Appendix 1: Invitation to complete the online questionnaire and reminder

Dear Sir/Madam XX,

My name is Julia Menon, and I am a research assistant. I'm currently performing a case study, on behalf of ZonMw, regarding their funding program "Meer Kennis met Minder Dieren (MKMD)".

ZonMw aims to evaluate the impact of performing synthesis of evidence / systematic reviews of animal studies (and preclinical studies) on researchers and their research.

In this context, we are approaching all researchers who performed or are performing systematic reviews with ZonMw funding and/or coaching.

Therefore, we kindly invite you to fill out an online questionnaire. We would be very grateful if you could take the time to participate.

The questionnaire should take about **15 min** only and can be found at the following link: https://www.questionpro.com/t/AQwH0ZiBJV
Please, fill the questionnaire online **before the 8th of August**.

All your information will be kept anonymous and confidential. The only purpose of this analysis will be to produce an internal report for ZonMw.

If you need any extra information, feel free to contact me at this e-mail or at the following email: Erica van Oort (ZonMw) at mkmd@zonmw.nl

Thanking you in advance,

Yours Sincerely,

Julia Menon

Reminder

Dear Sir/Madam XX

You were sent an invitation 2 weeks ago to participate in a questionnaire, with the aim to evaluate the impact of ZonMw's program on performing synthesis of evidence / systematic reviews on researchers and their research. We understand that you may be busy or unavailable due to summer plans, therefore this kind reminder. We sincerely hope you can participate during the summer season.

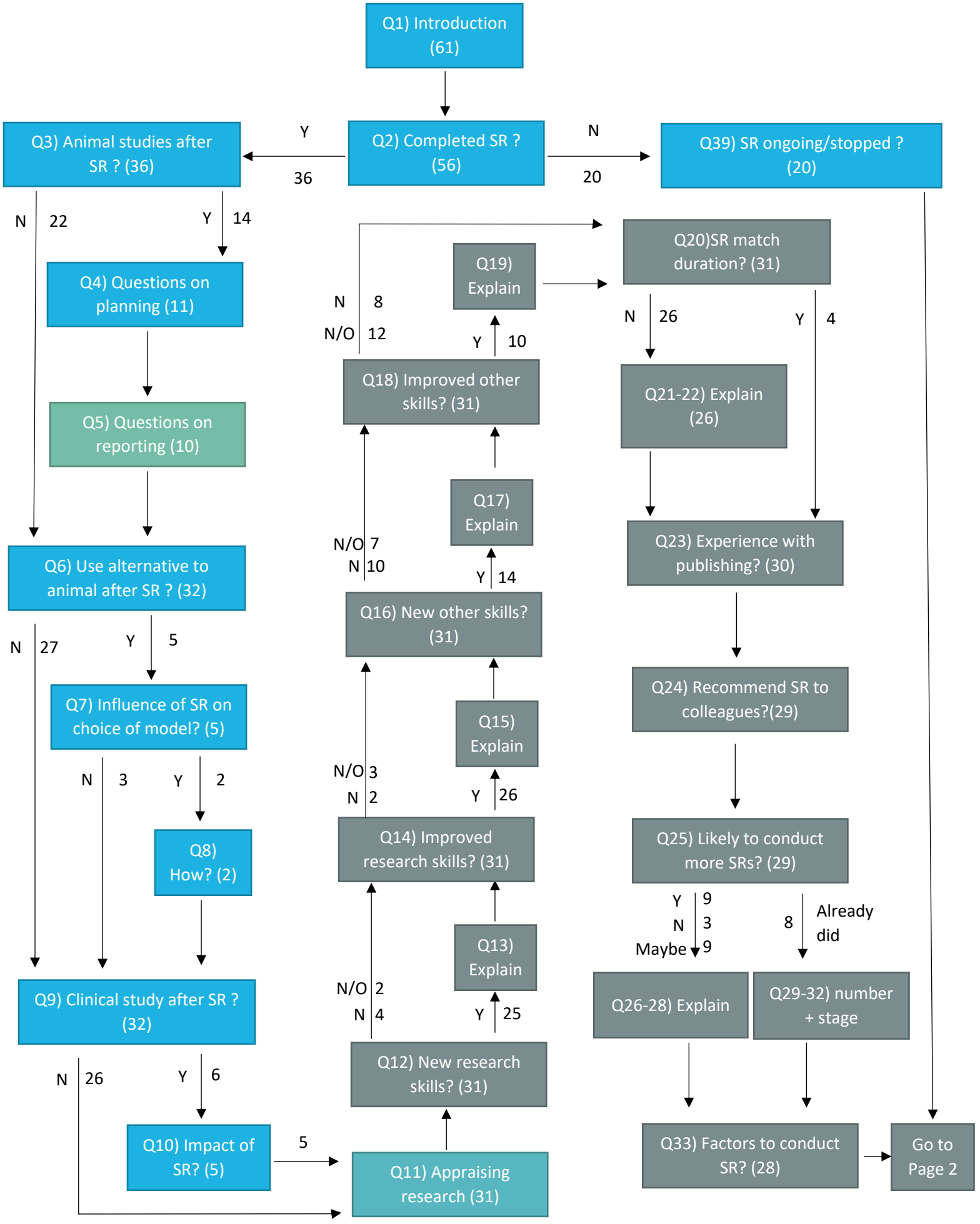
If you need any extra information, feel free to contact me at this e-mail or at the following emails: Erica van Oort at mkmd@zonmw.nl

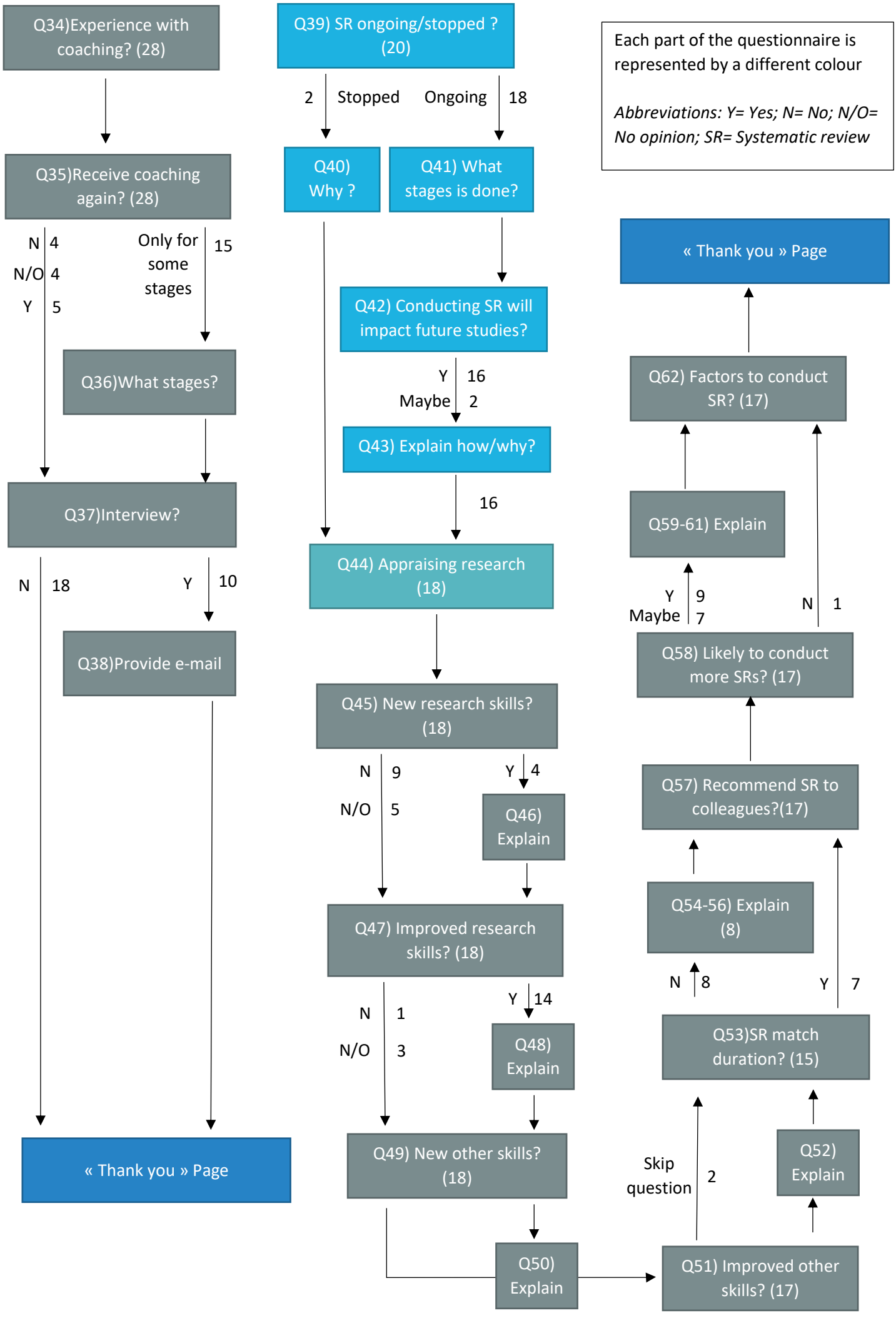
Thank you in advance for your time,

Yours Sincerely,

Julia Menon

Appendix 2: Organisation of the questionnaire and number of respondents per questions




Q34)Experience with coaching? (28)
Q35)Receive coaching again? (28)
N 4
N/O 4
Y 5
Only for some stages 15
Q36)What stages?
Q37)Interview?
N 18
Y 10
Q38)Provide e-mail
« Thank you » Page
Q39) SR ongoing/stopped ? (20)
2 Stopped
Ongoing 18
Q40) Why ?
Q41) What stages is done?
Q42) Conducting SR will impact future studies?
Y 16
Maybe 2
Q43) Explain how/why?
16
Q44) Appraising research (18)
Q45) New research skills? (18)
N 9
N/O 5
Y 4
Q46) Explain
Q47) Improved research skills? (18)
N 1
N/O 3
Y 14
Q48) Explain
Q49) New other skills? (18)
Q50) Explain
Q51) Improved other skills? (17)
Skip question 2
Q52) Explain
Q53)SR match duration? (15)
N 8
Y 7
Q54-56) Explain (8)
Q57) Recommend SR to colleagues?(17)
Q58) Likely to conduct more SRs? (17)
Y 9
Maybe 7
N 1
Q59-61) Explain
Q62) Factors to conduct SR? (17)
« Thank you » Page
Each part of the questionnaire is represented by a different colour
Abbreviations: Y= Yes; N= No; N/O= No opinion; SR= Systematic review

Appendix 3: Paper version of the questionnaire

Dear researcher who received funding from ZonMw to conduct a systematic review,

You are invited to participate in our questionnaire, which aims to gather information for a case study report on the ZonMw funding program, "Meer Kennis met Minder Dieren (MKMD)". It should take about 15 minutes to complete.

The main topic of the study is to evaluate the **impacts of performing a systematic review of preclinical studies**. It aims to assess both **impacts on research** (e.g. methods and models used after performing a systematic review) and **impacts on the researcher** (e.g. point of view, behaviour in research such as reporting, writing, research appraisal after completing the review).
Therefore, you will be asked several questions about your opinions and behaviour after performing your systematic review, such as designing and planning experiments, writing papers, appraising research and your personal experiences with performing a systematic review.

Do not worry if you have not finished your systematic review as yet or if it stopped ! Your input is still highly valuable feedback.

Your participation in this study is completely voluntary. If you feel uncomfortable answering any questions, you can withdraw from the survey at any point. Additionally, all your information will be kept anonymous and confidential, as this research follows and complies with the data protection act of 2018 and is solely for internal use within ZonMw.

We kindly thank you for your participation and your time!
Please start with the questionnaire now by clicking on the "Next" button below.

Introductory question

Have you completed a systematic review of preclinical studies? (*)

Yes ☐ No ☐

Have you performed primary animal experiments after conducting your systematic review?

Yes ☐ No ☐

----------Page Break----------

Designing and planning experiments

The following section focuses on your research projects during or after completing the preclinical systematic review. Questions are centred around the topics you addressed, the way you planned your experiments and methods and models you chose.

Please choose the answer that best fits the following statements: (*)

Conducting a systematic review had an impact on…	*Completely Disagree*	*Mostly Disagree*	*Slightly Disagree*	*Neither disagree nor agree*	*Slightly Agree*	*Mostly Agree*	*Completely Agree*
The topics I addressed in (future) research	☐	☐	☐	☐	☐	☐	☐
The use of a planning guideline, e.g. PREPARE, for my following research	☐	☐	☐	☐	☐	☐	☐
The time allocated for planning my following research	☐	☐	☐	☐	☐	☐	☐
The procedure I used for planning my following research	☐	☐	☐	☐	☐	☐	☐
The animal modelI chose inmy following research	☐	☐	☐	☐	☐	☐	☐
The intervention I chose in my following research	☐	☐	☐	☐	☐	☐	☐
The use of blinding inmy following experiments	☐	☐	☐	☐	☐	☐	☐
The use of randomization in my following experiments	☐	☐	☐	☐	☐	☐	☐
The use of power calculation in my following experiments	☐	☐	☐	☐	☐	☐	☐
Other experimental design aspects you chose inmy following experiments	☐	☐	☐	☐	☐	☐	☐
Avoiding duplication of (part of) the investigation	☐	☐	☐	☐	☐	☐	☐

If applicable, for the questions you answered with “mostly agree” or completely agree” could you briefly explain your answers?

----------Page Break----------

Writing manuscripts

The following section will focus on the primary study papers you wrote and their content after completing your preclinical systematic review.

Please choose the answer that best fits the following statements: (*)

When writing subsequent papers, conducting a systematic review had an impact on…	*Completely Disagree*	*Mostly Disagree*	*Slightly Disagree*	*Neither disagree nor agree*	*Slightly Agree*	*Mostly Agree*	*Completely Agree*
My use of reporting guideline, e.g. ARRIVE	☐	☐	☐	☐	☐	☐	☐

Reporting an ethical statement	☐	☐	☐	☐	☐	☐	☐
Reporting a justification for the chosen animal model							
Reporting my animal model provider	☐	☐	☐	☐	☐	☐	☐
Reporting housing conditions	☐	☐	☐	☐	☐	☐	☐
Reporting my animal model characteristics (e.g. species, sex, weight)	☐	☐	☐	☐	☐	☐	☐
Reporting of randomization	☐	☐	☐	☐	☐	☐	☐
Reporting of blinding	☐	☐	☐	☐	☐	☐	☐
Reporting of a power calculation/sample size calculation	☐	☐	☐	☐	☐	☐	☐
Publishing in an open access journal	☐	☐	☐	☐	☐	☐	☐
If applicable, publishing negative data	☐	☐	☐	☐	☐	☐	☐

----------Page Break----------

Have you performed preclinical research with alternatives to animal models after conducting your systematic review?

Yes ☐ No ☐

If "yes": did your systematic review influence your choice to use an alternative model?

Yes ☐ No ☐

If "yes": please explain **how** your systematic review influenced your choice of model?

Have you performed clinical research after conducting your systematic review?

Yes ☐ No ☐

If "yes" how did the SR impact your clinical research?

Appraising research

The following section focuses on the way you appraise research after performing a preclinical systematic review.

Please choose the answer that best fits the following statements: (*)

When appraising research papers, conducting a systematic review had an impact on…	*Completely Disagree*	*Mostly Disagree*	*Slightly Disagree*	*Neither disagree nor agree*	*Slightly Agree*	*Mostly Agree*	*Completely Agree*
Your critical sense when reading research papers	☐	☐	☐	☐	☐	☐	☐
Your critical sense towards peers' research	☐	☐	☐	☐	☐	☐	☐
Your critical sense toward your own previous research	☐	☐	☐	☐	☐	☐	☐
The way you appraise the overall research quality in your field	☐	☐	☐	☐	☐	☐	☐

----------Page Break----------

Your skills after conducting the preclinical systematic review

The following section focuses on skills you may have acquired by conducting your preclinical systematic review.

Did you **learn** new research skills by conducting the systematic review? (*)

Yes ☐ No ☐ No opinion ☐

If yes, what new research skills did you learn?

Did you **improve** your existing research skills by conducting the systematic review? (*)

Yes ☐ No☐ No opinion☐

If yes: what research skills did you improve?

Did you **learn** new skills beyond research skills by conducting the systematic review? (*)

Yes ☐ No ☐ No opinion ☐

If yes: what new skills did you learn?

Did you **improve** existing skills beyond research skills by conducting the systematic review? (*)

Yes ☐ No ☐ No opinion☐

If yes: what skills did you improve?

Your experience with conducting a preclinical systematic review

The following section focuses on your personal experience of performing a preclinical systematic review. It addresses questions about your experience with the coaching, your personal opinion and future perspectives.

Conducting and publishing the review

Please choose the answer that best fits the following questions:

Did completing the review match your expectations in term of duration? (*)

Yes ☐ No, it was longer ☐ No, it was shorter ☐

If "No": Can you please state how much (how many weeks) longer or shorter?

Which stages of the systematic review went slower or faster than expected? (multiple answers can be picked)

☐ Writing protocol

☐ Searching for all the evidence

☐ Study selection / screening

☐ Data extraction study characteristics

☐ Risk of bias assessment/study quality assessment

☐ Data extraction of outcome data

☐ Data analysis/synthesis

☐ Writing the manuscript

☐ Publishing the manuscript

Please tell us briefly what happened:

What was your experience with publishing your systematic review? (response of both journals/editors and reviewers)

Opinions and future perspectives

Would you recommend conducting a preclinical systematic review to your colleagues/peers? (*)

Yes ☐ No ☐ Maybe ☐ No opinion ☐

Is it likely that you will conduct another preclinical systematic review? (*)

Yes ☐ No ☐ Maybe ☐ I already conducted another review ☐ No opinion☐

If “yes”: Could you please explain why?

If “no”: Could you please explain why not?

If “maybe”: Could you please explain why?

If “I already conducted another review”:

How many preclinical reviews did you conduct? (please fill in the corresponding number)

If “I already conducted another review”:

Did you complete this/these systematic review(s)?

☐ Yes, I did

☐ No, it is a current project

☐ No, the project stopped (please specify why) _____

☐ Other (please specify) _____

Which factors would encourage you to conduct another preclinical systematic review?

What was your experience with the coaching?

Would you like to receive coaching again? (*)

Yes ☐ No ☐ Only for some stages of the systematic review ☐ No opinion ☐

If “only for some stages of the systematic review”: for which stages would you like support?

☐ Writing protocol

☐ Searching for all the evidence

☐ Study selection / screening

☐ Data extraction of study characteristics

☐ Risk of bias assessment/study quality assessment

☐ Data extraction of outcome data

☐ Data analysis/synthesis

☐ Writing the manuscript

☐ Publishing the manuscript

☐ Other (please specify) _____

For further analysis of this topic, we would like to perform interviews (± 1 hour) with some of the participants of this questionnaire.

Would you in principle be willing to take part in a semi-structure interview concerning this topic? If yes, you will be sent all of the required information in the near future.

Yes ☐ No☐

Please give us your e-mail so we can contact you regarding the interview.

----------Page Break----------

Thank you for completing this questionnaire

We are very grateful for your contribution and your time

Branching: if they answered no to the introductory question

Your ZonMw funded preclinical systematic review is ….

ongoing ☐ stopped ☐

If "ongoing":

Please provide information regarding the stage of your systematic review (*)

Stages	*Stage started*	*Stage finalized*
Writing protocol	☐	☐
Searching for all the evidences	☐	☐
Study selection / screening	☐	☐
Data extraction of study characteristics	☐	☐

Risk of bias assessment/study quality assessment	☐	☐
Data extraction of outcome data	☐	☐
Data analysis	☐	☐
Writing the manuscript	☐	☐

If "stopped":

Could you please tell us why the systematic review stopped?

----------Page Break----------

Do you think that conducting this systematic review will have an impact on the way you design, conduct and/or report future experiments?

Yes ☐ No ☐ Maybe ☐ No opinion ☐

If "yes" or "maybe": Please explain briefly how

Appraising research

The following section focuses on the way you appraise research now that you are accustomed to preclinical systematic review methods.

Please choose the answer that best fits the following statements: (*)

When appraising research papers, performing a systematic review had an impact on…	*Completely Disagree*	*Mostly Disagree*	*Slightly Disagree*	*Neither disagree nor agree*	*Slightly Agree*	*Mostly Agree*	*Completely Agree*
Your critical sense when reading research papers	☐	☐	☐	☐	☐	☐	☐
Your critical sense towards peers' research	☐	☐	☐	☐	☐	☐	☐
Your critical sense toward your own research	☐	☐	☐	☐	☐	☐	☐
The way you appraise overall research quality in your field	☐	☐	☐	☐	☐	☐	☐

----------Page Break----------

Skills after performing the preclinical systematic review

Did you **learn** new research skills by conducting the systematic review? (*)

Yes ☐ No ☐ No opinion☐

If yes, what new research skills did you learn?

Did you **improve** your research skills by conducting the systematic review? (*)

Yes ☐ No☐ No opinion☐

If yes: what research skills did you improve?

Did you **learn** new skills beyond research skills by conducting the systematic review? (*)

Yes ☐ No ☐ No opinion ☐

If yes: what personal skills did you learn?

Did you **improve** your skills beyond research skills by conducting the systematic review? (*)

Yes ☐ No ☐ No opinion☐

If yes: what personal skills/soft skills did you improve?

Your experience with conducting a preclinical systematic review

The following section focuses on your personal experience of performing a systematic review. It addresses questions about your experience with the coaching, your personal opinion and future perspectives.

Conducting the systematic review

Please choose the answer that best fits the following questions:

So far, did the review match your expectation in term of duration? (*)

Yes ☐ No, it was longer ☐ No, it was shorter ☐

If "No": Which stages of the systematic review went slower or faster than expected? (multiple answers are possible/can be picked)

☐ Writing protocol

☐ Searching for all the evidence

☐ Study selection / screening

☐ Data extraction of study characteristics

☐ Risk of bias assessment/study quality assessment

☐ Data extraction of outcomes data

☐ Data analysis

☐ Writing the manuscript

Please tell us briefly what happened:

Opinions and future perspectives

Would you recommend conducting a preclinical systematic review to your colleagues/peers? (*)

Yes ☐ No ☐ Maybe ☐ No opinion ☐

Is it likely that you will conduct more preclinical systematic reviews in the future? (*)

Yes ☐ No ☐ Maybe ☐ No opinion☐

If “yes”: Could you please explain why?

If “no”: Could you please explain why not?

If “maybe”: Could you please explain why?

Which factors would encourage you to conduct another preclinical systematic review?

----------Page Break----------

Thank you for completing this questionnaire

We are very grateful for your contribution and your time

Appendix 4: Informed consent form

Informed Consent Form for Participants in the Qualitative Study

"Conducting preclinical systematic reviews – the impact on research and researchers "

Principal Investigator

Julia Menon on behalf of ZonMw; Erica van Oort, ZonMw representative

Telephone: +33 6 26 36 84 38

Julia.menon@radboudumc.nl

mkmd@zonmw.nl

This Informed Consent Form has two parts:

• Information Sheet (to share information about the study with you)

• Certificate of Consent (for signatures if you choose to participate)

You will be given a copy of the full informed consent form

Part I: Information Sheet

You are being asked to take part in a research study. Before you decide to participate in this study, it is important that you understand why the research is being done and what it will involve. Please read the following information carefully and ask the researcher if anything is not clear or if you need more information.

Introduction

I'm Julia Menon, research and teaching assistant. I'm currently performing a case study for ZonMw regarding their funding program "Meer kennis met minder dieren (MKMD)/More Knowledge with Fewer Animals".

Purpose of the Study

The ZonMw funding program "MKMD" has been running since 2012. Within the program the Module 'kennisinfrastructuur'/knowledgeinfrastructure is focused on education and coaching for preclinical systematic reviews and funded many projects in the Netherlands. ZonMw would like to evaluate the reach of their program, notably by assessing the usefulness of funding preclinical systematic reviews. Therefore, we aim to investigate the impact of conducting systematic reviews, both on research and the researchers.

Procedure

This research will involve your participation in a one-hour interview, where you are kindly asked to respond to several open-questions. During the interview, I (Julia Menon) will interview you

via teleconference, using *GoTo meetings,* and will record our exchange for further analysis. If you do not wish to answer any of the questions during the interview, you may say so, and we will move on to the next question. No one else but I will be present unless you would like someone else to be there. We can then invite them to the call.

The information recorded is confidential; it will be transcribed verbatim. Only the ZonMw representative for this project (dr. Erica van Oort) will have access to the recording and the information documented during your interview. Additionally, your information will be used for an internal ZonMw report only. The entire interview will be recorded, but no-one will be identified by name in the data analysis or in any other future steps of publication. The recording will be destroyed after 16 weeks.

Participant Selection

You are being invited to take part in this research because we feel that your experience with the preclinical systematic reviews would be highly valuable. In particular, to highlight how conducting a systematic review impacted your subsequent projects and your opinion on (the quality of published) animal research.

Voluntary Participation

Your participation in this study is voluntary. It is up to you to decide whether or not to take part in this study. If you choose to take part, you will be asked to sign this informed consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason. Withdrawing from this study will have no bearing on your job or any work-related evaluations or report. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

Risks

The questions asked during the interview will be related to your experience with conducting your ZonMw funded/coached systematic review, and on the impacts it may have had on your subsequent research project and yourself. If you do not feel comfortable with this topic for personal, work-related, or other reasons, you may decline to answer any or all questions, and you may terminate your involvement at any time.

Benefits

There will be no direct benefit to you, but your participation is likely to help us identify the impacts systematic reviews may have and can support ZonMw to continue and/or reform the current grants.

Confidentiality

Confidentiality, privacy and anonymity is the main priority in our study. Every effort will be made by the researcher to preserve your confidentiality by the following:

- Assigning a code name to your collected information, as well as on all research notes and documents
- No mention of your profession, age, or any distinct characteristic that may be associated with your person.
- Interviews will be done and recorded on a trustworthy software.
- Digitally secure your data
- Access will be limited to the ZonMw representative (dr. Erica van Oort), and I (Julia Menon)
- Ensure destruction of the recording within 16 weeks after the original interview.

Participant data will be kept confidential except in cases where the researcher is legally obligated to report specific incidents. These incidents include, but may not be limited to, incidents of abuse and suicide risk.

Contact Information

If you have questions at any time about this study, you may contact the researcher whose contact information is provided on the first page.

Part II: Certificate of Consent

To be filled by the participant

I have read and I understand the provided information and have had the opportunity to ask questions.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost.

I have had the opportunity to ask questions and any questions I had have been answered to my satisfaction.

I understand that I will be given a copy of this consent form.

I voluntarily agree to take part in this study.

Name of Participant _____

Signature

Date _____

To be filled by the investigator

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Name of Investigator_____

Signature

Date _____

Appendix 5: Interview guide

Interview Guide

Note for the researcher: green text in italics is not said out loud but only an indication. Bullet points under some questions are meant to assure that discussion does not become out of topics + give the possibility to ask open questions on the go

Introduction

Good morning/good afternoon

Thank you for giving me some of your time today. Before the interview, we will first read through the informed consent form together to provide you with a brief recap of the goal of our study and the setting of the interview. If you have any question, please do not hesitate.

Do you have any questions for the moment?

Read the ICF

Is the aim of the interview clear?

Start the recording

Breaking of the ice and setting context

1) To start, could you please briefly introduce yourself?
    - Their background
    - Their role in their institute

In the first part of the interview, I will ask you some questions regarding your experience with the systematic review, and then in a second part, we'll discuss the impact of systematic reviews. Some of these questions you already answered in the questionnaires, but I would like to know your opinion further regarding these topics.

Experience with the systematic review

2) So, we'll start with some questions about your systematic review:
    a) Could you please tell me about the topic of your systematic review and when you started this project?

    b) Why have you conducted this systematic review?
        - What factors incited you to conduct this SR?

3) Now we'll focus on more details with the content of your review, in particular on the results that you had.

As you know, when starting a systematic review, you need to write a precise protocol, which helps to lay out what will be done in a transparent way. However, it can be difficult to predict what you will find.

a) In your case, did your expectations align with your final results?

- *Number of studies lower/higher than expected:* Was the number of studies lower or higher than expected?
- *Studies available or unfindable full text:* Did you have any issues with collecting all studies full text?
- *Quality of studies:* What did you expect from the quality of studies?
- *Unexpected findings*: Did you encounter any unexpected findings?

b) Was there sufficient evidence to draw conclusions?

c) Was there enough quality to draw conclusions?

4) Now I would like to ask you more in-depth questions regarding your experience with doing a systematic review, in particular related to your skills and insights.

By doing this review, what insights did you gain?

- *Awareness:* How has it changed your awareness/experience in your field?
- *Critical sense*: Did it change your critical sense?
- *Skills:* Which of your skills did you gain or improve since you are familiar with the methods of a systemic review?

Impacts – change in behaviour/attitude

We'll continue with the second part of the interview. We will focus on the insights you gained from this systematic review and how they impact your subsequent research projects, including the ones you're doing right now. Could you please tell me what type of project your conducted beside or after your review? E.g. animal studies, clinical studies etc.

5)

a) After your review or beside it, what type of research did you do?
   i) For instance, animal research, clinical research.

If they use animal models:

b) Since you have completed your systematic review, do you consider using alternatives to animal models?

If yes: Why? Are any alternatives available?

6) Has your opinion changed regarding the overall quality of animal research?

7) In what way did the insights that you got from the systematic review influence the way you conduct animal research?
   - *Model/methods:* Did it impact the models and methods you chose? Could you please elaborate?
   - *Critical planning:* did it impact the way you plan future experiments? How?
   - *Reporting:* did impact the way you reported your model and methods? How?
   - *Make it easily accessible:* did it influence you to make your next research accessible?
   - *Avoid duplication:* did it enable you to avoid duplication?

8) As said earlier, results gained from a systematic review can be unpredictable and are prone to generate new hypotheses. In your case, did conducting this systematic review give directions to your future projects or inspire new projects?

   - *Topic:* Did it change the topic of your research? E.g. you used to focus on protein A and now on protein B.
   - *Models:* Did you base your research on other animal models? E.g. discover that animal A is better suited than previous model they were using
   - *Further methods*: Did it trigger the development of further methods? E.g. realise that no induction of a model was done during the treatment and decided to write a protocol for it
   - *Project outside animal*: Did it trigger the start of new projects outside of animal research? E.g. make a letter, a mobile app.

9) You were talking earlier about how much insights you gained by conducting this systematic review.
   a) Is it common to perform systematic reviews of animals in your field?
      i) How is it received by journals or reviewers?
   b) How valuable do you think systematic reviews of animals are in your field?
      - Can an SR be of any benefit for translational purposes?
   c) In your opinion, what can be done to promote systematic reviews of animals in your field?

10) Do you have any ideas or comments you could add about this topic that we did not yet discuss?

Conclusion

Thank you for your participation and for allowing me to use some of your time. This information is very valuable to us. Would you like to be kept up to date with the results of the project?

Stop recorder