one aspect, resulting in a total of 533 aspects.

Comments about negative aspects were made by 410 researchers (53%) (Table 6). Again, four of them explicitly stated that they had none. Regarding the submission process some researchers complained about language issues.

"If you submit a project in English, in the middle of the online submission process you have to change the language and submit some points in the regional language."

Among technical aspects of BASEC, frequent comments were about redundant or exhaustive information that is required during BASEC submission.

"Too many documents, some information had to be given several times."

Researchers recurrently mentioned that for "small" projects exhaustive information was requested during submission, so that the volume of requested information was no longer proportional to the study type.

"The effort in relation to time and content is high. It is not in relation to the size of the project. For example, the effort and time that need to be spent is as high for a single case study as for a huge research project like an RCT. This means that the costs for ethical approval in a single case study are disproportionately high."

This was followed by complaints that instructions concerning the documents required for submission are unclear, that questions or terms are unclear, and that more explanations are needed.

"It was not very clear which documents need to be included. Hence I prepared more documents that were actually needed for the application."

"The questions in the submission form weren't clearly described."

Other recurrent issues were that the system is slow or crashes, that navigation is user-hostile due to difficulties in finding relevant information or required documents, or because it is unclear which parts of forms/documents need to be completed (among other), and that the structure of BASEC does not fit well all types of research, especially non-medical research.

"Not very easy to find needed documents, very loaded."

"It is sometimes hard to fit the project into the structure of BASEC. In particular, that is why we indeed do research with humans - but not from a medical or biological perspective. We only ask participants about their attitudes, emotions etc. The portal however is mainly designed for projects, which do not stem from a humanities domain."

Table 6 - Negative aspects of BASEC submission process (A4)

A	**Aspects related to the legal framework:**	**Number of comments**
A.1.	Law too focused on medical interventional studies, other study types are overregulated and/or templates / BASEC do not match non-medical studies (especially if low risk)	2
A.2.	Legislation gives an advantage to industry because of the amount of paper work and related costs which industry can afford but not an investigator	1
B	**Aspects related to the submission process at the EC:**	
B.1.	Language issues	13
B.2.	Submission too complex overall	8
B.3.	Disagreements with EC about the scientific content	8
B.4.	No emphasis on ethical considerations by EC	8
B.5.	Charges not in relation to scale of submitted study	5
B.6.	Slow feedback/review by EC	4
B.7.	Communication with EC could be improved (e.g. one single person in charge for a specific project at EC)	2
B.8.	Unclear fees	1
B.9.	Request for only one EC for Switzerland	1
B.10.	Different application process than it used to be	1
C	**Technical aspects of BASEC:**	
C.1.	Redundant or exhaustive information had to be given	97
C.2.	Unclear instructions (concerning the required documents), questions or terms, need for explanations	54
C.3.	System is slow or crashes	31
C.4.	User-hostile navigation (including: hidden information/ required documents, ambiguity which parts are to be completed)	30
C.5.	Structure of BASEC does not fit all types of research projects, e.g. non-medical projects	28
C.6.	Issues with uploading of documents	24

C.7.	If submission of a small project, exhaustive information requested	22
C.8.	Time consuming	18
C.9.	Difficulty to define the study type	15
C.10.	Difficult to submit changes after submission (amendments or modifications cannot be submitted separately after submission)	14
C.11.	Word limit too restrictive in some fields	9
C.12.	Issues with multicentre studies (including data entry, submission of research protocol for each site)	6
C.13.	Changing templates over time	6
C.14.	Lack of flexibility in the process	5
C.15.	Lack of feedback when upload was successful	5
C.16.	Layout (bigger font, colour coding)	4
C.17.	Issues with SNCTP registration	4
C.18.	If submission of project of low risk for patients, exhaustive information requested	3
C.19.	Difficulties getting started with submission	3
C.20.	Submitting corrected versions twice, once with track changes, once without	3
C.21.	Overview of submitted projects difficult	2
C.22.	Cover letter	1
C.23.	Lack of notification between multiple submissions concerning the same project	1
C.24.	Mix of online forms and upload of documents	1
C.25.	No data/document sharing possible, only access by the submitting person	1
C.26.	No transfer of data possible from a previous submission	1
C.27.	Sub-studies can only be submitted as new independent project	1
C.28.	Problem if date in BASEC and submitted documents are inconsistent	1
C.29.	Unclear how to name the submitted files	1
D	**Other individual aspects (quotes):**	
D.1.	“Details about secure handling of material and data”	1
D.2.	“If we don't consult regularly the platform, access could be more complicated”	1
D.3.	“I found not very useful to write the project summary in 20 pages as in our cases, it was copy-pasted from the main parts of the whole document.”	1
D.4.	“New fields were added in between the lead EC decision and the reply to it. This was not preannounced. This leads to delay in our process, since we have then to clarify this additional information before we can submit the reply to conditions. If there are changes in the BASEC portal, this should be communicated in advance and a transition period should be in place.”	1
D.5.	“I had to go to the EC to present the project in person. This was a certain loss of productive time in my work.”	1
D.6.	“This Project is part of an international Project that had already been approved by the national EC at the University of Strasbourg, which was not at all facilitating the approval process. In association with the mis-categorisation of the contribution”	1
D.7.	“Need to reformat the protocol to the local context (no possibility of submitting as such the protocol previously approved in France)”	1
D.8.	“The Lead EC decision did not contain all of the submitted participating sites, therefore we had to claim”	1
	Total	**460**

*410 project managers entered text; 4 stated that they had no negative aspect; 3 excluded; 53 mentioned >1 aspect;

4.6. Additional comments by the survey respondents

Respondents made much use of the option to provide additional comments and suggestions in a free-text field at the end of both questionnaire parts. For a tabular overview of comments and suggestions see Appendix 5.

4.6.1. Comments in questionnaire Part A

Of the 770 researchers returning questionnaire Part A, 113 (15%) made an additional comment about the submission process. From aspects related to the legal framework, researchers most frequently mentioned that the law is too focused on medical interventional studies, and that other (non-medical) research is overregulated. Regarding the approval process of the ECs, researchers complained that redundant or exhaustive information had to be provided. They mentioned repeatedly the exhaustive information requested during submission for “small” project (e.g. retrospective study, "data collection studies").

"Some studies especially retrospective ones with no access to biological sample should be processed a lot faster and in an easier way."

A frequent comment regarding technical aspects of submission was the request for only one online platform for both Swissmedic and ECs.

"It would be helpful in the future to have only one electronic portal / submission platform for both, Swissmedic and Ethics Committee (one-stop-shop solution)."

It was often mentioned that the structure of BASEC does not fit all types of research projects, e.g. non-medical projects.

"Templates available on swissethics site are not suitable for nursing research projects."

4.6.2. Comments in questionnaire Part B

Of the 750 researchers returning questionnaire Part B, 69 (9%) used the field for additional comments and suggestions related to the HRA. An additional eight explicitly mentioned that they had no comment or suggestion.

Researchers mentioned here again that, in their view, the law is too focused on medical interventional studies and that other types of research with lower risk are overregulated. BASEC templates were regarded as not matching with the design of these studies.

“Most of our nutrition studies didn’t really fit in the process of the HRA. This complicates studies and leads to wasted time.”

Other recurrent themes were related to the submission process at the EC. Researchers mostly complained about the submission requiring exhaustive information, and being too much paper work, especially, in case of retrospective or “small” studies.

“There should be a simplified and less expensive application process for retrospective data base studies (e.g. two-page summary of the study protocol) and a first decision for these applications should be made within 4 weeks. Even though they might not generate a lot of research funding or even breath-taking new scientific findings, these studies are the backbone of daily science and teaching research in medicine.”

Similar complaints were put forward for studies with low risk.

"It would be nice to have a number of simplified templates and procedures for very low risk clinical investigations. At this stage, getting through ethics takes about 1 year for a student, and this is really hindering the productivity of research. This law and its very meticulous application is making our work really difficult, or almost impossible."

Respondents desired that all Swiss ECs should work on the same standards and procedures or that there should be only one responsible EC in the country. Some researchers seem to struggle with the role of the EC and expressed the opinion that the interpretation of the HRA should not be left to a single authority in charge.

5. Discussion

5.1. Summary of main findings

We invited researchers who submitted applications for ethical approval of their projects in 2017 to an online survey and asked them about their opinion on and experience with the Swiss Federal Act on Research involving Human Beings. About a third responded to either part of the survey questionnaire.

General attitude towards human research legislation: A range of aspects of the current legislation was deemed appropriate by most researchers. However, about 40% affirmed a statement that the HRA hinders scientific research and about two thirds supported the view that many researchers do not know the current legislation very well. About a quarter of the researchers expressed the opinion that the current legal framework was more burdensome than in other countries and another quarter did not; half of them were undecided. Respondents with industry- and investigator-initiated studies differed insofar as those with industry-initiated projects less frequently perceived the Swiss legislation as burdensome. Of the researchers who had been involved in international multi-site studies, about one out of seven affirmed that they had been excluded from projects once or several times. 13% of all respondents had decided to conduct research abroad in the past for various reasons including better availability of participants, lower costs, career options (e.g. fellowships) but also because of the legal and procedural requirements for research in Switzerland.

Compliance with HRA and related ordinances: About half of the researchers mentioned difficulties (to a varying degree) with selected aspects of the HRA when designing and planning their studies. These aspects included the general scope of the HRA, which of the ordinances (ClinO or HRO) was applicable, which chapter of these ordinances precisely, and which of the risk category to choose. ECs or Swissmedic made changes to the type of study in less than 10% of projects, and when they did, researchers mostly agreed with this change. When a change was requested, explanations given by the EC were clear in most cases.

About half of the projects for which the risk classification was changed were in category A and a quarter each in categories B and C. The few researchers who disagreed with changes by the EC mostly had chosen category A in the first place. In general, researchers thought that the EC's requests were mostly justified. About 20% disagreed with requests concerning research methods. More than half of them answered that the EC had given maximum, considerable or at least average weight to a range of domains, and that it had the expertise to do so. Domains in which the ECs' role was perceived as being strong reflected their traditional core competencies such as protection of study participants. However, for each of the domains scientific relevance, choice of inclusion criteria, sufficient funding, suitability of research infrastructure, qualification and experience of project team, and study feasibility 20% or more researchers deemed that ECs had given little or no weight to it. Similarly, 20% or more researchers attributed little or no expertise to the EC for the domains scientific relevance, scientific quality, sufficient funding, suitability of research infrastructure, qualification and experience of project team, and study feasibility.

When those who had prior experience with two or more Swiss ECs were asked whether those committees evaluate projects to a common standard, this was affirmed by 44%, while 19% thought that such standards mostly or largely differed between ECs (37% were undecided). More than 70% of respondents would prefer more standardisation across ECs and almost half favoured a reduced number of ECs with either one per language region or a single committee serving the whole country. A range of 13 specific aspects of the legislation was deemed appropriate, in general. Researchers agreed with four statements describing features of the current risk classification. At least 10% of researchers judged that risk classification is either not straightforward, not appropriate or that projects in category A do not benefit from substantially reduced administrative workload. About 30% of researchers with trials on medicinal products or medical devices answered that the alleviated requirements for liability insurance did only slightly or not at all reduce the administrative workload.

Only 10% of projects (total 77) were subject to approval by Swissmedic and the respondents were asked about their interaction with Swissmedic. Three out of four researchers submitted their application at about the same time when they submitted it to the EC. Most agreed that parallel submission to both authorities was an advantage, and also judged that the responses received by Swissmedic were clear and relevant.

A third of projects (total 248) used biological material or health-related data, predominantly in a university (hospital) setting. Material or data were mostly (81%) from previous projects conducted by the same researchers, and much less so obtained from others in the same institution or from abroad. About half of researchers deemed anonymised material or data as more or equally useful as coded or uncoded material or data, and half of them considered them less useful or not useful at all.

Experience of researchers with BASEC submission and contact with authorities: Among the websites of KOFAM, Swissmedic and swissethics, the latter was used most often prior or during the submission process. Researchers contacted their EC most of the time before submission of the application. Responses by the EC were mostly regarded as clear, relevant and timely. More than half of researchers deemed the submission process using the BASEC portal as clear, concise, convenient and appropriate when asked for each of these domains separately. Results of a constructed overall score indicated that researchers had a good to medium level of satisfaction. Most respondents considered the overall submission process and contacts with either EC or Swissmedic good or very good. However, a recurrent comment was the demand for a single submission portal for both authorities. Researchers complained about the exhaustive information that is requested even when submitting a small-scale study (e.g. with straightforward collection of retrospective data or a simple non-invasive measurement only). They thought that certain types of studies without a medical intervention were overregulated. The BASEC portal was criticised by some for not being adapted to all types of research projects, and “non-medical projects” in particular.

5.2. Strengths and limitations

We made substantial efforts to contact the researchers of eligible projects and to remind them. It must be noted that (i) we asked them to devote substantial time and effort to complete a complex questionnaire in two parts, (ii) that we asked about critical issues such as approval of their studies in a non-anonymised fashion, and (iii) that the survey was in a foreign language for most (if not all) respondents. We used several methodological safeguards including in-built plausibility checks for questions about quantitative data. We consider the achieved response rate of about 35% satisfactory given the above-mentioned challenges. Surveyed projects do not differ from all eligible projects except for a minor difference in the type of research project. We found substantial overlap between researchers completing both parts of the questionnaire. This is not unexpected given that many research projects are rather small single-centre studies with key persons ensuring multiple roles at the same time (e.g. responsible investigators also managing the BASEC submission).

Several persons were contacted for more than one project. In some cases, the information available in the BASEC portal did not allow to identify whether a generic email account was used by several persons or by one single person. In the survey instructions, we advised that the most competent person should

answer the survey. However, our survey methods did not allow us to check individually whether this had been followed. Respondents needed to understand the survey questions and instructions in English but were free to answer in their language in free-text fields. Most did not use this option and wrote comments in English. We asked several non-native English speakers to read and comment on the draft questionnaire during its construction but refrained from a formal pilot phase in a larger sample for time reasons. We are confident that the questions were phrased with sufficient clarity despite their sometimes very complex content. However, data collection in an online survey does not allow checking whether questions were understood correctly. When we analysed the survey results we did not identify any patterns that would suggest that a larger part of respondents misunderstood a question.

5.3. Interpretation and conclusions

A large majority of researchers judged that core aspects were regulated adequately by the HRA and the derived ordinances, and that ECs are competent in fulfilling their role in enforcement. Overall, the results of this survey confirm the appreciation and satisfaction of active researchers with regard to their interaction with the competent authorities (i.e. ECs and Swissmedic) and swissethics. Consequently, substantial changes to the legislation do not seem necessary. Nevertheless, some results and the multiple comments made by the respondents point to areas in which improvements may be warranted. For instance, the requirements for ethical approval of studies other than clinical trials were perceived as overly burdensome and not in relation to the often-limited scale and complexity of such studies. This is likely more relevant for investigator-initiated studies conducted in academic institutions (as compared to industry) because research teams dispose of smaller budgets for their projects and often are unable to build and sustain teams that acquire some routine with application processes. Among researchers who were excluded from international multi-site studies in the past, almost all had submitted an investigator-initiated study in 2017. About one out of seven researchers chose to conduct projects abroad and specifically not in Switzerland in the past. Again, most of them applied for approval of investigator-initiated projects in 2017. This may point to a subgroup of academic researchers who might perceive the conditions of research in humans in Switzerland as less favourable than elsewhere. Our data suggest that the current legal framework may be one factor in such decisions and that other aspects such as higher costs and smaller numbers of available study participants play a role, as well. A more in-depth analysis may be warranted to find out who exactly is affected and whether measures need to be taken to improve the conditions for research in humans in Switzerland without compromising the protection of research participants.

The respondents commented on differences in the processes between ECs. Most of them would like to see more standardisation. Although it remains unclear how such differences impact on the research practice, we think that transparently aligned processes across ECs would further increase the trust of researchers in the current Swiss regulation. Of note, almost half of the respondents were in favour of two models with a single EC for either a language region or the whole country. Most researchers relied on online resources such as the swissethics website for information prior to or during submission of projects for ethical approval. Currently, researchers need to consult several platforms for relevant information, forms or templates (in particular if approval by Swissmedic is needed) and this likely adds to the perceived complexity of processes, in particular for small-scale projects. Researchers were generally satisfied with the BASEC submission portal but complained about the amount of information that had to be entered and perceived redundancies. It might be helpful if the current set of required items in BASEC was revisited and carefully checked at regular intervals. We assume that most researchers would welcome if any existing redundancies could be reduced and the overall processes be simplified even more.

To our knowledge, this survey is one of the most comprehensive studies about the regulatory environment of research on human beings in Switzerland. We are confident that its results will be informative in any efforts to improve the current implementation of the legal framework as defined by the HRA and derived ordinances. Any such improvements are likely to strengthen the country's profile as a place for competitive high-quality health research.

6. Acknowledgements

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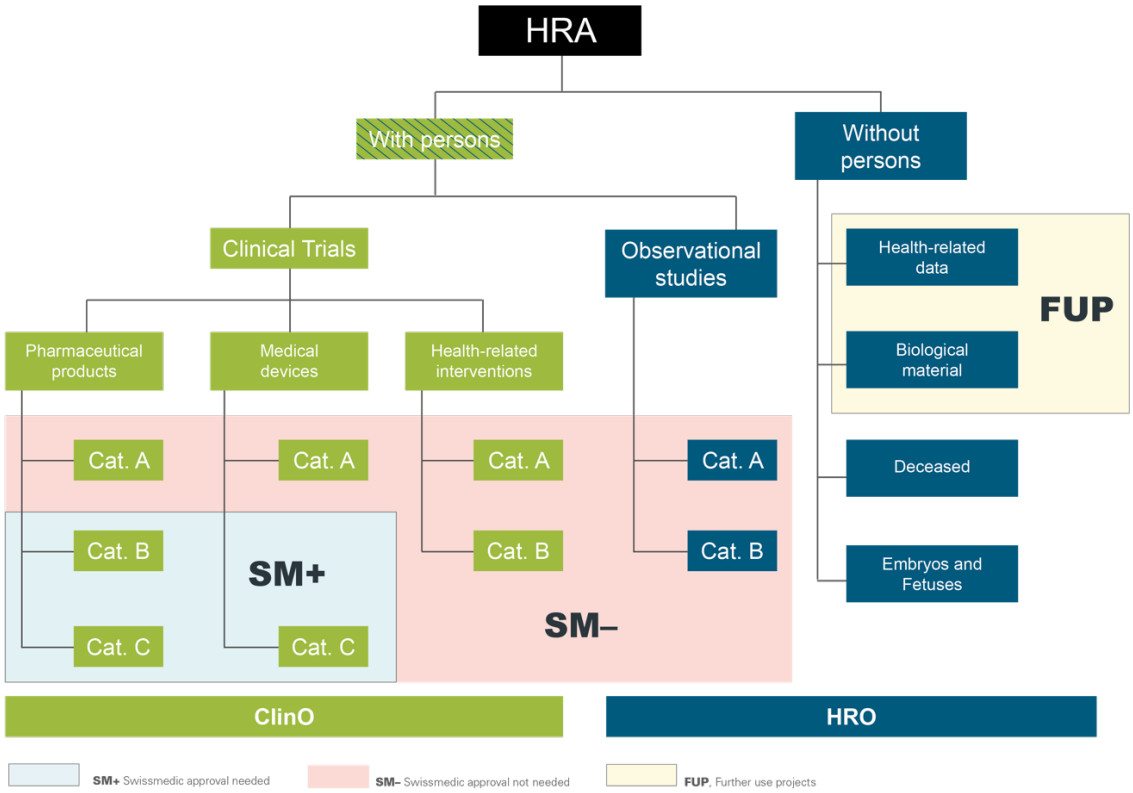
Finally, we are grateful to the Swiss researchers and study collaborators who participated in our survey or helped along so that questionnaires were filled in by the most knowledgeable person.

Appendices

1. Questionnaire Part A and B

See separate document.

2. Overview of types of studies according to HRA and its ordinances



ClinO = Clincial Trials Ordinance, chapters 2-4; HRO = Human Research Ordinance, chapters 2 and 3

3. Full report of survey results

See separate document.

4. Generalisability of survey results – comparison of eligible and respondent projects

	Eligible projects submitted in 2017	Respondent projects	
		Questionnaire Part A	Questionnaire Part B
Number	2275*	768	748
Type of research project (%)			
Clinical trial (ClinO)	541 (23.8)	204 (26.6)	177 (23.7)
Further use (HRO chapter 3)	879 (38.6)	252 (32.8)	248 (33.2)
Research with persons (HRO chapter 2)	826 (36.3)	312 (40.6)	323 (43.2)
Deceased, embryos (HRO chapters 4 and 5)	29 (1.3)	0 (0.0)	0 (0.0)
Type of clinical trial (%)			
Medicinal products (ClinO chapter 2)	203 (37.5)	81 (39.7)	64 (36.2)
Medical devices (ClinO chapter 2)	140 (25.9)	47 (23.0)	49 (27.7)
"Other clinical trials" (ClinO chapter 4)	181 (33.5)	71 (34.8)	61 (34.5)
Combination of drugs & devices (not defined in ClinO)	6 (1.1)	2 (1.0)	1 (0.6)
Transplant products (ClinO chapter 2)	8 (1.5)	2 (1.0)	1 (0.6)
Gene therapy (ClinO chapter 2)	2 (0.4)	0 (0.0)	1 (0.6)
Transplantation (ClinO chapter 3)	1 (0.2)	1 (0.5)	0 (0.0)
Risk category (%)			
A	1080 (79.0)	402 (77.9)	408 (81.6)
B	91 (6.7)	43 (8.3)	33 (6.6)
C	196 (14.3)	71 (13.8)	59 (11.8)
Investigator-initiated project (%)	2003 (88.0)	669 (87.1)	664 (88.8)
Design (%)			
Mono-centre	1671 (73.5)	561 (73.0)	566 (75.7)
Multi-centre (CH)	126 (5.5)	43 (5.6)	44 (5.9)
Multi-centre (intl.)	478 (21.0)	164 (21.4)	138 (18.4)
Leading EC (%)			
KEK-ZH	613 (26.9)	197 (25.7)	186 (24.9)
EKNZ	455 (20.0)	145 (18.9)	140 (18.7)
CER-VD	398 (17.5)	138 (18.0)	150 (20.1)
KEK-BE	356 (15.6)	123 (16.0)	121 (16.2)
CCER	269 (11.8)	93 (12.1)	82 (11.0)
EKOS	99 (4.4)	37 (4.8)	31 (4.1)
CE-TI	85 (3.7)	35 (4.6)	38 (5.1)
Approval (%)			
Ordinary	400 (18.0)	159 (21.1)	140 (19.1)
Simplified	1537 (69.3)	502 (66.5)	506 (68.9)
Presidential	282 (12.7)	94 (12.5)	88 (12.0)

*Includes 29 projects with deceased, embryos of foetuses and 59 projects with wrong email addresses that were excluded from the survey

5. Additional comments and suggestions about the application process

This table is based on the free-text answers that are documented in the Full Report of Survey Results in Appendix iv (p.145) and in Appendix vi (p.163).

	Additional comments	**Part A (project managers)**	**Part B (investi-gators)**
A	**Aspects related to the legal framework:**		
A.1.	Law too much focused on medical interventional studies; other study types are overregulated and/or templates/portal do not match with non-medical studies	11	11
A.2.	Too strict in general, too many regulations including the ordinances		2
A.3.	Legislation gives an advantage to industry because of the amount of paper work and related costs which industry can afford but not an investigator		2
A.4.	Some kind of "passive consent" should be possible in some studies (e.g. in schools (Informed consent may lead to selective participation)		2
A.5.	Data protection regulations are too strict		1
A.6.	Training regarding the HRA at the university level and submission support service		1
A.7.	General request to "reform" the HRA		1
A.8.	Unrealistic obligation to obtain informed consent for retrospective studies		1
A.9.	The mandatory usage of CE-certified diagnostic tests is too strict		1
A.10.	Non-certified devices and the risk classification should be revised		1
A.11.	Overregulation studies using already collected data or biological material		1
B	**Aspects related to the process at the EC:**		
B.1.	If submission of a 'small' project (e.g. retrospective study, "data collection study") exhaustive information is requested	13	14
B.2.	Redundant or exhaustive information had to be given/ too much paper work	9	
B.3.	Inconsistencies between ECs; all EC should work on the same standards and procedures; different application of Art. 34 among ECs; it should be clear whether final contracts should be submitted through BASEC	3	6
B.4.	Personal contact to EC was helpful	7	
B.5.	Information requested during submission too exhaustive for studies with low risk for patients		6
B.6.	Participating ECs not clear	6	
B.7.	Problem that the EC seem to be the only authority to interpret the HRA, interpretation of the HRA by the EC too strict	2	4
B.8.	Unclear fees or costs of the submission	3	1
B.9.	Too expensive	3	
B.10.	Formal things more important than content/patients	1	2
B.11.	No emphasis on ethical considerations	2	1

B.12.	Overall positive	3	
B.13.	Overall too time-consuming	2	1
B.14.	Exhaustive information requested for research in vulnerable persons	1	1
B.15.	Request for only one EC for Switzerland		2
B.16.	Clear and helpful instructions	2	
B.17.	Overall too complex	2	
B.18.	Submission difficult when interdisciplinary research	1	
B.19.	Role of the EC should be better explained to investigators		1
B.20.	Inconsistency between Swissmedic and EC	1	
B.21.	Outcome of the jurisdictional inquiry (i.e. submission for ethical approval required) was different from the outcome of the actual submission (not HRA relevant)		1
B.22.	Authorisation by Swissmedic requires a lot of work		1
B.23.	Helpful feedback/ review by the EC	1	
B.24.	Slow feedback/review of EC	1	
B.25.	Communication issues	1	
B.26	Since the reform of 2014 ethical boards in Switzerland have become more professional		1
B.27	More gender-balanced composition of the committees		1
B.28.	Disagreements with EC about the scientific content		1
C	**Technical aspects of BASEC:**		
C.1.	Request for only one online submission platform both for Swissmedic and EC	10	2
C.2.	Convenience of electronic/online submission	6	
C.3.	System is slow or crashes	4	
C.4.	Difficult to submit changes after submission (amendments or modifications cannot be submitted separately after submission)	3	1
C.5.	Unclear instructions (concerning the required documents), questions or terms, need for explanations	3	
C.6.	Adding or changing date/ version number to every document (not only the changed documents) is very time consuming	3	
C.7.	Layout could be improved	3	
C.8.	Language issues	3	
C.9.	Illogical answers can be given in BASEC		2
C.10.	Difficulty to define the study type		2
C.11.	User-hostile navigation	2	
C.12.	Uploading issues	2	
C.13.	Overview of submitted projects difficult	2	
C.14.	Templates should contain in each chapter the link to the necessary information		1
C.15.	Full document titles not visible	1	
C.16.	Lacking feedback system of successful uploading	1	
C.17.	Access to BASEC after approval by the sponsor should be possible	1	

C.18.	Less work because no synopsis required anymore	1	
C.19.	More templates should be provided, e.g. recruitment advertisement, consent forms	1	
C.20.	Registration section was confusing	1	
C.21.	Upload of SAE should be possible anytime*	1	
C.22.	Full document title not visible	1	
C.23.	In case of digital data collection, the need to submit to different ethics committees and pay fees individually is burdensome		1
C.24.	"The new General Data Protection Regulation (GDPR) should be implemented in the templates of the Patient information"*		1
C.25.	Informed consent template for studies including already collected biological material or patient data is too complicated for patients		1
C.26.	Protocol templates for non-clinical trials should be available also in English*		1
C.27.	Submission process should be more interactive including face to face meetings with the researchers		1
D	**Other specific aspects:**		
D.1.	Survey is useful for research community, result should be discussed at a conference		1
D.2.	“We are not responsible for Swissmedic Submission, only EC, so all Swissmedic questions don't apply for us”	1	
D.3.	"Swissmedic was not helpful"	1	
D.4.	“We were asked to keep the identification list for the small qualitative study for 10 years, which does not make any sense in my view. There will not be any need to return to the list for identification of a patient. I think that the EC should not apply the HRA "by the letter" but consider what makes or does not make sense.”	1	
D.5.	“Due to a change in the BASEC Portal beginning of the year I had to enter additional information and documents although the trial was already approved. As I did not expect that, I was not prepared and the submission of an amendment needed to be postponed as I had to collect the new documents before.”	1	
D.6.	"The trial is not yet initially approved due to study design."	1	
D.7.	“It was difficult to understand why the first submission was not good enough. We had a special project and for us it was so difficult to explain this project in order to not have misunderstanding with the commission. When I did the course GCP (after the acceptance of the project), I understood a lot about what I had to do during the submission. Now, I think for the future project it would be simpler and surely I would contact the CTU to ask their professional opinion.”	1	
	Total	**138**	**79**

128 project managers entered text in the free-text comment field; 7 stated that they had no comment; for 1 comment no category was found; 18 researchers mentioned more than one aspect in their comment for a total 138 aspects. 77 researchers entered text in the free-text comment field; 8 stated that they had no comment. 10 mentioned more than one aspect in their comment for a total of 79 aspects.

*addressed by a change that was already made in the BASEC system