

BLUETONGUE CONTROL STRATEGY, INCLUDING RECOURSE TO VACCINE

– A CRITICAL REVIEW –

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Summary: *The bluetongue epidemic that has prevailed in Europe since 2000 is the first example of continental spread of the bluetongue virus (BTV) in large naive populations of susceptible animals. Based on the results of intensive surveillance and research in countries of the southern Mediterranean that have been affected by the infection, a new strategy for prevention and control of the disease was developed to limit direct losses and to reduce the consequences due to movement restrictions. The basic innovations that were introduced were the use of mass vaccination of all domestic ruminant species to limit the spread of BTV and the use of intensive active surveillance to limit, as far as possible, the zone where movement restrictions must be applied. The novel strategy that was adopted dramatically reduced the number of clinical outbreaks and ensured safer animal trade. In 2006, a BTV-8 epidemic occurred in north-western Europe. During the first BTV-8 epidemic in 2006, affected countries adopted a 'wait and see' approach. No vaccination was implemented until 2008 and, in many instances, the movement of animals was authorised within restricted areas, thereby facilitating the spread of infection. Derogations to the ban on animal movements similar to those applied in southern Europe were applied in northern Europe, although the conditions that made such derogations applicable in the Mediterranean (the existence of mass vaccination programmes and the establishment of widespread serological and entomological surveillance network) were not always implemented. The delay in administering vaccination was due to the choice of avoiding the use of modified live virus (MLV) vaccines, although this type of vaccine performed satisfactorily in the previous bluetongue epidemics in southern Europe. This had also been recognised in the 2008 vaccine conference organised by the European Commission.*

Bluetongue has demonstrated that the infectious agents present in southern Africa can easily adapt to the Mediterranean Basin, which should be considered as a unique entity, as far as the epidemiology of animal diseases is concerned. Therefore, any effective strategy for the prevention and control of animal disease in Europe must take into account this reality and recognise the need for regional surveillance networks that include all the countries that border the Mediterranean.

Key words: bluetongue – BTV – Europe – vaccination

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Introduction

Bluetongue was first reported over 125 years ago with the introduction of Merino sheep to southern Africa. Since then, bluetongue virus (BTV) strains have been identified in many tropical and temperate areas of the world, but the disease is restricted to ruminants in the temperate zones. Little, if any, clinical disease is observed in the tropical and subtropical areas of the world, except when non-native ruminants are introduced into a virus-endemic area [72].

Several different epistystems have been recognised around the globe as relatively stable relationships between several distinct strains of BTV (virus topotypes), different species of *Culicoides* and susceptible vertebrate species, despite extensive and ongoing trade and movement of ruminants between individual epistystems [10].

In the countries historically affected by bluetongue, the control strategy was based on the vaccination of exposed sheep and on clinical and serological surveillance. All international movements of animals of susceptible species and their potentially infectious products from infected countries and zones were strictly forbidden unless they were demonstrated as non infected, after a specified period of protection by vector attacks in an insect-proof environment, as required by the World Organisation for Animal Health (OIE) standards that included bluetongue in former 'List A' diseases. Animal movements from infected countries or zones were possible, however, towards countries/zones where the absence of *Culicoides* spp. likely to be competent BTV vector was proven [52].

The international situation changed as of 1998 when the Mediterranean epistystem changed dramatically and the largest bluetongue epidemic ever recorded was recorded. This epidemic brought about a significant change of attitude towards bluetongue in several countries and the perspectives of bluetongue control have changed worldwide accordingly. The OIE standards on bluetongue also underwent considerable changes and a new chapter on bluetongue surveillance was introduced [55].

The aim of this paper is to describe the history of bluetongue in Europe and to describe how control strategies adopted at the beginning of 2000 to date have been modified in parallel to the evolution of knowledge on vectors and virus distribution as well as in connection with the implementation of vaccination. Changes made to the OIE standards and to European Union (EU) legislation are also briefly described.

1. The strategy of bluetongue control in Europe

In the eastern Mediterranean, a bluetongue epistystem has been recognised since the first half of the 20th century. Bluetongue became endemic in the eastern Mediterranean Basin [71] with sporadic spillovers in Cyprus, Greece, Spain and Portugal [41, 46, 58].

1.1. The evolution of epidemiology of bluetongue in the Mediterranean

Between the autumn of 1998 and winter of 2002, successive waves of bluetongue epidemics due to BTV-9 and BTV-4 were recorded in the Balkans, giving rise to a number of clinical outbreaks that caused severe direct losses in several countries, namely: Albania, Bosnia-Herzegovina, Bulgaria, Croatia, Greece, Kosovo, the Former Yugoslav Republic of Macedonia, Turkey and Yugoslavia [56]. These epidemics could be considered to be part of the evolution of the historic Middle East epistystem. The spread of the virus has been linked partly to animal movements and partly to the spread of vectors by proximity [8, 56].

In December 1999, a completely new epistystem developed in the Mediterranean Basin.

In the central and western Mediterranean Basin BTV-2 was recorded in the north and east of Tunisia, from where it spread to Algeria during the summer of 2000 [40]. At the same time, BTV-2 appeared for the first time in Italy (Sardinia) [8] and France (Corsica) [54]. Spain was also affected (Balearic Islands) [39].

In November 2000, BTV-9 was isolated in the region of Calabria in Italy [8].

The infection of these Mediterranean countries rapidly became the largest bluetongue epidemic ever recorded both in Europe and North Africa [8].

The introduction of bluetongue to Sardinia and the Balearic Islands from the movement of animals or animal products has never been proved and appears unlikely. Introduction of BTV from one area into another by the transportation of animal products (semen, embryos), by inanimate (aeroplanes, ships) appears unlikely considering the pathogenesis of BTV infection and the nature of the vector. Therefore, it has been hypothesised that BTV-2 most probably entered Sardinia and the Balearic

Islands through passive windborne transport of infected vectors from BTV-2-infected regions of North Africa. Several dust storms from North Africa reached southern Italy and the Italian islands between June and July 2000; one of these reached Sardinia 25 days before the first reported case of bluetongue [8].

Subsequent waves of different BTV types (BTV-1 and BTV-4) occurred in southern Europe and spread on fairly regular and similar pathways. As an example, the spread of BTV-4 in an unvaccinated ruminant population in 2003 in Sardinia closely resembled the pattern and rapidity of spread of BTV-2 in the same population in 2000 [32]. The sole exception was BTV-16 the spread of which modified after entering Italy after the use of a modified live virus (MLV) vaccine that was eventually demonstrated to be inadequately attenuated.

At the end of 2006, a totally new Mediterranean episystem was created, in which the western episystem of African origin and the eastern episystem of Asian origin had merged into one. In 2007, BTV-8 eventually entered this episystem to form what might now be defined as the 'Euromediterranean bluetongue episystem'.

1.2. Bluetongue control strategy in Europe in 2000

Europe was not fully prepared to face a vector-borne epidemic of the magnitude of the bluetongue epidemic that started in 2000 in the Balkans and in central and western Mediterranean [32].

In the European Union, the strategy of bluetongue control was essentially based on stamping-out (as had been the case for most other OIE List A diseases, such as rinderpest, lumpy skin disease and other diseases). Vaccination was considered as a complementary measure to stamping out, to control direct losses and to limit the spread of infection. Veterinary legislation at the time reflected this strategy and Directive 92/119/EEC [24] only prescribed direct control measures that included the demarcation of a 3-km radius protection zone and a 10-km radius surveillance zone around each infected farm as well as the slaughter of all susceptible animals on the farm and possibly on neighbouring farms.

The situation was modified rapidly in the autumn of 2000 with Directive 2000/75/EC, as it became obvious that stamping-out was absolutely inadequate to deal with a vector-borne disease such as bluetongue, and the slaughter of all susceptible animals in the entire infected and at-risk areas was not considered an alternative.

The basic control strategy was based on strict movement controls of the susceptible animals from zones considered infected and vaccination was limited to sheep that were exposed in the protection zones. Intensive clinical, serological and entomological surveillance were used to define the areas that were subject to movement restrictions [33]. This strategy and legislation were both coherent with the OIE standards applicable at the time.

Restriction zones

EU Council Directive 2000/75/EC [25] considered three levels of zones in which movement restrictions should be applied, namely: a 20-km radius zone; a protection zone that included the infected zone and with a radius of at least 100 km around the infected holding in accordance with the OIE *Terrestrial Animal Health Code* standard; a surveillance zone with a radius of at least 50 km that extended beyond the limits of the protection zone.

In the **20-km radius zone**, all holdings had to be subjected to regular visits and, on each occasion, animals had to be examined clinically and pathology and laboratory tests were conducted to confirm the disease. A complete standstill of susceptible animals was to be applied to and from the holdings.

In the **protection zone**, an epidemiological surveillance programme had to be implemented, based on the serological and entomological monitoring of sentinel ruminants and vector populations, respectively. Animals in the protection zone were banned from leaving the zone unless it could be proved that the virus was not circulating. Vaccination could be applied depending on different scientifically justifiable strategies.

In the **surveillance zone**, measures similar to those in the protection zone had to be implemented, with the exception of the administration of vaccines which was prohibited.

The limitation of the movements of susceptible animal populations over a long period of time is very hard to impose. In particular, in case of diseases such as bluetongue, stakeholders and local veterinary

service had great difficulty in understanding why individual animals that were clearly not infected by the most sophisticated laboratory testing could not be moved freely to and from restricted areas.

In some cases (for instance in the south of Italy), livestock production was severely affected by these movement restrictions that affected century old customs, such as the seasonal grazing patterns. The measures were imposed to protect susceptible ruminant populations in free areas of the north of Italy and the rest of Europe.

Farmers were further frustrated because nobody was able to tell them when the situation might change and they had no possibility of doing anything to solve the problem.

The situation soon became unsustainable from the economic, social and political points of view.

1.3. Development of a new strategy

1.3.1. The quest for new tools

New tools had to be found to implement a strategy that would limit both direct losses and indirect losses due to movement restrictions. International standards had to be taken into account, as well as the need to protect susceptible animal populations in the free zones. A further constraint was the need to produce sufficient scientific data to justify the choices made.

An intensive surveillance and research effort had been launched since 2000 in the individual affected EU member states to identify vector presence, abundance and dynamics as well as establish BTV epidemiology in the European context [4, 30, 32, 38, 56, 63]. While these studies were able to describe the epidemiological evolution of bluetongue in Europe, they also demonstrated the existence of other competent *Culicoides* spp. vectors besides *C. imicola*. In particular, the *Obsoletus* complex [64, 70] was demonstrated as playing a significant role in BTV transmission in some areas. The latter findings provided a clear warning of the possibility of the further expansion of bluetongue well above the 40°N indicated by the OIE standard as the most northerly distribution limit, into northern Europe, which indeed happened later. They also demonstrated that BTV could readily infect new areas through the movement of animals from infected zones when inappropriate risk mitigating measures were applied [33]. This might seem to contradict reports by some authors [45, 73], but the difference is likely to be due to the fact that while the latter reported on rather stable epizootics, a new system was developing in Europe, into a typically dynamic situation.

In addition, further studies were conducted on the efficacy of different chemical compounds to treat livestock to protect them from *Culicoides* attacks [8, 13] or to treat larval breeding sites or adult resting areas with an aim to significantly reduce the vector population [62]. Although a certain level of efficacy was recorded experimentally after the application of some pyrethroid-based products, the limitations did not enable basing any control strategy on direct control measures against *Culicoides*. The use of these compounds, therefore, was limited during animal transportation, as an ancillary measure to reduce the probability of infection. The same results have recently been confirmed also in a comprehensive review [28].

In 2000, only MLV vaccines were available. The efficacy of these vaccines in protecting sheep from the disease had been proved extensively in other continents although reservations existed on their safety [73]. No experience existed in the use of bluetongue vaccines in cattle and data on their efficacy in blocking viraemia in sheep was scarce. Several studies on vaccination were performed to assess the level of protection against disease and infection in susceptible species. Both controlled and field studies on the vaccination of cattle, in particular, were conducted to assess whether vaccination would block viraemia and whether MLV vaccines affected either reproduction or milk production or had any adverse effects on the foetus [35, 42, 48, 49, 50, 64, 66, 69]. Several studies were also performed to assess the effect of MLV vaccine on milk production in sheep during lactation as well as other adverse effects [7].

The results of these studies encouraged the development of a new bluetongue control strategy.

The effort of the researcher workers in performing these studies should be highlighted. Much time was devoted to this work with meagre financial resources which was a significant constraint; apart from a few enlightened government agencies, traditional research bodies, including those of the EU, did not consider bluetongue to be a research priority at that time.

1.3.2. The new strategy design

A new strategy had to fulfil two mandatory objectives, as follows:

- 1) limit virus circulation in the environment to reduce the extent of the protection and surveillance zone and thus facilitate thus the movement of animals;
- 2) immunise animals to ensure they were resistant to wild virus infection and did not contract disease or introduce infection to susceptible free populations.

The strategy did not consider the possibility of eradicating BTV, although the results of mass vaccination, when correctly applied, demonstrated the disappearance of circulating BTV, as was the case in the Balearic Islands which were declared free from BTV-2 and BTV-4 in 2006 [22], or in Tuscany, where Massa Carrara, Pisa, Livorno and Grosseto Provinces were declared free from BTV-2 infection in 2005 [19], 2006 [21], and 2008, respectively.

While a strategy that was solely based on direct control measures (movement restrictions) did not appear capable of limiting the spread of infection effectively when ruminant and midge population densities and dynamics were able to sustain BTV circulation, a control policy based solely on vaccination of sheep did not seem appropriate to meet the objective of the new strategy either.

Voluntary vaccination of sheep only, as practised in most areas of the world, such as Australia, South Africa and United States, reduces losses incurred by disease and, in cases of low densities of other susceptible species, might also lead to a marked reduction in virus circulation. When a large bovine population exists, however, a cycle between cattle and vectors develops, irrespective of whether sheep and goats are present and BTV may establish itself in the area. Therefore, neither a strategy based on direct control measures alone, nor a strategy based solely on the vaccination of sheep and goats, appeared appropriate to reduce virus circulation and, consequently, to lift movement restrictions while ensuring the safe trade of susceptible animals [11]. On the contrary, a control strategy based on the vaccination of the entire susceptible domestic ruminant population could have induced sufficient population immunity levels that would meet the objectives considered above [11].

Webster *et al.* [73] described the potential vaccination strategies for bluetongue control to include the following:

- 1) vaccination of cattle only;
- 2) vaccination of both sheep and cattle;
- 3) vaccination of sheep only;
- 4) no vaccination.

In Europe the strategies adopted until 2003 were as follows:

- 1) direct control measures (movement restrictions) without vaccination, such as those adopted in Greece;
- 2) vaccination of sheep only adopted in the Balearic Islands and in Corsica [57], together with movement restrictions outside the affected area.

Italy proposed an innovative strategy to the EU based on the analysis of both data generated by controlled experiments and factual field data collected by intensive serological and entomological surveillance. The choice of the new strategy was made after assessing (in the spring of 2001) the range and magnitude of consequences without vaccination or vaccinating all susceptible domestic livestock (cattle, sheep and goats) or just sheep and goats in affected areas [33].

In the absence of a vaccination strategy, a quantitative assessment estimated the spread of infection to the free regions of Italy within 4-6 months from the beginning of the new epidemic season. Vaccination, on the contrary, could reduce both direct economic losses and virus circulation significantly. To achieve a significant reduction in virus circulation, however, at least 80% of the BTV-susceptible populations had to be immunised to reach the goal of reducing the number of secondary cases to less than 1% of that expected to occur in the absence of vaccination [33].

Directive 2000/75/EC only considers the possibility of vaccination in the protection zone and does not provide specific criteria on the design of vaccination campaigns. Therefore, each EU member state had to decide whether to vaccinate or not and to design and implement its own vaccination strategy. The veterinary services of Italy decided to mass vaccinate all domestic BTV-susceptible species (sheep, goats and cattle) with the MLV vaccine types against the wild BTV strains circulating in the various zones of the country, as revealed by the intensive surveillance programme that was launched in 2000.

The strategy proposed by Italy and finally approved by the EU was to associate vaccination, considered insufficient *per se* to ensure effective control of BTV, with intensive surveillance, based on the inclusion of serology, virology and entomology capable of recognising the presence and type of circulating viruses as well as the vector species involved and to define, with the highest possible level of precision, the effective spread of virus circulation [11].

Strict movement controls of susceptible animal were maintained but one of the consequences of the new strategy that combined mass vaccination and intensive surveillance was the reduction of the restriction zones from three to one. Systematic intensive clinical and serological surveys of all susceptible animals, first in a 20-km radius and then in a 4-km radius around any observed cases that revealed positive serology was performed in 2002 and 2003. It demonstrated that in vaccinated populations, the circulation of BTV could only be very limited within the infected herd. As a consequence, the infected zone of 20 km was maintained as the sole area of restriction for 60 days when clinical and serological monitoring of all susceptible ruminants in an area of 4 km around the first evidence of virus presence gave negative results.

1.3.3. Results of the new strategy

Reduction of bluetongue virus circulation

The validity of the model proposed by risk analysts can be easily inferred by observing the data of vaccination relative to Italy, Corsica and Spain, as well as the development of BTV spread in some European countries and regions.

The structure of the ruminant populations and certain local situations in Italy made it very difficult to reach the target of 80% population coverage unless cattle were also vaccinated. Therefore, Italian legislation required the vaccination of all domestic ruminants (cattle, sheep and goats). Only two regions of Italy met the objective of vaccinating at least 80% of their populations against BTV-2 (namely Sardinia and Tuscany). In these two regions, very low levels of bluetongue infection were recorded in 2002 compared to 2001 (Table 1). A total of 24 cases were reported in Sardinia and no case in Tuscany. Clinical surveillance data were confirmed by serology on sentinel animals, as follows: in Sardinia 25 out of 4,393 and in Tuscany 5 out of 691 sentinel animals revealed positive serological reactions in 2002, respectively [33]. On the contrary, BTV spread widely in the southern regions that did not even get close to the established target of vaccinated population.

Table 1.– Results of vaccination campaigns in some regions of Europe

Country	Region	Year before vaccination ⁽¹⁾				Year of first vaccination campaign ⁽²⁾			
		Diseased sheep	Flocks with diseased sheep	Vaccination target species	Vaccin. coverage (%)	Diseased sheep	Flocks with diseased sheep	Vaccination target species	Vaccin. coverage (%)
Italy	Sardinia	239 178	6 090	Sheep, goats, bovines	0%	24	6	Sheep, goats, bov.	>80%
	Tuscany	693	158	Sheep, goats, bovines	0%	0	0	Sheep, goats, bov.	>80%
	Campania	3	1	Sheep, goats, bovines	0%	1 568	238	Sheep, goats, bov.	<60%
	Other southern regions	10 357	496	Sheep, goats, bovines	0%	776	76	Sheep, goats, bov.	<60%
Spain	Balearic Islands	5 455	NA	No vaccin.	No vaccin.	0	NA	Sheep	78.3%
France	Corsica	2 765	NA	No vaccin.	No vaccin.	13 141	NA	Sheep	65.1%

(1) Italy (2001), Spain (2000), France (2000)

(2) Italy (2002), Spain (2001), France (2001)

NA data not available

In the Balearic Islands, two of the four islands, Majorca and Minorca, were affected in the epidemic that occurred in the summer of 2000. Sheep and goats represented 88% of the BTV-susceptible population of the islands. Mass vaccination of sheep and goats was performed; 78.3% of the total susceptible animal population were vaccinated. In 2001, no case of bluetongue was reported ([Table 1](#)). In 2003, a new incursion of bluetongue due to BTV-4 affected the islands and a further vaccination campaign of all sheep with MLV vaccine was implemented.

Mainland Spain was affected by an epidemic of BTV-4 in 2004. The vaccination of all sheep and cattle that had to be moved was performed during the first year with MLV and with inactivated vaccines thereafter. No BTV-4 virus circulation occurred in 2007 and levels were very low in 2006.

In 2000, BTV was reported for the first time and vaccination was performed, covering 65.1% of the total sheep and goat populations (Report of the *Rencontre des services vétérinaires bilatérale France-Italie* held in Ajaccio on 25 September 2001). As expected, the spread of infection was uninterrupted and, in 2001, 13 141 new cases were reported in sheep ([Table 1](#)).

Portugal was involved in the 2004 epidemic of BTV-4 that affected in the Iberian peninsula. Likewise, in Spain, vaccination of all sheep and cattle to be moved was performed with MLV and inactivated vaccines. There was no circulation of BTV-4 in 2007.

Restoration of animal trade

The novel strategy adopted in the Mediterranean EU member states led to both a dramatic decrease in the number of clinical outbreaks and to a significant reduction in BTV circulation. Therefore, it has led to safer animal trade as shown by the data on animal trade in Sardinia. Before the epidemic of bluetongue, Sardinia was involved in intensive cattle trade to continental Italy, particularly to the northern regions. Due to the bluetongue epidemic and the enforcement of existing legislation since August 2000, trade came to a complete standstill. Trade was resumed in 2002 after mass vaccination and a total of 1,019 animals were shipped to continental Italy, 92% of which, during the last two months of the year. During the first six months of 2003, a total of 3,097 animals were sent from Sardinia to continental Italy, compared to a total of 8 animals in the same period of 2002 [11]. No BTV-2 has ever been recorded in the regions from where most of Sardinian cattle were shipped. Subsequently, all exports were again interrupted due to the presence of BTV-4.

As soon as the surveillance data collected after the mass vaccination became available, a new risk assessment was conducted, taking into account the results obtained from mass vaccination [33]. The analysis led the European Commission to:

- 1) authorise domestic movements of vaccinated animals directly for slaughter when at least 80% of the susceptible populations had been vaccinated in the area of origin [14];
- 2) develop a new approach to the definition of areas subjected to movement restrictions, with a significant reduction in the restricted areas when at least 80% of the susceptible population had been vaccinated;
- 3) allow countries to despatch vaccinated slaughter animals from 'lower risk areas' —even with active infection— and from 'higher risk areas' where viral circulation had not been detected to free areas within their national territory [15];
- 4) modification of the demarcation of the 20-km protection and surveillance zones by merging these into a single restricted zone [16, 18].

All of this legislation was based on scientifically documented information that had been examined by the Standing Committee of the Food Chain and Animal Health, in accordance with the specific procedures stipulated in Directive 2000/75/EC. In all of these amendments, vaccination of both animals to be moved, their population of origin and a risk assessment were specifically considered as conditions for derogation from the Directive's no-movement provisions from restricted zones.

Adverse events observed in the use of live virus attenuated vaccines

A possible drawback of the use of MLV vaccines for the control of bluetongue is the possibility that the vaccine virus crosses the placental barrier causing infection of the foetus and consequent abortion, stillbirth or neonatal mortality [29].

To evaluate possible adverse effects of vaccination with MLV vaccines, a number of preliminary studies were conducted prior to and during the initial phases of the bluetongue mass vaccination campaign. No adverse effects on reproduction (abortion or teratogenic defects) were observed in cattle immunised with the monovalent BTV-2 vaccine, or bivalent BTV-2 and BTV-9 vaccine, either in controlled or in field conditions [42, 48].

The only effect on milk production was a transient 30% decrease in production that lasted for about a week after vaccination with bivalent BTV-2 and BTV-9 vaccine to sheep [67, 68]. In Sardinia, a study involving more than 18,000 dairy cows in 220 herds vaccinated with BTV-2 MLV did not demonstrate any negative effects either on the quality or quantity of milk produced [35].

Adverse vaccination effects (deaths, abortions, stillbirths) were monitored in the field by collecting information on adverse vaccination effects (type of damage observed and dates of vaccination) and collecting samples from the animals to detect and identify both vaccine and field strains of BTV. During the first vaccination campaign in Italy, 312 of 87,245 holdings on which vaccination was performed, notified adverse effects, representing 0.16% of cattle herds and 0.50% of small ruminant flocks vaccinated. In 47 of these holdings (0.01% of vaccinated cattle herds and 0.09% of vaccinated sheep and goats flocks), the presence of vaccine virus was confirmed by the laboratory.

As a purely indicative quantitative assessment of the adverse event observed, one can examine data collected between 1991 and 2001 in the United States by the Vaccine Adverse Event Reporting System (VAERS). During the study, 1.9 billion doses of 27 different types of human vaccine were administered and the prevalence of adverse events was 11.4 per 100,000 (equivalent to 0.01%) [74].

A possible further drawback of the use of MLV vaccine is the possibility of reversion to virulence of the vaccine viruses and reassortment between vaccine and field strains of the virus [26].

The spread of BTV-16 in Italy has been used as an indication of reversion to virulence of a MLV vaccine [5, 60]. While it is true that the BTV-16 strain used in the vaccine and the virus isolated in the field appear to be the same virus [5, 59], the phenomenon does not appear to be due to reversion to virulence of the vaccine strain, but rather to an insufficient attenuation process of the virus used in manufacturing the vaccine [1, 26].

The reassortment of BTV strains has been monitored constantly in Italy over the last eight years. No reassortment between vaccine and field strains has been observed, while it has been witnessed between vaccine virus strains present in the same vaccine [51]. In addition, the reassortment suggested in a BTV-16 strain isolated in Italy has been attributed by the authors [5] to the reassortment of two vaccine strains. This latter evidence is particularly strange as the virus was isolated when BTV-16 vaccines had not yet been used in Italy. It appears odd that reassortment did not generate a number of BTV serotypes that far exceeded the 24 presently known serotypes and that a constantly changing pattern of the pathogenicity of virus strains was not observed. The segments of the genome that code for the virus structures determining its antigenic and pathogenic characteristic might be influenced by reassortment on very rare occasions, if ever at all.

Claims of the factual dangers of the use of MLV vaccine against bluetongue due to either reversion to virulence of the vaccine viruses and reassortment between vaccine and field strains of the virus [61] remain hypothetical for the time being and are not supported by factual scientific data.

Effects of the 1999-2002 epidemic on international bluetongue standards

The evolution of bluetongue in the Mediterranean had a considerable effect on the international bluetongue scenario. The epidemiology of bluetongue worldwide was considered fairly stable and, apart from extending the infective period, the international OIE standards remained almost unchanged since the previous modification in 1993, following the Second International Symposium organised in Paris by the OIE in 1992 [53].

The changes in the bluetongue situation in the Mediterranean prompted the OIE to organise the third International symposium on bluetongue that was held in 2003 [43, 44]. The recommendations of the symposium led to significant changes in OIE standards. In addition to extending the limit of the northern latitude to 50°N, the possibility of freely moving seropositive and vaccinated animals was also recognised. The infective period was reduced and standards for bluetongue surveillance were introduced, together with a case definition of bluetongue.

These standards remain unchanged, despite the thorough review of the situation at a special meeting of the *ad hoc* group on bluetongue held in Paris in October 2006, after the BTV-8 incursion. No significant amendment to the bluetongue chapter of the *Code* has been proposed recently.

2. Incursion of bluetongue virus serotype 8 into Northern Europe

In August 2006, a new BTV serotype (BTV-8) was detected in the Netherlands. The infected area was close to the borders with France, Belgium and Germany where cattle population densities are between 2 to 5 times the EU average [3] (Table 2).

Table 2.– Cattle population in the countries affected by the epidemic of bluetongue virus serotype 8

		Cattle population (head)	Surface (km ²)	Cattle density (animals/km ²)
Countries first affected in 2006	Belgium	2 573 400	30 300	84.9
	Netherlands	3 820 000	33 800	113.0
	Germany	12 608 500	357 000	35.3
	Luxembourg	193 100	2 600	74.3
Countries first affected in 2007	France	19 123 800	544 000	35.2
	United Kingdom	10 078 000	243 800	41.3
European Union		88 750 800	4 215 100	21.1

It is uncertain how BTV-8 reached north-western Europe, but the absence of BTV-8 circulation in the Mediterranean Basin suggests that it was not a simple linear extension of earlier outbreaks but was probably introduced by a distinct route and mechanism [27]. Sequence analyses of Seg-2 from the Dutch isolate demonstrated that the virus originates in a western lineage from sub-Saharan Africa but is distinct from the BTV-8 vaccine strain (http://www.iah.bbsrc.ac.uk/dsRNA_virus_proteins/BTV-8-Seg-2-tree.htm; http://www.iah.bbsrc.ac.uk/dsRNA_virus_proteins/ReoID/btv-8.htm; http://www.reoviridae.org/dsrna_virus_proteins/ReoID/BTV-mol-epidem.htm).

In 2006, the disease was observed in Belgium, Germany, Luxembourg, the Netherlands and France and a total of 2 047 outbreaks (clinical outbreaks) were reported. In 2007, the infection spread rapidly and extensively across France (15,379 outbreaks) and Germany (11,485 outbreaks) and reached Denmark, the Czech Republic, Switzerland and the United Kingdom. A total of 40,919 clinical outbreaks due to BTV-8 were notified in the affected countries. From January to 31 July 2008, a total of 6,082 BTV-8 outbreaks were reported in France (5,995), the United Kingdom (68), Spain (11), Italy (5), Switzerland (2) and the Czech Republic (1).

The cessation of BTV circulation in some areas and the high number of outbreaks in others (i.e. France) during the winter of 2008 may be linked to the different interpretations by EU member states of the definition of 'bluetongue outbreak' in EU legislation. Until October 2007, EU provisions had not taken into account the case definition of the OIE *Code* and notification was consequently focused on clinical evidence. Although EU Regulation (EC) 1266/2007 [23] has a definition of outbreak that differs slightly

from the OIE standard, it has adopted the OIE standard definition of a 'case' of bluetongue. Some difficulties, however, in the notification of cases still exist because some member states notify cases only if virus circulation is considered active either upon clinical observation or laboratory testing, whereas others notify cases on the basis of positive serology without any further consideration of virus circulation.

2.1. Bluetongue control strategy in Northern Europe

In 2006 a 'wait and see' approach [73] was adopted during the first BTV-8 epidemic by the countries affected, apart from movement restrictions imposed by France. It is possible that some northern Europe experts who lacked recent practical experience with bluetongue were not convinced at the end of 2006 of the possible re-emergence of BTV-8 after the 2007 winter season, notwithstanding the experience of southern Europe.

When the second BTV-8 epidemic commenced in 2007, no effective structured surveillance network was in place in northern Europe to detect BTV infection. The definition of restricted zones (protection and surveillance zones), therefore, was made following the notification of clinical cases and this made the preparation of up-to-date picture of the spread of BTV very difficult.

No vaccination was implemented and, in certain instances, the movement of animals at risk was permitted within the restricted areas, thereby facilitating the spread of infection [47]. Derogations to Directive 2000/75/EC, similar to those applied in southern Europe were applied in northern Europe, although the conditions that made such derogations applicable in the Mediterranean (the existence of mass vaccination programmes and the establishment of a widespread serological and entomological surveillance network) were not always present. These animal movements and the absence of vaccination might well explain the rapidity and the extent of BTV-8 spread that was resembled what happened in Sardinia in the absence of vaccination in the first four weeks of the 2000 epidemic. Furthermore, it must be noted that in northern Europe the spread in one year affected a geographic area that was larger than that affected over eight years in the Mediterranean where vaccination, surveillance and animal movement controls had been applied [31].

2.1.1. Restricted zones

Since the beginning of the epidemic of BTV-8 (when disease was detected), a single restricted zone was created in most affected member states; others maintained the three areas (20-km, protection and surveillance zones) during the first epidemic 'wave', thereafter moving to the approach of the 'single restricted zone'. This complied with the provisions of Decisions 2003/828/EC and 2005/393/EC that authorised such an approach in the countries of southern Europe.

The adoption of single restriction zones in many member states affected by BTV-8 was automatic. The 20 km, protection and surveillance zones were merged and standstill measures limited in southern Europe only after the implementation of surveillance systems and the mass vaccination of susceptible species. Changes to the restrictive levels between territories in southern Europe were based on a risk analysis that evaluated the effects of vaccination [36], sensitivity of sentinel systems [9] and probability of BTV spread by animal movements [33].

The adoption of a single restriction zone within which animals could move freely in the absence of effective risk mitigating measures, in some cases meant that potentially viraemic animals moved to the borders of the restricted zone and could have considerably altered the effectiveness of the preventive value of the restrictions applied.

In October 2007, the approval of Commission Regulation (EC) 1266/2007 [23] introduced important criteria to harmonise surveillance and reporting of the BTV. The regulation also introduced two important changes to the animal movement restrictions that had previously been stipulated in Decision 2005/393/EC, namely:

- 1) removing the required approval of the member state of destination in case of movements of animals from the restricted zones of another member state;
- 2) eliminating *de facto* the standstill measures on animal movements within restricted zones for animals with clinical signs of bluetongue.

The risk of BTV spread by animal movements was further increased by the use of insecticides/repellents as a means to fulfil the obligation of protecting animals against attacks of midges.

In compliance with the OIE standard, Regulation (EC) 1266/2007 introduced the possibility of moving animals from restricted zones after keeping them for a given period 'protected from the attack from *Culicoides* likely to be competent BTV vectors'. This possibility had existed since 2001 and 'protection' had been previously been interpreted as keeping the animals in insect-proof premises, such as quarantine stations. Insecticides/repellents were used only to protect the animals for short periods of time during transport. In several countries affected by BTV-8, the use of insecticides/repellents instead was considered to be an effective stand-alone method for long-term protection of the animals against *Culicoides* attacks.

Furthermore, the idea that simply the use of insecticides/repellents associated with individual animal testing for virus could be sufficient to certify animals from restricted areas as safe for trade, complicated matters further. The lack of effectiveness of these assumptions (already anticipated by a number of experts), was demonstrated by the events that occurred in Italy from August 2007 to February 2008. During this period, 624,741 cattle were introduced from the infected countries. They were introduced in accordance with the provisions of Regulation 2007/1266/EC, including animals that gave negative results to the polymerase chain reaction (PCR) and that were protected from *Culicoides* attack by using insecticides for 60 days prior to the date of shipment. The Italian Veterinary Services traced and tested 64,295 of these animals and 280 of them, located on 86 farms, were found to be positive by the PCR test. BTV-8 was isolated in 32 animals on 20 farms located in the four regions of Italy [37]. At the end of March 2008, the first outbreak of BTV-8 was detected in northern Italy (Verona Province), providing a further field demonstration of the risk posed by unsafe animal movements.

According to the OIE standards for bluetongue, animals from infected zones can be traded freely in the so-called 'seasonally free' periods of the year in which 'surveillance demonstrates no evidence either of BTV transmission or of adult *Culicoides* likely to be competent BTV vectors' either in the country of origin or in the country of destination or in both. In Europe, this was used extensively with considerable success since 2001. It was applied as part of the strategy of bluetongue management and control, following intensive investigations on the species of bluetongue potential vectors, areas of distribution and seasonal population dynamics. In northern Europe, the same strategy was applied without the full knowledge of *Culicoides* population dynamics although it was demonstrated that some of the *Culicoides* species involved in BTV transmission were different from those recorded in southern Europe and might, therefore, have different seasonal patterns [1, 20]. Therefore, common sense, expertise and experience were required to successfully implement the solid principles underlying EU legislation and OIE standards.

2.1.2. Vaccination policy

Another important difference in the BTV management strategy between southern and northern Europe has been the timeliness of vaccination of susceptible populations. The BTV-8 epidemic commenced in 2006 and no vaccination was performed during the first two epidemics up until the end of 2007, despite of the availability of a MLV vaccine against BTV-8.

In January 2008, a conference on bluetongue vaccination strategies was organised in Brussels and the very valuable expertise acquired by the southern member states affected by bluetongue, especially in regard to the successful use of vaccination using both MLV and inactivated vaccines was acknowledged. It also recognised that the use of any of both types of vaccine was better than experiencing the disease and it would be hard to justify adopting the 2007 approach when controlling the disease in 2008, given the availability of vaccines.

While the local epidemiological situation largely influences the choice of the most adequate type of vaccine and vaccination strategy, it is clear that there is no scientific, economic or management justification to exclude the use of any of the existing vaccines for emergency vaccination that should be performed within the existing EU legal framework for bluetongue control and eradication, as is the case for any other former OIE List A diseases.

In conclusion, emergency mass vaccination has been recognised as the most efficient strategy, taking into account the current EU situation and the European Commission has clearly stated that its strategy with regard to bluetongue is mass vaccination with all available vaccines. The EU Commission has also made available substantial funding for vaccination campaigns in member states.

At present, all EU member states infected by BTV use vaccination as a tool to control the disease. Only inactivated vaccines are used but Italy also uses BTV-1 MLV vaccine in addition to inactivated vaccines against the other serotypes present. Several vaccination schemes are implemented in the various member states. Voluntary vaccination of cattle and sheep is implemented in the United Kingdom and the Netherlands, while mandatory vaccination is performed in Belgium, Denmark, France, Germany, Italy, Luxembourg, Portugal and Spain. No country in Europe outside the EU is vaccinating against bluetongue, at present, but in Switzerland, vaccination of cattle, sheep and goats against BTV-8 is compulsory.

The EU vaccination strategy, in line with the legislation in force, does not envisage the protection of zones free from the disease that are at particularly high risk of BTV introduction. Vaccination can be implemented in restricted zones only. It would appear, therefore, that it is used more as a tool to reduce direct losses in the animal populations of infected zones and to facilitate trade of the animals of the same zones, than to limit the spread of infection to free susceptible animal populations in contiguous to infected non-restricted zones.

2.1.3. Surveillance and the information system

When bluetongue was limited to the Mediterranean countries of Europe, the origin of the incursions in EU member states was generally beyond the EU.

The intra-European transboundary spread of bluetongue, until 2006, has only been documented from Sardinia to Corsica [59] and suspected from Greece to Italy [32, 33], probably because the effort made by affected individual countries had limited the spread of infection within each country. The need to harmonise national information systems and the implementation of an integrated bluetongue information system was not considered necessary to be compulsory by neither the EU or by the member states until BTV-8 spread to northern Europe. In 2007, the European Commission decided to establish a mandatory Web-based surveillance network to collect, store and analyse bluetongue surveillance data [23].

This Web-based surveillance network (BTNET: bluetongue network) is a Web-based geographic information system (GIS) that is able to collect, store, and analyse bluetongue surveillance data. It has been developed in a similar network that was coordinated by the OIE in several countries of the Balkans and consists of two components, namely: one supranational and one national that can be used as a stand-alone element or can be integrated.

The EU-BTNET offers a visualisation system for the retrieval of technical, scientific, legislative and epidemiological information on bluetongue. Information is presented in map, tabular, graph and text formats.

Data from the official Animal Disease Notification System (ADNS) of the EU are used to illustrate BTV occurrence in EU member states. In addition, information collected from the OIE World Animal Health Information System (WAHIS) complete the picture for the rest of the European continent and Mediterranean Basin. The geographic distribution of bluetongue infection is presented according to the localisation of outbreaks, when the information for each single outbreak and its geographic coordinates are available (i.e. for ADNS-derived data and WAHIS immediate notifications). Therefore, the outbreak database is structured to collect and store data from both ADNS and WAHIS.

Data on the serological and entomological surveillance as well as on vaccination in EU member states are entered by each competent authority of the member states.

2.2. Lessons learnt

The following lessons can be learned from the recent experiences:

- 1) The fact that the infection did not cause any symptoms in cattle and that some serotypes did not cause severe disease in the sheep complicated matters because bluetongue, apart from some zones where it caused significant disease in sheep, eventually began to be seen as a 'minor' disease. Therefore, most animal owners and veterinarians had great difficulty in accepting the burden of the control strategy. They considered that it was unjustified because it imposed measures that were considered disproportionate to the relative gravity of the disease and they considered there was no reason to limit movements of animals that were healthy and

uninfected, in a context in which animal movement was both essential for the livelihood of properties and an historical animal husbandry practice.

- 2) Increasing numbers of animal owners and veterinarians convinced themselves that a 'wait and see' policy that allowed the spread of infection would be the choice strategy. They reasoned that if infection became endemic, movement controls would have no value and free animal movements could be resumed. Therefore, they regarded the use of vaccines as an obstacle to the spread of infection and to what they perceived as the solution to their problem. Before vaccination could be demonstrated as being capable of avoiding both the direct losses incurred by sheep farmers and the indirect losses incurred by both sheep and cattle owners due to movement prohibition, the attitude to avoid vaccination prevailed in many areas. Vaccination was recognised as necessary only in the zones where bluetongue had caused severe losses in sheep.
- 3) A further problem arose due to the difficulty of having good quality vaccines in the quantities required and in sufficient time to perform vaccination during the seasons in which wild virus did not circulate. Furthermore, farmers who did not receive compensation for indirect losses incurred by movement restrictions, began to attribute all kinds of adverse effects to the vaccine that were largely exaggerated in relation to those that did effectively occur. The fact that cattle were vaccinated for the first time in the world against bluetongue and that MLV vaccines were used complicated matters further. These two latter aspects, in particular, were emphasised with a score of opinion sought and given by experts who opposed both the vaccination of cattle on the grounds of this being unheard of and the use of MLV vaccines on the grounds that these vaccines were dangerous.
- 4) The need for an effective communication campaign on the strategy chosen was underrated and no effort was made to activate coherent risk communication directly involving farmers, other stakeholders and politicians. Furthermore, there was sufficient time to inform and train veterinarians adequately, in particular those working as official field veterinarians. They were the people who had the greatest difficulties as they had to implement measures that they did not fully understand. It was incredibly difficult to grasp the scientific reasoning behind the fact that BTV was an infection that affected 'territories' rather than individual animals or farms. Even today, after eight years, much difficulty still remains in some areas in understanding why official veterinary measures must be based on monitoring a territory rather than individual animals or on herd testing results.
- 5) The spread of BTV-8 in northern Europe indirectly confirms the validity of the strategy applied in southern Europe. The virus introduced in a yet unexplained manner after fifteen months has spread across eleven countries and over 750,000 km². It has infected an area larger than the sum of all the areas infected in eight years by all the other five BTV types, affecting four countries of southern Europe.
- 6) The possibility of a new incursion of BTV from other epizootic systems is an ever present threat. The most likely paths would be the same experienced with the viruses currently circulating, namely: the Middle East and North Africa, although other routes cannot be excluded as demonstrated by the BTV-8 event. Preparedness for such a situation appears necessary both in terms of early warning and vaccine availability. While the former should be organised as soon as possible as a surveillance system involving all countries of the Mediterranean Basin and in countries of Eastern Europe, coordinated by the OIE, surveillance in northern Europe should also be maintained. In particular, susceptible population immunity levels relative to virus circulation should be monitored closely to avoid a more serious epidemic.

Although at first sight, the control strategy and the legislation in force appear to be the same as those applied for other BTV serotypes, some fundamental differences should be recognised between the two situations, as follows:

- a) *Demarcation of restricted zones.* The first difference is that movement controls in northern Europe was less effective than in southern Europe due to a lack of experience and expertise. Indeed, combining the 20 km, protection and surveillance zones was done in the absence of risk mitigating measures (vaccination *in primis*) as applied in the case of Italy, Spain and Portugal. How the merging of the three zones facilitates the spread of BTV can be demonstrated by observing the rapidity of BTV-4 spread in southern Spain from September to November 2004, when legislation did not authorise the merging of restricted areas and the

spread of BTV-1 in the same zone from August 2007 to October 2007, after the zones had been merged. The latter closely resembles the spread of BTV-8 in northern Europe in 2006.

- b) *Use of insecticides/repellents.* The second difference has been the false assumption that the use of insecticides and repellents alone can be sufficient to confer protection against a *Culicoides* attack and that if it is associated with individual animal testing before movements, it could offer the safety of the animals moving from infected to free zones.
- c) *Vaccination strategy.* The third reason is that in the case of the BTV-8 epidemic, no vaccination was applied during two entire epidemic seasons. The reasons for the delay in implementing vaccination are twofold. The first was caused by the advice of experts in northern Europe who suggested that the 2006 epidemic would wane during the winter months of 2006-2007 and, therefore, no action should be taken as a new epidemic appeared unlikely. The second was the unjustified fear of MLV vaccines.

Scientific facts, as well as field data derived from the application of millions of vaccine doses in different animal species have been considered less significant than inferences based on hypothetical events. It is interesting to consider that while vaccination of humans is currently performed mainly with MLV vaccines such as those for rabies, polio, smallpox, measles, mumps and vaccination with MLV vaccines against animal disease such as rinderpest, swine fever, rabies, brucellosis, infectious bovine rhinotracheitis to mention just a few, has led to eradication; in Europe MLV vaccines are still considered dangerous by some experts and their use is feared.

It is worth mentioning that according to some authors [26] if inactivated bluetongue vaccines are available, they should be used in preference to others, while MLV vaccines should be considered only after a specific risk/benefit analysis.

Bluetongue vaccines are intended for use only in animals against a disease that does not have any human health implications. One would consider it logical that in such cases any risk/benefit analysis should have economic implications. It is, therefore, difficult to understand why such an analysis should not also be conducted for inactivated vaccines. Using some simple arithmetic to compare real current costs to vaccinate 1 million sheep and 1 million cattle against bluetongue with either an inactivated or a MLV vaccine in one EU member state, the cost for the use of the former would be €1.34 and €4.23 million higher for sheep and cattle, respectively, as shown in [Table 3](#).

Table 3.– Cost of bluetongue vaccination in a single European country

	Cost of vaccine/dose		Costs of inoculation		Cost to immunise 10 ⁶ animals		Cost differences between modified live virus and inactivated vaccines/1 × 10 ⁶ animals
	Inactivated	Modified live virus	Inactivated	Modified live virus	Inactivated	Modified live virus	
Sheep	€0.37	€0.15	€0.50	€0.25	€1 740 000.00	€400 000.00	€1 340 000.00
Cattle	€0.69	€0.15	€2.00	€1.00	€3 380 000.00	€1 150 000.00	€4 230 000.00

The cost of potentially adverse effects after MLV vaccination can also be calculated. Notifications of such events are made frequently in Europe [26]. They represent approximately 0.1% in cattle and 0.5% in sheep, while laboratory confirmation represents approximately 0.02% of vaccinated cattle and 0.15% of vaccinated sheep. A worst case scenario can be envisaged, in which all notified events were actually due to vaccination and all led to the death of the animals. If the average value of one sheep is estimated as being as equal to €200 and of one bovine animal as equal to €1 000, the total loss incurred per 1 × 10⁶ vaccinated animals would, in both cases, be €1 million. Even if there was no adverse effect from the use of inactivated vaccines, the use of the latter would be negative from a cost/benefit point of view.

The statement of the European Medicines Evaluation Agency (EMA) [12] that bluetongue vaccines, which would enable a differentiation between infected and vaccinated animals, would be desirable is difficult to justify in the current specific context. OIE standards as well as

EU legislation [23] consider seropositive animals safe for trade irrespective of the fact that antibody is generated by contact with either vaccine or wild virus antigen.

The fact that MLV vaccines performed satisfactorily in the early phases of the bluetongue epidemic in southern Europe was eventually recognised in the 2008 vaccine conference organised by the European Commission that endorsed the use of both inactivated and MLV vaccines.

Conclusions

The bluetongue epidemic that has prevailed in Europe since the beginning of the 21st century is the first example of continental spread of BTV in large naive populations of susceptible animals. The traditional control strategies used in countries in which the relationship virus-vector-vertebrate host has reached an equilibrium over a relatively long period of time, were inadequate to control the situation. Furthermore, there was no experience in the control of insect-borne viral animal diseases when the first European member state faced an incursion of bluetongue in 2000.

Population densities of susceptible species of the type encountered in Europe is certainly another element that explains the speed and the extent of spread of the infection. The principal epidemiological features of the infection were the same as those observed elsewhere. As expected, BTV has been very efficient in finding the *Culicoides* species with the best competence and capacity to sustain its survival. Therefore, it has been a relative surprise to recognise how new *Culicoides* spp. never previously considered as competent vectors of BTV, have been able to sustain BTV infection cycles, together with other species, such as *C. imicola*, that until recently was considered the only important vector of BTV in the Mediterranean.

The transport of infected vectors by the wind was also demonstrated, first in the Mediterranean then in northern Europe, to be a significant determining factor in the spread of BTV over long distances. Animal movements that were always considered of no importance for BTV spread has also been demonstrated to contribute to the spread of the infection over long distances.

Therefore, the bluetongue epidemic has created the need to design a new strategy for prevention and control of the disease due to the inadequacy of the consolidated methods, particularly given the need to move animals from infected to free zones.

The basic innovations that were introduced were the use of mass vaccination in all domestic ruminant species to limit the spread of BTV and the use of active surveillance to limit, as far as possible, the zone in which movement restrictions should be applied.

The strategy was successful in limiting the spread of BTV even within countries affected by multiple BTV types. BTV was eradicated from some limited areas of affected territories, namely those in which vaccination and movement controls were applied in accordance with the strategy design.

The implementation of the strategy had limitations due mainly to factors linked to the speed with which multiple serotypes entered countries that had never previously experienced either bluetongue or any other animal disease transmitted by vectors.

Although the present use of vaccines and the vast immunisation of susceptible ruminants due to wild virus circulation reduces the probability of further spread of BTV infection due to the virus that is already present, preventive measures in force should be maintained, in particular surveillance and vaccination.

It should also be recognised that bluetongue has provided yet another example of how a disease historically present only in one hemisphere can enter and spread with ease in the other hemisphere. Today, when faced with events such as the bluetongue epidemic, there is temptation to attribute the occurrence to concurrent climatic changes. The similarity of the ecology of the two hemispheres is often underrated as is the fact that there are a number of disease agents, for instance in southern Africa, that could spread rapidly in Europe by finding naive susceptible animal populations. Should this happen, the consequence would be far worse than those incurred by bluetongue.

The epidemiology of bluetongue has demonstrated that the infectious agents present in southern Africa can easily access the Mediterranean countries of North Africa. It has also been shown that the Mediterranean Basin represents a unique entity in regard to the epidemiology of animal diseases. Any effective strategy for the prevention and control of animal disease in Europe, therefore, must take into account this reality and recognise the need for regional surveillance networks that include all countries that border the Mediterranean Sea.

Relevant components of disease management, such as risk assessment, early warning, contingency planning, the organisation and management of vaccine banks, would be much more efficient and effective for most of the European countries if surveillance networks were organised on a trans-Mediterranean basis. A small-scale example of this type of regional surveillance network already exists and the OIE has been instrumental in the development and implementation of such a network. This experience could be expanded in both scope and geographic range, in particular with the perspective of the new European neighbourhood policy (ENP) in the Mediterranean Basin according to which the European Commission considers that 'for agricultural products, convergence with EU standards for sanitary and phytosanitary controls will greatly enhance reciprocal trade between the partner countries and the EU. Exchanging information and close co-operation with international organisations responsible for the control of animal and plant diseases and improved sanitary conditions to protect consumers are top priorities [17].

Finally, three additional elements should be taken into account in bluetongue prevention and control. The first is the problem of unlawful animal movements that are a very serious threat in regard to the introduction of foreign animal disease and might also have been the cause of the introduction of some BTV serotypes into certain countries of Europe. The second is the need to organise vaccine antigen banks for the various BTV serotypes that are not yet reported in Europe. It is obvious that a serious analysis should be conducted before a decision is made on what types of vaccines should be used and, in particular, the need to demonstrate the efficacy and safety of both multivalent inactivated and MLV vaccine in case of need of vaccines that include more than two BTV type antigens. The third is the monitoring of the frequency of BTV-8 transplacental transmission to verify its relevance in relation to BTV spread.

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