



Surveillance analysis Tool for  
Outcome-based Comparison  
of the confidence of FREEdom



## **STOC free: WP5, Deliverable 3**

**Annual report year 3**

**10 March 2019-9 March 2020**

**Comparison of the confidence in freedom from infection based on  
different control programmes between EU member states: STOC  
free**

September 2020





**This study was awarded a grant by EFSA and was co-financed by public organisations in the countries participating in the study**

## Summary

The STOC free project runs from 10 March 2017 until 9 March 2021 and aims to construct a generic framework that will allow a standardised and harmonised comparison of the output of different control programmes (CP) of cattle diseases that are not regulated by the EU. During the first year, the dynamics of BVD infection were evaluated in a conceptual model. Based on those results and the aim of the project, Bayesian networks were considered the best modelling method for output-based evaluation of surveillance. Detailed CP information was collected for BVDV in the six participating countries and the most important key aspects for inclusion in the STOC free model were identified.

In the second year, a first version of STOC free model was developed and tested on simulated data. The risk factors that need to be included in the model were defined as were the most important aspects of CPs. Default values for risk factors for BVDV infection to be included in STOC free model were deducted based on a meta-analysis and the data collection tool was finalised. Even though the data collection tool was final, it was foreseen that this tool will further advance concurrently with model development.

In year three, the sensitivity of the different model input parameters was evaluated on simulated data to obtain insight in the importance of each of the input parameters. Subsequently, the developed model was tested and validated using data from each of the partner countries. Based on the feedback the model was finalised and the report and corresponding computer code were delivered to EFSA. There were roughly three different BVDV situations needed to be taken into account in the model: 1. Endemic situation with a CP on herd level, 2. Endemic situation with a CP on animal level and 3. BVD free situation. The model was adapted to enable inclusion of both animal and herd level data. The model could not handle a country in a completely BVDV free situation given that it needs some infections to converge. In the latter situation a scenario tree model might be better suited. This is evaluated as part of the case studies.

In year four, we will finalise the case studies and work on aspects for future generalisation of the methods to other diseases. For these aspects collaboration with the SOUND control consortium is foreseen. The COVID-19 outbreak complicates the dissemination of the project results to other scientists and stakeholders. The project team is looking at several options to maximize dissemination such as postponing the workshop and looking at online possibilities.

## Background

Several European Member States (MS) have implemented control programmes (CP) for endemic infections that are not regulated by the EU. Therefore, the design of these programmes is tailored to each country's specific situation and vary extensively. This large variation results in difficulties when comparing these programmes, highlighting the need for methods to objectively and quantitatively compare programme outputs e.g. confidence of freedom from infection.

In the STOC free project, six countries are collaborating to construct the generic framework to allow for standardised and harmonised comparison of the output of different CPs for cattle diseases that are not regulated by the EU. The framework will allow the integration of heterogeneous data and will result in standardised and comparable outputs.

During this project, BVD is acting as the case disease because of the large variations in both programme design and prevalence that exists between MS. The framework is being designed and optimised using pilot-scenarios describing the CPs in one of the consortium partner countries. Thereafter, information about BVDV CPs, combined with test specifications and demographic context information, will form the basis of case studies where the developed methods will be applied and optimised in all six consortium member states. In the final stage of the project, the developed methodology will be evaluated for possible generalisation to other cattle diseases.

## Overview of activities in year 1 and 2

First, a conceptual model was developed that represented the course and dynamics of BVD infection. Thereafter, possible statistical methods were explored that showed potential to be used in this context of output-based evaluation. Bayesian network models were chosen because of their flexibility and the possibility to include heterogeneous input information. The developed model was built on herd-level data and calculated the probability of freedom given the probability of becoming infected and the probability of clearing an infection. Risk factors included in the model are herd size, introduction of cattle into the herd and the risk from neighbouring herds (prevalence of disease and/or livestock density). The model was tested and validated using simulated data.

In WP2, the BVDV Cps were compared between countries and an approach was proposed to qualitatively compare elements that influence the likelihood, and associated uncertainty, that cattle from a herd categorized as BVDV-free are truly free from infection. The results were published in the [Journal of Dairy Science \(JDS\)](#). The data collection tool was adapted and tailored to the needs of the statistical model (WP1). A literature review and meta-analysis was initiated to obtain default values for input parameters to be included in STOC-free model. In total, 51 papers were included in the review and 18 papers were included in the meta-analysis. The paper is also published in [JDS](#).

In this document, the progress of the third year is described.

## WP5: management

*WP leader and co-leader: G. van Schaik and I. Santman-Berends (Utrecht University, the Netherlands)*

### *WP5: Highlights of year 3*

During the third year, monthly Skype meetings were held to discuss the challenges and to monitor the progress of the project. Face-to-face meetings were held in June 2019 (between PhD students), October 2019 (whole consortium) and February 2020 (people involved in the case studies). The second annual newsletter was delivered in September 2019 in which the progress of the second year was described. An interim report including the financial statement was produced in March 2019.

Additionally, the COST Action SOUND control finished its first year in the project. In this Action more than 100 researchers from 32 countries collaborate with the aim to stimulate and assist in initiatives to explore and implement a widely adaptable output-based framework. The STOC free work was presented to this group and the data collection matrix developed in STOC free is taken to the next level in SOUND control i.e. making it applicable throughout Europe and for multiple cattle diseases. More information on this COST Action can be found at (<https://www.sound-control.eu>, COST Action CA17110).

*Deliverables third year:*

- 5.3 Annual progress report year 2 delivered: September 2019

<https://stocfree.eu/sites/default/files/Annual%20report%20STOC%20free%20year%202020.final.pdf>

## WP1: Development of STOC-free model

*WP leader and co-leader: C. Fourichon and A. Madouasse, PhD student M. Mercat (ONIRIS, France)*

The aim is to develop a method (STOC free model) for the quantitative comparison of the confidence in freedom from infection in different CPs for non-regulated diseases in the EU.

### *WP1: Highlights of year 3*

During the third year, WP1 proceeded with the development of a statistical model based on the chosen method: a special type of Bayesian networks called a hidden Markov model, which allows incorporating infection dynamics in the estimation.

The initial version of the model that was developed on herd-level was expanded with an animal level module for countries that perform their CPs on animal level. The sensitivity of the different input parameters in the models were tested by evaluating the model results of the simulated data when incorporating a range of pre-defined parameter values. The results were discussed and the model adapted accordingly. After this exercise the model was coded as an R package, with an example dataset and the relevant documentation, and shared with the members of the team on the Github platform. Members could opt to start directly with their own data (WP3) or to apply the model on the sample data first. During the annual meeting in October 2019, a half day workshop was organised by the members of WP1. The aim of this workshop was to let the team members get acquainted with the model and to answer all questions so far. Between July 2019 and March 2020, each member was applying the model on the data of their own country and in this process feedback was provided which

led to several updates of the model. In April 2020 the model was finalised and delivered to EFSA together with the computer code.

*Deliverables second year:*

- 1.3 Description of statistical models delivered: April 2019  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/D1.3\\_STOCfree\\_model\\_description\\_summary.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/D1.3_STOCfree_model_description_summary.pdf)

- 1.4 STOC free model including PC code delivered: April 2020  
The documented STOC free R package is available from Github at the following address:  
<https://github.com/AurMad/STOCfree> . A paper documenting the package is currently under review and available as a pre-print at the following address:

<https://www.biorxiv.org/content/10.1101/2020.07.10.197426v3>

## **WP2: Development of STOC-free data**

*WP leader: S. More (UCD, Ireland), PhD student A. van Roon (Utrecht University, the Netherlands)*

The aims of WP2 are two-fold:

1. To develop a generic data collection framework named STOC free data, guided by the methodology developed in WP1, and
2. To use this framework to provide a thorough description of the BVDV control/eradication programmes (CPs) conducted in defined EU MS and, subsequently, to collect specific quantitative information about the CPs.

### **WP2: Highlights of year 3**

In year 3, the scientific paper that was written about the qualitative comparison of CP elements that influence the confidence of freedom of BVDV was accepted for publication in the [\*Journal of Dairy Science\*](#). The developed STOC free data collection tool was presented in the SOUND control consortium in which 32 European countries are represented and feedback was received for further generalisation of the tool. Based on the feedback the tool was further adapted to make it applicable throughout Europe and other cattle diseases as well.

In the literature review and meta-analysis, it was decided to include 51 papers for the review part and to include 18 papers for the meta-analysis. Criteria for inclusion in the meta-analysis were that quantitative data should be available and that the paper should originate from Europe. Based on the review, the most important risk factors for BVDV were identified i.e. introduction of cattle in the herd, herd size, herd type (dairy or beef) and neighbourhood risk. The meta-analysis resulted in default values for the most important risk factors that can be used as input in the model when country specific estimates for the risk factors are unavailable. The results of the literature and meta-analysis were written in a paper which was accepted for publication in the [\*Journal of Dairy Science\*](#).

## WP3: Case studies and generalisation

*WP leader and co-leader: J. Frössling and E. Agren (SVA, Sweden)*

The objective is to validate and optimise STOC free model and STOC free data that are developed in WP1 and WP2, respectively, in case studies that are conducted by all partners. Additionally, the generalizability to other diseases will be evaluated.

### *WP3: Highlights of year 3*

In year 3 the case studies were started and the results on the exercise in which the equivalence between the BVDV CP in the partner countries were reported to EFSA. In the participating six countries, roughly three different situations with regard to BVDV control can be distinguished: 1. Endemic situation on country level, CP on herd level (Netherlands, France, Scotland), 2. Endemic situation on herd level, CP on animal level (Germany and Ireland) and 3. BVDV free situation (Sweden). When a country is completely disease free, the model did not produce informative and realistic output given that it needs some infections to estimate the latent class (the true BVDV infection status). It was concluded that in this situation, a scenario tree model is better suited. For the countries that have a CP on animal level, an extra animal level module was developed that enables inclusion of raw animal level input data in the model. During the case studies several meetings between the members working on the case studies and the team that developed the model were held to discuss the challenges and possible solutions. Based on the feedback of the people working on the case studies, the model was updated several times to be able to incorporate the needs of the different countries. In year four it is foreseen to finish the case studies and to organise a workshop to gather input for the generalisability of the STOC free framework.

The work that is conducted within the COST Action SOUND control, which is closely linked to STOC free, will provide additional input on how to generalise STOC free model to other diseases. Additionally, within SOUND control aspects such as economics and sociology will also be taken into consideration.

#### *Deliverables third year:*

-3.1 Report on equivalence between BVDV CP in partner countries      delivered: March 2020

[https://www.stocfree.eu/sites/default/files/documents/Deliverables/STOC%20free%20D3.2.1%20Report%20on%20equivalence\\_final.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/STOC%20free%20D3.2.1%20Report%20on%20equivalence_final.pdf)

## WP4: Communication and dissemination

WP leader: J. Gethmann (FLI, Germany)

### WP4: Highlights of year 2

During the third project year, the progress of the STOC free was presented to the stakeholders of FESASS (March 2019). The different aspects of the STOC free project i.e. the developed model and the data collection tool were presented and discussed with the members of SOUND control.

Additionally, the project was presented and discussed with national stakeholder and in decision maker meetings. Up to the third year, three scientific papers resulting from the STOC-free project are accepted for publication:

#### *Deliverables third year:*

- 4.2 Presentations at international conferences On-going  
From March 2020 on, conferences and meetings were cancelled as a result of the COVID-19 outbreak. Posters could not be presented at SVEPM2020 and ICAHS4.

- 4.3 Publications in international journals On-going  
<https://stocfree.eu/progress/publications-presentations>

#### *Papers:*

STOC Free: An Innovative Framework to Compare Probability of Freedom From Infection in Heterogeneous Control Programmes.  
<https://www.frontiersin.org/articles/10.3389/fvets.2019.00133/full>

A description and qualitative comparison of the elements of heterogeneous bovine viral diarrhoea control programs that influence confidence of freedom.  
<https://www.sciencedirect.com/science/article/pii/S0022030220301697>

Quantification of risk factors for bovine viral diarrhoea virus in cattle herds: A systematic search and meta-analysis of observational studies  
<https://linkinghub.elsevier.com/retrieve/pii/S0022030220305798>

## Planning year 4

In year 4, the case studies will be finalised and the final reports will be written and delivered. As part of the dissemination, papers will be submitted to scientific journals that describe the model and the results of the sensitivity analysis on simulated data. Further, the development of the STOC free data collection tool and the results of the case studies will also be submitted for publication. Due to the COVID-19 outbreak that resulted in major travel restrictions from March 2020 on, it will be a challenge to present and disseminate the results of this project. Initially, a workshop on the STOC free project was accepted to be held on the ICAHS4 conference in May 2020. This conference is postponed to May 2022. We now need to determine whether we can proceed with an online workshop instead. The workshop for stakeholders that was foreseen for the beginning of 2021, may now be aligned with an

OIE meeting at the end of 2021. We can also present and disseminate our work through the possibilities that are provided within the COST Action SOUND control. However, no physical meetings are planned yet.

Monthly Skype meetings are held to discuss the progress of the project and additional meetings are planned when needed. The annual meeting is planned for 7 and 8 October 2020. The meeting was initially planned to be held in Dublin but will now be organised online given the COVID-19 outbreak. The final report will be delivered to EFSA in March 2021.

### List of previous deliverables

- 1.1 Guidelines for the design of conceptual models delivered: April 2018  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/1.1\\_conceptual\\_model\\_april\\_2018.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/1.1_conceptual_model_april_2018.pdf)
- 1.2 Guidelines for the identification and sources of data delivered: July 2018  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/1.2\\_final.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/1.2_final.pdf)
  
- 2.1 First version questionnaire delivered: April 2018  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/2.1\\_questionnaire\\_apr\\_2018\\_def.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/2.1_questionnaire_apr_2018_def.pdf)
- 2.2 Second version questionnaire delivered: July 2018  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/2.2\\_questionnaire\\_second\\_version.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/2.2_questionnaire_second_version.pdf)
- 2.3 Description of BVDV CPs delivered: July 2018  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/2.3\\_introduction.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/2.3_introduction.pdf)
  
- 4.2 Presentations at international conferences (Covid-19 allowing) On-going
- 4.3 Publications in international journals On-going  
<https://stocfree.eu/progress/publications-presentations>
  
- 5.1 Annual progress report year 1 delivered: September 2018  
[https://stocfree.eu/sites/default/files/Annual%20report%20STOC%20free%20year%201\\_format%20newsletter.pdf](https://stocfree.eu/sites/default/files/Annual%20report%20STOC%20free%20year%201_format%20newsletter.pdf)
- 5.2 Interim report (technical and financial) delivered: March 2019  
[https://www.stocfree.eu/sites/default/files/documents/Deliverables/5.2\\_2019\\_interim\\_technical\\_report\\_stoc\\_free\\_final.pdf](https://www.stocfree.eu/sites/default/files/documents/Deliverables/5.2_2019_interim_technical_report_stoc_free_final.pdf)