EFSA activities on TSE in 2018-2019

18th TSE EURL Annual Meeting

Torino, IT

12-13 September 2019

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European Food Safety Authority

CONTENTS

- CWD III opinion
- 2016-8 TSE EU summary reports
- Collagen & Gelatine

CWD III

ToR1

Revision of the state of knowledge, considering new sci data, about the differences:

a) between the strains found in different species i merica and in Europe and
b) between the strains found so far in moos eer and red deer in Europe;
c) with the main emphasis on transm (transmission paths), pathogenicity and prevalence o ferent strains and susceptibility of the different species/gen

ToR2

To revise the new scien idence on the zoonotic potential of CWD; to assess the transmission to humans through the consumption of nd meat products of cervids and to provide recommenda possible additional control measures to address the risks ide ed.

ToR3

Identify risk factors that can facilitate the spread of CWD in the European Union given the current situation of the disease.

Adoption: 25-26 September 2019

APPROACHES

- Literature searches: update form previous CWD opinions.
  - *in vivo* studies
  - *in vitro* studies
  - epidemiology, risk, introduction, spread

- Contacted researchers
  - *in vivo:* 17 research groups from FR, IT, ES, UK, DE, NL, Can and USA
  - *in vitro:* 11 research groups from FR, IT, ES, UK, SE, Can and USA

- Surveillance data: EFSA database

- List of groups of risk factors: evidence appraised scored-based system from weakest (biological plausible, hypothetical) to strongest (intervention studies)

- Personal communications: NRLs, individual researchers

TOR1: TRANSMISSIBILITY ACROSS SPECIES BARRIER

		CWD isolates													
	Country	USA				Canada						Norway			Finland
Species modeled	Rodent models	Elk	Mule deer	WT deer	Moose	Elk	Mule deer	WT deer	Moose	Red deer (exp)	Reindeer (exp)	Moose	Red deer	Reindeer	Moose
Mouse	conventional mice	Y/N	Y/N	Y		N	Y/N	ong/N				Y		Y	
Mouse	tg-mousePrP	Y				Y		ong				Y	ong	Y	
Hamster	hamsters							ong				ong		ong	
Hamster	tg-hamsterPrP			Y		ong						N		ong	
Bank vole	bank voles	Y	Y	Y		Y	Y	Y	Y			Y	Y	Y	Y
Deer	tg-cervidPrP (all variants)	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y	ong	Y	ong
Bovine	tg-bovinePrP	N		Y/N		Y/N	Y	Y/N		Y		ong/N	ong	ong	ong
Ovine	tg-sheepPrP (all variants)	Y		ong		ong/N	N	Y	N			Y/N	ong	ong	ong
Porcine	tg-porcinePrP					ong/N		ong/N				ong	ong	ong	
Human	tg-humanPrP (all variants)	N	N			ong/N	N	ong/N	N	N	N	ong	ong	ong	
Vulture	tg-vulturePrP											ong	ong	ong	

TOR2: TRANSMISSIBILITY TO HUMANS: *IN VITRO*

Cell-free conversion assay	Very low levels of human recombinant PrP is converted by deer CWD PrP^{sc} ($wdPrP^{sc}$), less than by bovine BSE PrP ($bo\text{-}PrP^{bse}$)	Raymond et al., 2000
In vitro conversion of GdnHCl-treated PrP^{c}	Elk CWD converts human PrP, more easily than bovine, sheep or mouse PrP (brain homogenate)	Li et al., 2007
PMCA	Conversion of human PrP enhanced by preliminary PMCA amplification cycles on cervid PrP	Barria et al., 2011
SDS-based fibrillation assay	No human recombinant PrP conversion by $wdPrP^{sc}$, while converted by $bo\text{-}PrP^{bse}$	Luers et al., 2013
huPrP and 293F cells expressing human PrP / PMCA	Conversion of human PrP less efficient than BSE prion, 129 VV < 129 MM	Barria et al., 2014
RT-QuiC	Very efficient conversion of rec human PrP by CWD samples (better than BSE)	Davenport et al., 2014
PMCA	Efficient conversion of human PrP, depending on human genotype, cervid genotype and cervid species	Barria et al., 2018

TOR2: TRANSMISSIBILITY TO HUMANS *IN VIVO*

Tg40 (MM, 1x) Tg1 (MM, 2x)	No transmission from elk CWD	-	Kong et al., 2005
Tg440 (MM, 2x)	No transmission from 4 elk, 2 MD and 2 WTD isolates	-	Tamgüney et al., 2006
Tg35 (MM, 2x) Tg45 (MM, 4x) Tg152 (VV, 6x)	No transmission from MD CWD	-	Sandberg et al., 2010
TgHu MM (1x) TgHu MV (1x) TgHu VV (1x)	No transmission	-	Wilson et al., 2012
Tg40 (MM, 1x)	No transmission of CWD, except in mice expressing chimeric human PrP (expressing 4 elk AA)	- (+ in chimeric)	Kurt et al., 2015
Tg66 (MM, 8-16x) TgRM (MM, 2-4x)	Clinical suspicion but no IHC or immunoblot confirmation. Faint positive RT-QuiC reactions	+/-	Race et al., 2019
Tg66 (MM, 8-16x)	No transmission	-	Mitchell et al. (2011)
TgRM (MM, 2-4x)	No transmission	-	Cervenakova et al. (2014)
Squirrel monkey	IC transmission from MD CWD	+	Marsh et al., 2005
Squirrel monkey cynomolgus macaque	IC and oral transmission to squirrel monkey, no IC or oral transmission to macaques after 6 years	+ Squirrel - macaque	Race et al., 2009
Squirrel monkey cynomolgus macaque	IC and oral transmission to squirrel monkey, accelerated transmission after secondary passage. No IC or oral transmission to macaques after 10 years	+ Squirrel - macaque	Race et al., 2014
Squirrel monkey cynomolgus macaque	IC and oral transmission to squirrel monkey, no IC or oral transmission to macaques even after 13 years	+ Squirrel - macaque	Race et al., 2018
Cynomolgus macaque	No IC transmission to macaques after 7 years	- macaque	Comoy et al., 2015
Cynomolgus macaque	No transmission	-	Schmaedicke et al., 2012 (PRION)
Cynomolgus macaque	Wasting and mild neurological signs in IC and orally challenged macaques.	+ with clinical signs no pathognomonic for BSE	Czub et al., 2018 (PRION oral)

+: transmission; -: no transmission; +/-: inconclusive

TOR2: THE RISK OF HUMANS TO CWD

- Epidemiological studies: association between human and animals TSE

- Risk of CWD to humans: probability of transmission to humans through the handling and/or consumption of meat and meat products from cervids.

  Unknowns:

  - No tissue infectivity data
  - uptake of the infectious agent by a new host
  - amount of agent present in food portions
  - age of the host at exposure
  - possible potentiating effects of intercurrent disease or injury of the host

- Exposure to the CWD agents:

  - at individual level: consumption
  - at population level: strains, species, prevalence

TOR3: RISK FACTORS SPREAD

- Criteria for selection:
  - ✓ biological plausibility
  - ✓ hypothetical: epi studies
  - ✓ Evidence: association with disease

- Strength of evidence:
  - ✓ from biological plausibility to intervention studies

- Preventability: risk management options

- Disease forms (continuum):
  - ✓ Contagious: peripheral distribution (CWD in NA, CS). Horizontal transmission via live animals, human activity, fomites and/or scavengers or via the feed chain.

  Vs

  - ✓ non-contagious: little or no detectable involvement of peripheral tissues (BSE, atypical/Nor98 scrapie). Environmental contamination

TOR3: RISK FACTORS SPREAD

1. Natural movement of live wild deer from infected areas
2. Man-mediated movement of live farmed/free-ranging deer from infected areas
3. Failure to separate live farmed and free ranging deer
4. High deer density
5. Species-specific social organization
6. Sex-related behaviours
7. Natural or man-mediated animal aggregation
8. Consumption of forage grown on contaminated soil
9. Fallen stock or inappropriate disposal of carcasses and slaughter by-products
10. Movement of other animals (working dogs, scavengers, predators)
11. Transfer of inanimate vehicles of contamination (fomites)
12. Environmental persistence of prions
13. Host genetics

NEW DATA COLLECTION SYSTEM

- **TSE data collection tool v 1.3.5**

  Direct into the tool

  XML files

- **Wiki manual: GitHub**

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Manual for the reporting of surveillance data on Transmissible Spongiform Encephalopathies (TSE) using the EFSA TSE Data Reporting Tool

The TSE data reporting tool is an open source Java client tool running on Windows and is developed for members of the TSE Network for the reporting of surveillance data on TSEs according to Regulation (EC) 999/2001 (part I.A, chapter B.I of annex III); in particular, for Bovine Spongiform Encephalopathy (BSE) in bovine animals, Scrapie in small ruminants (sheep and goats), random genotyping in sheep, Chronic Wasting Disease (CWD) in cervids and TSE in other species.

The tool allows countries to submit and edit their data and automatically upload them into the EFSA Data Collection Framework (DCF) as XML data files.

All the documentation of the TSE reporting tool can be found in this wiki that will automatically open in your default internet browser every time you open the TSE data reporting tool. In addition, a manual for data reporting via XML file (for users not using the tool) is available at this link.

Please note that, in order to be able to upload and submit the data to DCF, a data provider account is required. If you are not registered as a data provider for the TSE data collection please send an

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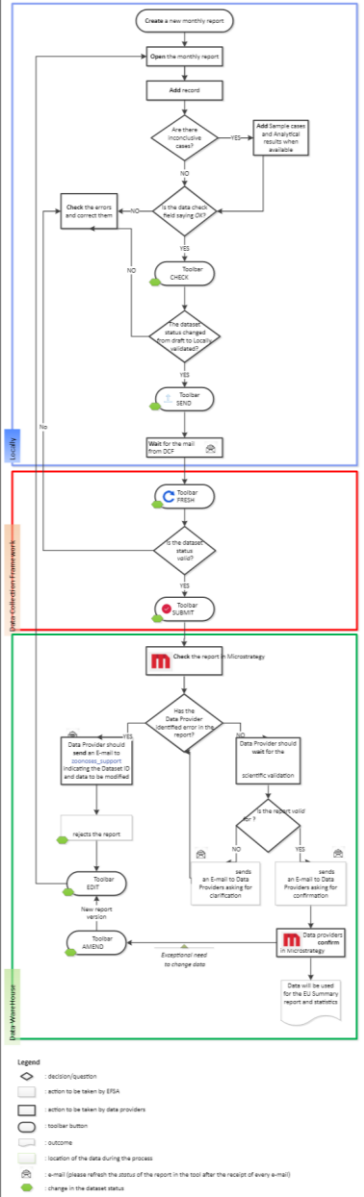
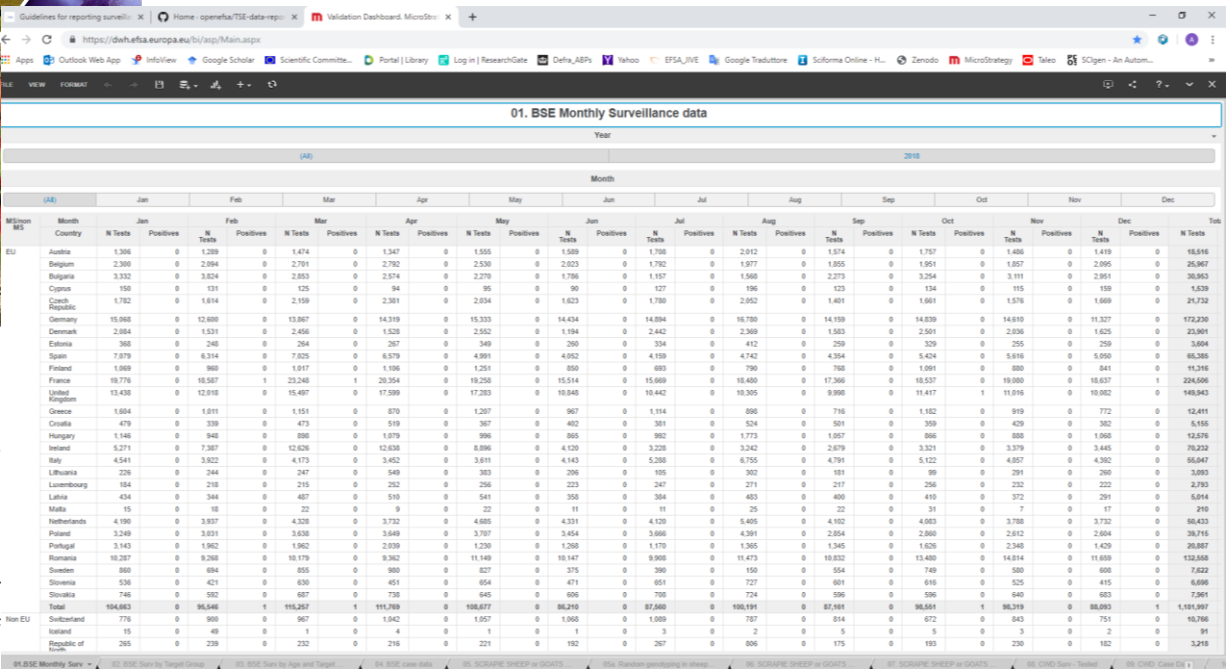
    - BSE (cattle)
    - Scrapie (sheep and



NEW DATA COLLECTION SYSTEM

- **Guidelines for reporting:** XML, business rules, structure…



TECHNICAL REPORT

APPROVED: 9 July 2019

doi:10.2903/sp.efsa.2019.EN-1675

Guidelines for reporting surveillance data on Transmissible Spongiform Encephalopathies (TSE) in the EU within the framework of Regulation (EC) No 999/2001

European Food Safety Authority (EFSA),
Mario Monguidi, Alban Shahaj and Anca-Violeta Stoicescu

Abstract

These guidelines are specifically aimed at guiding the reporting of information under the framework of Regulation (EC) No 999/2001/EC. The technical aspects for the reporting of surveillance data on Bovine Spongiform Encephalopathy in bovine animals, scrapie and genotyping in small ruminants (sheep and goats) and Chronic Wasting Disease in cervids are covered. The guidelines explain the individual data elements of the Standard Sample Description model which are relevant for the data collection on Transmissible Spongiform Encephalopathies. These guidelines are given in order to support the reporting countries in data submission using eXtensible Markup Language data file transfer through the Data Collection Framework according to the protocol described in the EFSA Guidance on Data Exchange.

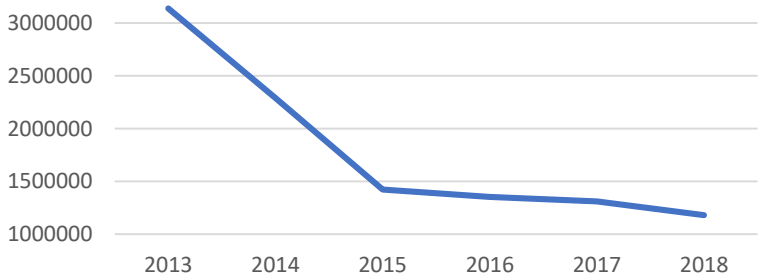
- **Microstrategy Dashboard:** fixed reports to visualize data

2017-8 TSE REPORTS: CATTLE

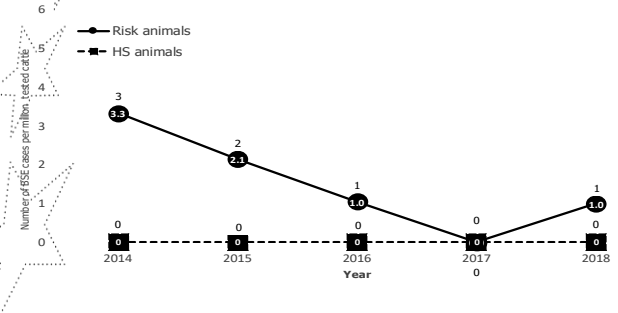
2017: EU + (NO + IS + CH)
2018: EU + (NO + IS + CH + MK)

TESTED

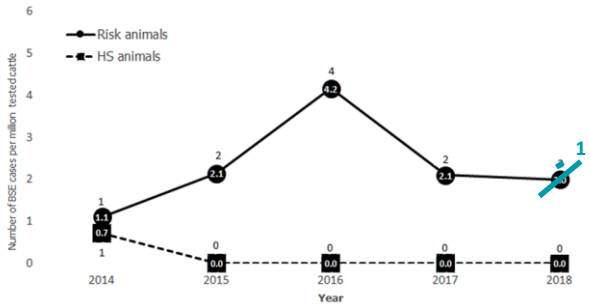
- 2015-2018: 3-5% reduction per year
- 1,331,238 in 2017
- 1,181,997 in 2018.



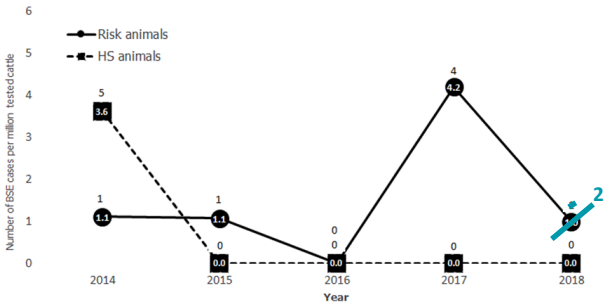
C-BSE



H-BSE



L-BSE



BSE CASES 2018

Country	UK – classical 1	FR - atypical 1	FR – atypical 2	FR – atypical 3
Surveillance target group	Fallen stock	Emergency Slaughter	Fallen stock	Fallen stock
Case type	Classical	L-BSE	H-BSE	L-BSE
Month and year of birth	April 2013	May 2010	November 2001	September 2008
Age at detection (in months)	65	92	194	123
BARB status	Yes	No	No	No
Clinical Symptoms	Falling, recumbent	No clinical symptoms	No clinical symptoms	Aggressive animal
Cattle type	Beef	Dairy	Beef	Dairy
Breed	Aberdeen Angus	Prim'Holstein	Limousin	Limousin
Herd size	22	119	30	296
Herd type	Beef	Dairy	Suckling	Beef
BSE: bovine spongiform encephalopathy; H-BSE: H-type BSE; L-BSE: L-type BSE.				

BSE CASES 2013-2018

	2013	2014	2015	2016	2017	2018
DE		2 (1H,1L)				
ES		1 (1C) 1 (1L)	1 (1L)	1(1H)	3 (1H, 2L)	
FR	2 (2H)	3 (1H,2L)		1(1C) 3 (3H)	2 (1H-1L)	3(2H-1L)
RO		2 (2L)				
IE	1 (1H)		1 (1C)		1 (1L)	
PL	1 (1L)					
PT		1 (1C)				
SI			1 (1H)			
UK	2 (2C) 1 (1H)	1 (1C)	1 (1C) 1 (1H)			1(1C)
NO			1 (1H)			
9 (9C)- 30 (17H, 13L)	2 (2C) 5 (4H-1L)	3(3C) 8 (2H, 6L)	2 (2C) 4 (3H-1L)	1(1C) 4 (4H)	0(0C) 6 (2H, 4L)	1 (1C) 3 (2H, 1L)

2016-8 TSE REPORTS: SHEEP

TESTED

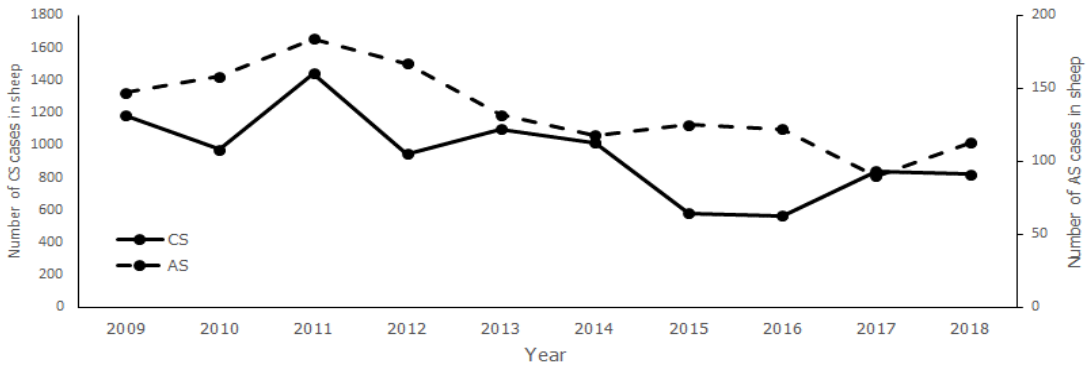
2018 EU: 325,386 in 2018 (+3.4% EU)
2017 EU: 314,547 in 2017 (+10% EU)
2016 EU: 286,351 in 2016

Increase in TSE-infected flocks (+10,680)

CASES

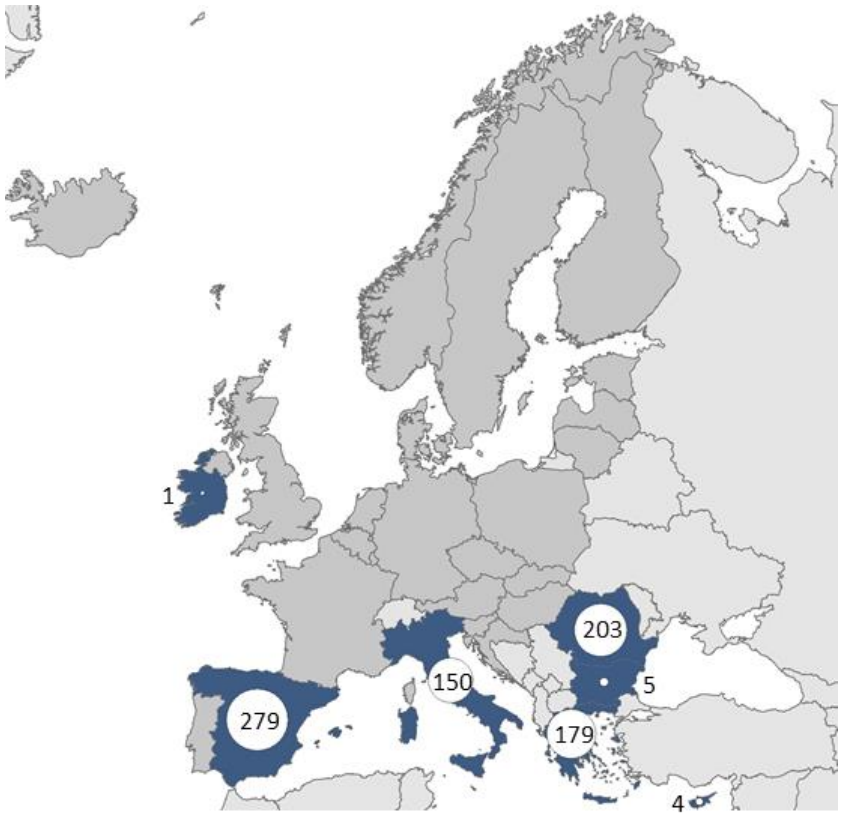
2018 EU - 934: 821 (C) 113 (A) 21% index (99,105)
2017 EU - 933: 843 (C) 104 (A) 25% index (145, 89)
2016 EU - 685: 554 (C) 122 (A) 32% index (112, 106)

EL,ES,IT,RO: 88.6%

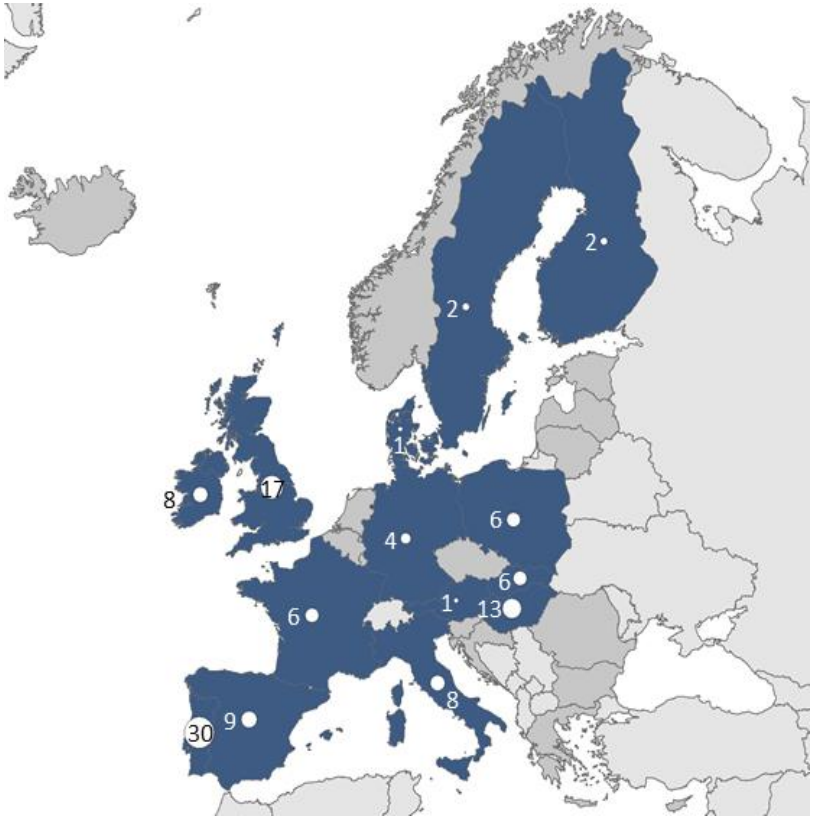


2018 TSE REPORT: SHEEP

Classical scrapie



Atypical scrapie



2016-8 TSE REPORTS: GOATS

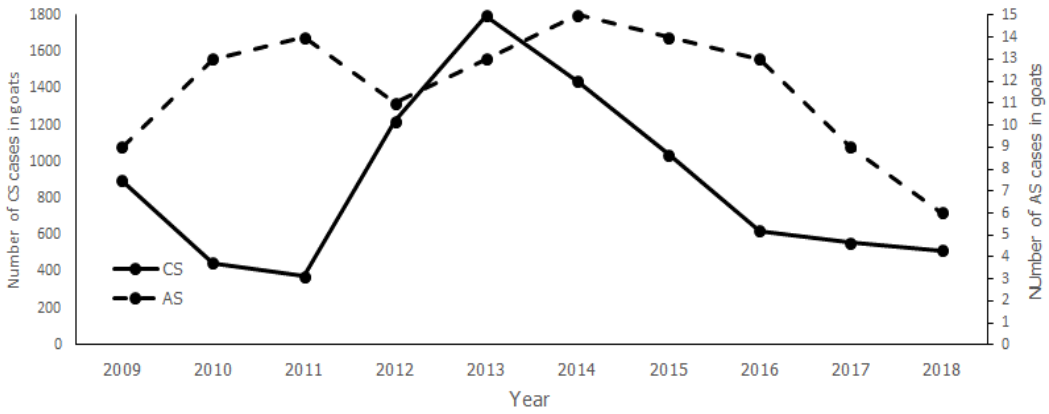
TESTED

2018 EU: 138,128 in 2018 (+ ~18%)
2017 EU: 117,268 in 2017 (+ ~6%)
2016 EU: 110,832 in 2016

CASES

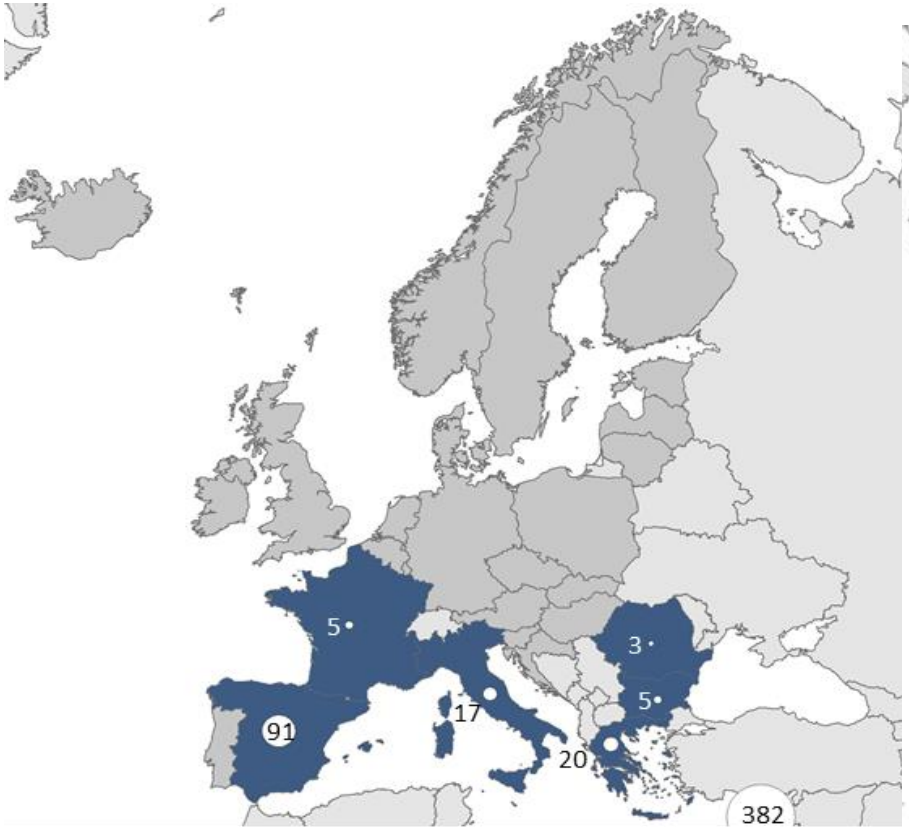
2018 EU - 523: 517 (C) 6 (A) 8.4% index (38-6)
2017 EU - 567: 558 (C) 9 (A) 8.6% index (42-7)
2016 EU - 634: 621 (C) 13 (A) 6.8% index (30-13)

CY: from 485 to 382



2018 TSE REPORT: GOATS

Classical scrapie



Atypical scrapie

2018 TSE REPORT: CERVIDS

TESTED

- 8,185 by 12 reporting countries
- EE,FI,LT,LV,PL,SE (mandatory): 5,110 (62.4%)
- AT,DK,HU,IT,ES,RO: 3,075 (37.6%). RO: 2,387
- NO: 33,037

CASES

- FI: 1 moose
- NO: 6 reindeer + 1 moose

2018 TSE REPORT: CERVIDS

	PSU			Tested	% Risk
Country	Number PSU declared	Number of PSU tested (%)	Median number of cervids tested (min-max)	Total	Tested
EE	15	10[c] (66.6%)	4 (1-78)	217	54.4%
FI	349	153 (43.8%)	2 (1-44)	663	84.8%
LT		Not available		1,835	15.2%
LV	100	145 (145%)	4 (1-20)	1,054	5.8%
PL	16	16 (100%)	63 (8-197)	1,141	75.5%
SE	210	54 (25.7%)	2 (1-13)	200	95%

COLLAGEN & GELATINE: BACKGROUND

Collagen:

"means protein-based products derived from hides, skins, bones and tendons of animals"

main fibrous structural protein of tendons, bones, cartilages and skins

Gelatine:

"natural, soluble protein, gelling or non-gelling, and obtained by the partial hydrolysis of collagen produced from bones, hides and skins, tendons and sinews of animals"

Commission Regulation (EU) No 142/2011)

COLLAGEN & GELATINE: BACKGROUND

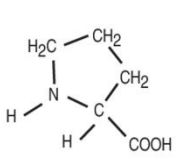
- **Collagen:**

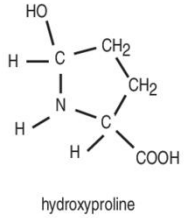
  Main fibrous structural protein of tendons, bones, cartilages and skin

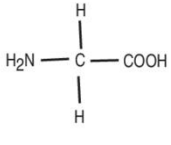
  Very large and complex proteinic structure: up to 1400 amino acids Triple helix

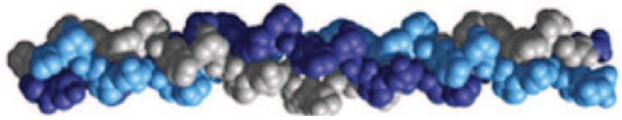
  Contains 19 different amino acids

  Dietary supplements, functional foods, super foods









COLLAGEN & GELATINE: BACKGROUND

- **Gelatine:**

  Polymer with a high molecular weight ~300.000 Da
  White, odourless and tasteless powder

  Hydrophilic properties: gelling, thickening

  Easy to digest, low calorific value (<4 kcal/g)

  Contains 18 different amino acids

  Dairy, bakery products, pet food

  Protects vitamins enriching food/feed from light and oxygen

COLLAGEN & GELATINE: BACKGROUND

For the production of collagen/gelatine intended for use in food:

- hides and skins of farmed ruminant animals
- "*derived from animals which have been slaughtered in a slaughterhouse and whose carcases have been found fit for human consumption following ante-mortem and post-mortem inspection*"

Section XIV, Annex III, Regulation (EC) No 853/2004

COLLAGEN & GELATINE: BACKGROUND

Regulation (EC) No 1069/2009

Category 3 material shall comprise the following **animal by-products**:

b) hides and skins, including trimmings and splitting thereof, horns and feet, including the phalanges and the carpus and metacarpus bones, tarsus and metatarsus bones, of…

ruminants which have been tested with a negative result in accordance with Article 6(1) of Regulation (EC) No 999/2001

n) hides and skins, hooves, feathers, wool, horns, hair and fur originating from dead animals that did not show any signs of disease communicable through that product to humans or animals, other than those referred to in point (b) of this Article

COLLAGEN & GELATINE: BACKGROUND

- Continue revision of the feed ban (TSE Road Map 2)
- 100.000 tonnes of foodstuffs containing ruminant collagen and/or gelatine currently go for disposal and therefore underutilized
- EU protein deficit due to EU legislation on TSE and food and feed controls.
- Assess the BSE risk posed to animals by the authorisation to feed non-ruminant farmed animals including fish with collagen and gelatine derived from ruminants

COLLAGEN & GELATINE: BACKGROUND

FEED

PAP and constituents of animal origin	Ruminants	Unweaned ruminants	Non ruminants	Aquaculture	Pets and fur animals
Ruminant PAP (ruminant blood included	UA	UA	UA	UA	A
Non-ruminant PAP	UA	UA	UA	A	A
Non-ruminant blood meal	UA	UA	UA	A	A
Insect PAP	UA	UA	UA	A	
Fishmeal	UA	A	A	A	A
Ruminant collagen and gelatine	UA	UA	UA	UA	A
Non-ruminant collagen and gelatine	A	A	A	A	A
Ruminant blood products	UA	UA	UA	UA	A
Non-ruminant blood products	UA	UA	A	A	A
Hydrolysed proteins from ruminants other than those derived from hides and skins	UA	UA	UA	UA	A
Hydrolysed proteins from non-ruminants	A	A	A	A	A
Hydrolysed proteins from ruminants derived from hides and skins	A	A	A	A	A
Di and tricalcium phosphate of animal origin	UA	UA	A	A	A
Milk and milk products	A	A	A	A	A
Colostrum and derivates	A	A	A	A	A
Eggs and egg products	A	A	A	A	A

UA: unauthorised; A: authorised.

COLLAGEN & GELATINE: TORS

ToR1

To estimate the cattle BSE risk (C-, L- and H-BSE) pose[illegible]e use of ruminant collagen/gelatine produced in accordance [illegible]ction XIV and XV of Annex III to Regulation (EC) No 853/2[illegible]**OOD)** in feed intended for non-ruminant animals including [illegible]ulture animals

ToR2

To estimate the cattle BSE risk (C[illegible]d H-BSE) posed by the use of ruminant collagen/gelatine cla[illegible]s Category 3 **(ABP)** as referred to in Article 10 of Regulatio[illegible] No 1069/2009 and produced in accordance with Regulat[illegible]) No 142/2011 for feed intended for non-ruminant animal[illegible]uding aquaculture animals.

Deadline: 30 September 2020

Thank you

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