Biological Hazards & Animal Health and Welfare Unit (BIOHAW)

MINUTES OF THE WORKING GROUP ON RABIES – WAITING TIME AFTER RABIES ANTIBODY TITRATION TEST

TELE-conference, 3rd May 2022

(Agreed on 10th May 2022)

Participants

- Working Group Members:
  - Helen ROBERTS (chair)
  - Julio ALVAREZ
  - Emmanuelle ROBARDET
  - Søren SAXMOSE NIELSEN
  - Arjan STEGEMAN
  - Steven VAN GUCHT
  - Vlad VUTA

- Hearing Experts[1]:
  - Thomas MÜLLER

- From EFSA BIOHAW Unit:
  - Sotiria-Eleni ANTONIOU

[1] As defined in Article 17 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work: http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf.

1. Welcome and apologies for absence

The Chair welcomed the participants.

Florence Cliquet sent her apologies for her absence.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

4. Scientific topic(s) for discussion

The meeting concerned the Mandate received by the EC under article 31 of Regulation (EC) 178/2002 for scientific and technical assistance on the risks related to a possible reduction of the waiting time after rabies antibody titration to 30 days compared to 90 days in the current EU legislative regime.

Discussion on pending comments

The comments by the Panel members, the reviewers and the EC were discussed and applied.

Uncertainty Analysis

A presentation was delivered and a discussion on the evidence dossier (already shared with the WG experts) was conducted with the WG experts to provide them explanations on how to quantify the impact of the uncertainties identified in the assessment performed. The WG experts replied on the specific questions providing their estimation and their probability judgement of their certainty.

Conclusions and Recommendations

The conclusions and the recommendations amended and agreed based on the comments and the uncertainty analysis.

5. Tasks distribution

The WG experts should review and comment the final version of the report by Friday 6 May.

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Biological Hazards & Animal Health and Welfare Unit (BIOHAW)

MINUTES OF THE WORKING GROUP ON RABIES – WAITING TIME AFTER RABIES ANTIBODY TITRATION TEST

TELE-conference, 5th April 2022

(Agreed on 21st March 2022)

Participants

- Working Group Members:
  - Helen ROBERTS (chair)
  - Julio ALVAREZ
  - Emmanuelle ROBARDET
  - Søren SAXMOSE NIELSEN
  - Arjan STEGEMAN
  - Steven VAN GUCHT
  - Vlad VUTA

- Hearing Experts[1]:
  - Thomas MÜLLER
  - Florence CLIQUET
  - Guillaume CROZET

- From EFSA BIOHAW Unit:
  - Sotiria-Eleni ANTONIOU

[1] As defined in Article 17 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work : http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf.

1. Welcome and apologies for absence

The Chair welcomed the participants.

There were no apologies for absence.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

4. Scientific topic(s) for discussion

The meeting concerned the Mandate received by the EC under article 31 of Regulation (EC) 178/2002 for scientific and technical assistance on the risks related to a possible reduction of the waiting time after rabies antibody titration to 30 days compared to 90 days in the current EU legislative regime.

1. Results of the literature review

There was a discussion on the results of the literature review. The experts considered the publications included sufficient and no other publications were proposed.

For the studies on experimental trials it was clarified that information from the time from inoculation to the onset of clinical signs wasn't available at individual level in all studies and instead the ranges of each group of dogs was provided.

The graph with the ranges of all publications was presented and it was agreed to include all publication with all routes of inoculation (intramuscular, intranasal, intracerebral) and to add dots for each dog wherever it was available.

The dogs that are moving as pets accompanying their owners (non-commercial movements) are not registered into TRACES system. The requirement of registration the commercial movements of dogs into TRACES will be clarified with the colleagues from EC and the available data will be shared with the WG.

For 3 publications by Fekandu there was a suspicion that they came from the same experiment. It was decided to keep the one with more information at individual level (Fekadu, Shaddock, et al., 1982) and from the rest to keep only the groups of animals with different routes and doses of inoculation and different results.

For the analysis, only the publications with the intramuscular inoculation are going to be used since they simulate better the route of transmission in the field.

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[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

There was a discussion on the publication of Tierkel et al., 1949 about the observation of a death occurred 255 days post inoculation. The experts explained that this could be a late response that can happen and therefore not to exclude this observation from the dataset.

Some additional clarifications on specific publications were requested from the contractors.

2. Assessment of the risk of rabies introduction

The data from experimental trials and cases in the field are going to be used for the estimation of the incubation period. From experimental trials the data of the intramuscular inoculation are going to be used and more specific the time from inoculation to the onset of clinical signs.

It was discussed that the animals 21 days after vaccination have not developed immunity and they are considered unvaccinated having equal probability to get infected. The type B risk.

3. Quantitative risk assessment of rabies being introduced into mainland France through worldwide non-commercial dog and cat movements

Dr Guillaume Crozet was invited to the WG meeting as Hearing Expert and he presented his work on quantitative risk assessment of Rabies being introduced in France. The results are available to the WG to be used and included in the Scientific Report.

4. Uncertainty

The methodology of the Uncertainty analysis and the way it will be incorporated in the Scientific Report was presented to the WG.

5. Distribution of tasks

The experts will finalise the part that the sections that they have been assigned to work with by Monday 11th April and to review and comment by Monday 18th of April.

5. Next meeting(s)

The next WG meeting was agreed to take place on 3rd of May. If needed shorter WG meetings may be arranged to discuss and work on specific topics.

Biological Hazards & Animal Health and Welfare Unit (BIOHAW)

MINUTES OF THE WORKING GROUP ON RABIES – WAITING TIME AFTER RABIES ANTIBODY TITRATION TEST

TELE-conference, 24th March 2022

(Agreed on 28th March 2022)

Participants

- Working Group Members:
  - Arjan STEGEMAN
- From EFSA BIOHAW Unit:
  - Sotiria-Eleni ANTONIOU

1. Welcome and apologies for absence

There were no apologies for absence.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

4. Scientific topic(s) for discussion

The meeting concerned the Mandate received by the EC under article 31 of Regulation (EC) 178/2002 for scientific and technical assistance on the risks related to a possible reduction of the waiting time after rabies antibody titration to 30 days compared to 90 days in the current EU legislative regime. In fact, it was a meeting to inform the expert on the new Mandate and the outcome of the previous WG meeting that he was not able to join.

1. Presentation and discussion of the Mandate and the Terms of Reference

The Mandate and the Terms of References were presented. It was clarified the Mandate was received by the EC in the context of article 31 of Regulation (EC) No. 178/2002, therefore the output will be a Scientific Report that will be published by 31st of May 2022. The draft Scientific Report will be presented to the AHAW Panel on 4 May 2022.

2. Interpretation of terms of references

It was clarified and agreed that the Mandate concerns dog movements from non-EU Countries to EU Countries following the requirements of the EU Regulation in terms of individual identification of the dog, the vaccination, the titration test, the time intervals, the documents/certifications that accompany the dog. In addition, it is assumed that good veterinary practice has been applied through vaccination, clinical examination, and blood sampling for the titration test, given that all these activities are conducted by an authorised or official veterinarian.

The following topics were also discussed and clarified:

The threshold of 0.5 IU/ml is high enough to be considered as a true positive result and in addition it is a test with high specificity.

Some scenarios of vaccinated healthy dogs, with VNT >= 0.5 IU/ml have been discussed and it seems that mainly the risk is related to primary vaccination if the infection occurred before vaccination or after vaccination and before the development of the protective immunity.

The Type B risk as described in Smith et al 2021 publication is different from the type B risk.

3. Literature Review

The protocol of the Literature Review (LR) had been shared before the WG meeting. There were no moments on the protocol and the expert proposed to have the information on the onset of clinical signs and the deaths at individual level to allow us to get the distribution.

The structure of the LR report and the tables with the results presented and discussed with the expert.

4. Structure of the Scientific Report document

The main structure of the Scientific Report was discussed.

5. Distribution of tasks

Review of the results of the LR by 30 March 2022.
Construct the distribution of the incubation period from the datasets.

6. Next meeting(s)

The short deadline of this Mandate and the Easter (Catholic and Orthodox) holidays generated limitations to find a convenient date for all the WG experts. Nevertheless, 5 April and 3 May will

be the dates for the next WG meetings. If needed shorter WG meetings may be arranged to discuss and work on specific topics.

Biological Hazards & Animal Health and Welfare Unit (BIOHAW)

MINUTES OF THE WORKING GROUP ON RABIES – WAITING TIME AFTER RABIES ANTIBODY TITRATION TEST

TELE-conference, 21st March 2022

(Agreed on 25th March 2022)

Participants

- Working Group Members:
  - Helen ROBERTS (chair)
  - Søren SAXMOSE NIELSEN
  - Julio ALVAREZ
  - Emmanuelle ROBARDET
  - Vlad VUTA
  - Steven VAN GUCHT

- Hearing Experts[1]:
  - Thomas MÜLLER
  - Fernanda DOREA

- European Commission and/or Member States representatives:
  - Thierry CHALUS
  - Moritz KLEMM

- From EFSA BIOHAW Unit:
  - Sotiria-Eleni ANTONIOU
  - Inma AZNAR

[1] As defined in Article 17 of the Decision of the Executive Director concerning the selection of members of the Scientific Committee, the Scientific Panels, and the selection of external experts to assist EFSA with its scientific work: http://www.efsa.europa.eu/en/keydocs/docs/expertselection.pdf.

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies for absence have been received from Arjan STEGEMAN (WG member) and Florence CLIQUET (Hearing expert).

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

4. Scientific topic(s) for discussion

The meeting concerned the Mandate received by the EC under article 31 of Regulation (EC) 178/2002 for scientific and technical assistance on the risks related to a possible reduction of the waiting time after rabies antibody titration to 30 days compared to 90 days in the current EU legislative regime.

1. Presentation and discussion of the Mandate and the Terms of Reference

The Mandate and the Terms of References were presented. It was clarified the Mandate was received by the EC in the context of article 31 of Regulation (EC) No. 178/2002, therefore the output will be a Scientific Report that will be published by 31st of May 2022. The draft Scientific Report will be presented to the AHAW Panel on 4 May 2022.

2. Interpretation of terms of references

It was clarified and agreed that the Mandate concerns dog movements from non-EU Countries to EU Countries following the requirements of the EU Regulation in terms of individual identification of the dog, the vaccination, the titration test, the time intervals, the documents/certifications that accompany the dog. In addition, it is assumed that good veterinary practice has been applied through vaccination, clinical examination, and blood sampling for the titration test, given that all these activities are conducted by an authorised or official veterinarian.

The following topics were also discussed and clarified:

The Virus Neutralisation Test (VNT) is not a test to confirm or rule out rabies, it is a regulatory tool to check the level of immunity after vaccination. The threshold of 0.5 IU/ml is high enough to be considered as a true positive result.

The dogs that are moving as pets accompanying their owners (non-commercial movements) are not registered into TRACES system. The requirement of registration the commercial movements of dogs into TRACES will be clarified with the colleagues from EC and the available data will be shared with the WG.

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Primary rabies vaccination is considered to be the first vaccination in puppies or older dogs. Revaccination is only valid if it was carried out within the period of protective immunity conferred by the previous vaccination and in line with the vaccine manufacturers instructions.

Some scenarios of vaccinated healthy dogs, with VNT >= 0.5 IU/ml have been discussed and the WG concluded that mainly the risk is related to primary vaccination if the infection occurred before vaccination or after vaccination and before the development of the protective immunity.

3. Literature Review

The protocol of the Literature Review (LR) had been shared with the WG experts before the WG meeting. Fernanda Dorea on behalf of the contractor, presented the protocol and provided clarifications to the experts. The WG agreed on the protocol, and they proposed to delete from the exclusion criteria the *no English* language, for publications on the cases of the infected dogs that have been moved from non-EU-countries into EU. The contractor will check for additional publications and the WG will support with the translation if necessary.

The eligible publications of the literature review on experimental studies and the raw datasets were shared with the WG and no objections expressed for those that have been already included. The experts provided some additional publications that were included in Smith et al 2021 article, publications, on cases of imported infected dogs and cats in France and on risk assessment. The publications have been forwarded to the contractor to check for their eligibility.

The structure of the LR report and the tables with the results presented to the WG experts. The WG proposed to present the results on the incubation period at animal level or group of animals if the information at animal level is not available, instead of the min and max incubation period.

4. Structure of the Scientific Report document

The document has been presented to the WG experts and the main structure of the Scientific Report was discussed.

5. Distribution of tasks

The contractor will provide the draft report on Literature Review on Friday, 25 March 2022. The WG experts will review the report by 30 March 2022. The contractor will implement the comments and the final version is going to be incorporated into the Scientific Report document before the WG meeting on 5 April 2022.

6. Next meeting(s)

The short deadline of this Mandate and the Easter (Catholic and Orthodox) holidays generated limitations to find a convenient date for all the WG experts. Nevertheless, 5 April and 3 May will be the dates for the next WG meetings. If needed shorter WG meetings may be arranged to discuss and work on specific topics.