Methodology of the biological risk classification of animal pathogens in Belgium

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Summary

The biological hazards posed by micro-organisms have lead to their categorisation into risk groups and the elaboration of classification lists. Current classification systems rely on criteria defined by the World Health Organization, which cover the severity of the disease the micro-organism might cause, its ability to spread and the av   of prophylaxis or efficient treatment. Animal pathogens are classified according to the definitions of the World Organization of Animal Health, which also consider economic aspects of disease. In Europe, classification is often directly linked to containment measures. The Belgian classification system however, only considers the inherent characteristics of the micro-organism, not its

use, making the risk classification independent of containment measures. A common classification list for human and animal pathogens has been developed in Belgium using as comprehensive an approach as possible. Evolution of scientific knowledge will demand regular updating of classification lists. This paper describes the Belgian risk classification system and the methodology that was used for its peer-reviewed revision (with a focus on animal pathogens).

Introduction

Pathogenic micro-organisms represent only a small part of the microbial world but receive much attention due to their potentially harmful effects on human, animal or plant health.
In the last decades, this attention has grown due to the emergence of new (and known) infectious diseases inducing local epidemics as well as worldwide pandemics. Along with the research and diagnosis of those etiological agents, (bio)safety concerns have highlighted the biological risks associated with their deliberate use   laboratories, animal facilities and production plants, and their transboundary movements (import and export). It was soon recognized that micro-organisms could be categorized into different risk groups on the basis of their inherent characteristics and the biological hazards they could represent for human health and/or the environment (including animal health).

The World Health Organization (WHO) has defined criteria for the classification of micro-organisms into 4 risk groups, taking into account the   ty of the disease pathogens may cause to human or animal health, their ability to spread amongst the population and the availability of prophylaxis or efficient treatment (15). For animal pathogens, the classification system is mainly based on the definitions of the World Organisation for Animal Health (OIE), which categorizes animal pathogens into 4 groups according to their risk to animal health,

and since 2008, their risk to human health (16). In general, the classification of animal pathogens considers not only environmental risks, but also socio-economic aspects, particularly disease control of livestock. Both accidental release into the environment from laboratories, and deliberate or inadvertent introductions into the country are taken into account. As a result, factors linked to import regulations are also one of the issues considered during the classification.

In an overview of different classification systems (1), it is clear that the United States and many European countries have relied on these criteria to develop their classifications; moreover, a lot of national regulations aimed at protecting human and/or environmental health against harmful effects of pathogenic organisms refer to lists in which these organisms are classified into risk groups. Classification lists should ideally be dynamic and based on the continuous acquisition of scientific knowledge. This paper aims to describe the methodology that was adopted during the revision of the Belgian classification lists, and more specifically the revision of the animal pathogens classification. The strength of the chosen methodology is that it focuses on the latest knowledge of animal pathogens, and aims to harmonise the criteria and arguments used for assignment into different risk classes. We feel that this provides a solid approach that will facilitate regular revisions in a broader context.

Classification systems in Europe

Germany (Zentrale Kommission für die Biologische Sicherheit (ZKBS)) and Switzerland (Swiss Agency for the Environment, Forests and Landscape (SAEFL)) published reference lists for bacteria, fungi, viruses and parasites (12, 7), whereby 4 risk groups are considered with respect to their risk for humans and for the environment (animals and plants). In order to comply both with the contained use regulation (12) and occupational safety (11), non pathogenic organisms (e. g. some vaccine strains, cell lines, organisms used for genetic engineering) are included in risk group 1. These lists also contain opportunistic pathogens, which represent a risk for immunocompromized individuals, as well as organisms that could not be assigned to a definite risk group. The pathogenicity of organisms for animals is indicated without assigning them to a definite risk group (an exception is made in the Swi s

list for parasites where two separate lists exist: risk groups for parasites pathogenic to humans and those for parasites pathogenic to animals).

The UK classifies animal pathogens into 4 disease-producing groups (10). There are separate classification lists for animal and human pathogens. In a review report on the regulatory framework for handling animal pathogens (6), the classification systems for both human and animal pathogens were compared, and the need for harmonisation of these regulations was recognized. Today, the implementation   a single regulatory framework for human and animal pathogens is in progress.

There is often a direct link between the risk group of a pathogen and its containment level (in Germany and the Netherlands, and to a lesser extent Switzerland). For instance, in the Netherlands, the categorisation of animal viruses was   riginally based on containment measures for work with human pathogens. However, it was difficult to maintain a linear relationship between risk group and containment level, since the work with solely animal pathogens does not represent a threat to human health   d protection of the worker is not required. Therefore, in a revised classification for animal viruses, the following criteria were taken into account: enzootic character, transmission via vectors, route of infection, stability in the environment, mortality and availability of a vaccine (8).

In Belgium, classification lists for human, animal or plant pathogens provide a tool for identifying biological hazards associated with the (contained) use of pathogenic organisms as such, or as donor or recipient organisms in genetic engineering (5). The classification only takes into account the intrinsic properties of the organism,   the nature of the (laboratory) work, nor the containment level linked to it. With regard to animal pathogens, factors such as geographical distribution, transmission via vectors or carriers and economic impact - requiring in some cases sanitary measures - were considered. The Belgian classification defines 4 risk groups, using the term "risk class". The classification lists are limited to human, animal and plant pathogens, which are classified into three risk classes, as non pathogenic organisms of risk class 1 are not included. Pathogenic micro-organisms for either humans or animals or for

both are compiled in a single list, with risk classes assigned with regard to humans as well as with regard to animals.

The first Belgian classification lists were established in 1998, taking into account relevant European Community legislation, international and national classification schemes as well as relevant scientific publications. Since these lists reflect the state of knowledge at the time they were devised, they now needed to be updated. Our aim was to revise the existing lists in terms of taxonomy and risk groups. The revised lists are not exhaustive but are intended be representative in terms of the variety of pathogens that are prevalent and/or used (e.g. in research) in Belgium.

Methodology

Procedure for revision

The revision of the classification lists with respect   taxonomy and biological risk class was conducted by the Division of Biosafety and Biology (SBB) of the Scientific Institute of Public Health, acting as an advisory body to the Regional Competent authorities for contained use of genetically modified organisms and/or pathogens. Prior to the revision of the risk classes, the lists were revised taxonomically. The revision of the nomenclature and the taxonomy was coordinated by BCCM (Belgian coordinated collections of micro-organisms) and the division of Mycology of the Scientific Institute of Public Health.

As a second step, an internationally recognized expert was chosen to coordinate Belgian animal health and biosafety experts in their review of the risk classes of animal pathogens in the taxonomically reviewed classification list. The working documents consisted of different lists of human and/or animal pathogens: bacteria, viruses (and unconventional agents such as TSE), fungi and parasites, with associated (unrevised) risk classes for humans as well as animals. The experts were asked to focus on organisms that represented a risk to animal health without considering the risk to humans in the case of zoonotic pathogens. Assessment of the zoonotic characteristics of animal pathogens was carried out at a later stage (during the

revision of human pathogens). Scientific knowledge was judged in the context of existing definitions of risk class in order to decide whether the assignment of a pathogenic organism should be modified or whether the lists should be extended.

During a start-up meeting, the criteria for classification of animal pathogens were discussed. It was agreed that the classification process should only consider the inherent characteristics of the micro-organisms and not the type of operation carried out within the laboratory or animal facility. The following method of working was proposed and a task allocation list was made. All experts were asked to i) go through the classification lists and propose the animal pathogens for which the risk class should be revised or ii) to contact experts within their field and coordinate the allocation of tasks amongst them. For each revision proposal, a revision form (table I) had to be completed that identified the given organism and documented the rationale for the proposed risk class revision. A single revision form was completed for a group of organisms belonging to a single family, if the   sion was applicable to all the mentioned members of that family. The revision form was also used to add organisms which were not previously included in the list.

The revision forms were collated by the SBB and the coordinator. All experts were asked to peer-review the revision forms and were invited to provide feedback. Based on this feedback, a compilation document was established. This document, containing the risk evaluations, was the working document for the plenary meeting. The meeting aimed to review the final proposals and reach unanimity with regard to the assignment of a given pathogenic organism to a given risk class.

Criteria for revision

In the assessment of the biological hazard of an organism, the following elements were considered:

- Impact of the disease or severity of the infection (pathogenicity);
- Infectivity (the virulence of the strain, the infective dose, the mode of transmission, natural route of infection);

- Host range (e.g. reservoir) and spectrum of specificity of target-species (age, sex);
- Genetic stability;
- Potential of survival outside host (e.g. ability to form resistant spores) and dissemination in the community or the environment (e.g. zoonosis, presence of vectors, reservoir);
- Availability and effectiveness of prophylactic or therapeutic measures (vaccination or antisera, antibiotics, chemotherapeutic agents, taking into consideration the possibility of emergence of resistant strains);
- Active control or eradication programs for the disease in Belgium;
- Production of allergens or toxins

Based on the aforementioned elements, Belgian legislation defines criteria for classification of organisms into 4 biological risks classes, taking into account the theoretical maximum hazard incurred by immunocompetent humans, healthy animals and plants (table II). These criteria are published in the reference lists of the Belgian regional decrees on contained use of GMOs and/or pathogens (2, 3, 4) and were used as a starting point for revision of the classification of animal pathogens.

At the start-up meeting, it became evident that the criteria for a given risk class did not apply equally to all pathogens (due to their specific characteristics). It was therefore decided to introduce the following *additional specifications* for how to apply or weight the criteria:

- o The characteristics of the pathogen should correspond   much as possible to the criteria considered for a given risk class.
- o Though all criteria should be used, some criteria should be considered more important that others. This is the case for the epizootic, enzootic and exotic character of the pathogen (in order of importance).
- o Although criteria that address the economic and/or sanitary importance of a pathogen should be taken into account, criteria that are inherent to the pathogen should be considered first and foremost.

- As the severity of the disease can vary with different strains of a given pathogen, the mean pathogenicity that is expected and/or observed is taken into consideration.

Results and Discussion

Rationale for the chosen methodology

In the Belgian classification system, the assignment of a risk class depends on the inherent properties of the organism, independent of the activit s (e.g. diagnosis, research, animal experiments) undertaken with it. This means that a clear distinction is made between the biological risk class of the pathogen and the risk class of the activity. In a risk assessment, both need to be considered in order to define the containment level and specific safety measures that should be adopted in order to protect hu   health and the environment. Hence the risk class of the activity may be equivalent to the risk class of the micro-organism or it may be higher or even lower. Consequently, work with the same pathogen can be undertaken under different containment levels, depending on the risk assessment of the activity. It also means that changing the biological risk class of the pathogen will not necessarily lead to an altered risk class of the activity or containment level. This approach to assigning a biological risk class ensures the resultant classification lists are not bound to containment levels. The requirement of different conta   levels, as a consequence of different biosafety regulations for human and animal pathogens, as found in the UK and the Netherlands, is therefore avoided. Hence, the Belgian   im to support a case by case risk assessment of the activity that should ultimately determine adequate containment measures with respect to the protection of human and animal health. This approach has been adopted by the Swiss advisory bodies, but to a lesser extent because even though a risk assessment based on a pathogenic organism's specific use can affect containment measures, the risk group of the organism itself principally influences the containment level.

More than 70% of new and emerging infectious human diseases are known to be zoonotic (7). It was chosen for the Belgian classification list   elaborate a common list for human and

animal pathogens. In that respect, this approach is in accordance with the present criteria for classification of the OIE (16). In addition, the Belgian classification assigns, if necessary, two different classes of risk to the same pathogen with respect to its pathogenicity for humans and/or animals. This enables the consideration of the risk of animal pathogens within a larger context and also ensures harmonization between different regulations concerning human and animal health.

Classifying human and animal pathogens in a single list enables a more comprehensive approach since it addresses the possibility that micro-organisms infecting animals may cross species barriers and infect humans and vice versa. However it also poses greater challenges for revising the classification. One of the reasons is that additional sources of scientific information (e.g. medical versus veterinary, domestic versus wild-life) must be consulted in order to conduct a comprehensive risk assessment. For   ance, new biological agents are continuously detected in animals, several of which showing no clear association with disease in humans and/or livestock (despite serological evidence of infection for some cases). Other micro-organisms have been shown to be transmitted from animals to humans and to cause disease in humans, without (yet) being transmitted amongst humans. A direct consequence of increased scientific knowledge in this field is that the classi   ation lists will need to be updated on a more regular basis.

Revision of animal pathogens

A compilation document with the peer-reviewed proposals for revision of risk class (57 in total, see Table III) was discussed in a meeting with the expert group, the coordinator and the SBB. No new proposals were made for fungi, except one (the skin fungus *Batrachochytrium dendrobatidis*, a pathogen for amphibians, for which a risk class 2   as proposed). The proposals were discussed one by one and unanimity was obtained on the risk classes for the proposed pathogens.

For the majority of revised pathogenic bacteria and viruses, lower risk classes were proposed and accepted, except 2 bacteria of which the risk class remained unchanged. In contrast,

parasites were often assigned a higher risk class and   parasites were added to the list. Table IV gives an overview of the conclusive arguments that were used for revision of the risk classes for bacteria, viruses and parasites, illustrated by some   les. The conclusive arguments are on the one hand criteria corresponding to the criteria for classification in the Belgian legislation, and on the other hand additional   eria. The criteria are listed in order of decreasing frequency of use.

The main arguments for reducing the risk classes for some bacteria and viruses were quite similar, although they did not appear in the same order of frequency. For viruses in particular, the reasons were linked to the situation in Belgium. For parasites, the main reason to either remove or add families to the list was the $degree$ of discomfort and illness. Parasites causing only slight discomfort and no disease were withdrawn from the list. On the other hand, parasites causing very serious discomfort or severe illness or mortality, and causing significant economic impact, were added to the list. Depending on the severity of the symptoms, the host range, the geographical distribution and the economic impact, the parasites were either classified in risk class 2 or 3. The vector-borne nature of some pathogens was taken into account in the risk assignment of the pathogen itself. However, parasites that are only acting as carriers for pathogens were excluded from the list. In contrast, vectors producing toxins or serious allergic disease were considered for inclusion on the list.

One of the major challenges when applying criteria for the classification of animal pathogens is understanding and interpreting these criteria in an unambiguous way. The discussions concerning the criteria for classification of animal pathogens during the start-up meeting were crucial from that perspective. A comprehensive note explaining the way in which the criteria had been interpreted by the experts was added to the revised classification list. The peer review considered the final proposals and reached unanimity with regard to the assignment of risk class.

Where new proposals were subject to revision, the experts aimed to ensure coherence between the risk classes of pathogens. Thus, it was decided that when the importance of the disease varied with different strains of a given pathogen, the mean pathogenicity (expected and/or observed) was taken into consideration to define the risk class. This is also reflected in the arguments mentioned for lowering the risk (see table IV).

In general, the chosen set of criteria for assigning a risk class worked fairly well for the majority of micro-organisms. However, additional factors were considered in some cases, since a classification based on a single set of criteria was not always possible. Even though the classification process aimed for coherence between those pathogens with comparable risks, a case by case evaluation was still needed for some specific pathogens, as is illustrated below.

Where the intrinsic properties of a certain pathogen could have led to its assignment to two different risk classes, assignment was ultimately based on the highest match with criteria defined for a single risk class. COGEM, the Dutch advisory body, came to the same conclusion for the classification of animal viruses (8). In other cases, though all criteria were used, some criteria were given higher priority than others. First consideration was given to the epizootic character of the pathogen, prior to its enzootic or exotic character, as an epizootic disease can have important economic consequences and would require sanitary regulations.

However, the enzootic character of certain pathogens nevertheless constituted a conclusive argument for assignment to a given risk class in some cases. This was illustrated by the case of the Marek's disease virus, occurring worldwide and constituting a serious economic threat to poultry. The development of the disease is prevented by vaccination, but poultry still remain carriers of the virus. Due to its enzootic character it was decided to reclassify the virus to risk class 2.

Though the severity of the disease remained at the forefront of experts' minds, in some specific cases criteria addressing the economic impact or sanitary importance of a pathogen

were taken into account. Infection by the Duck enteritis virus, for example, is known to be limited to anatidae (ducks, geese and swans). But since the anatidae population in Belgium is rather small, the economic impact is limited, so a reduction from risk class 3 to risk class 2 was considered justified.

Another example of weighing up different factors against each other is illustrated in the case of the Bluetongue virus (BTV): although the characteristics of the virus meet all the criteria defined for risk class 4, the virus does not cause high mortality or important economic losses. The dissemination of the virus is strictly dependent of the presence of the *Culicoides* insect vector. Based on these factors, a reclassification of the virus to risk class 3 was agreed. Nevertheless, it must be borne in mind that a change of climate might enhance the presence and/or survival of insect vectors in countries where they do not occur naturally. The actual risk class will thus also depend on the potential spread of the vector due to these climatic changes (14). After an outbreak of the disease in the Netherlands in 2006, a study suggested that the disease could be spread via an endemic species (*Culicoides obsoletus*). Hence the risk class of BTV, formerly classified as risk class 2, was increased to risk class 3 (9).

Conclusions

The Belgian risk classification process categorises human and animal pathogens into a common list using the most comprehensive approach possible. The risk class of an organism is determined independently from the activities undertaken with it, allowing case-by case consideration of the activities carried out with pathogens and the determination of appropriate containment measures. This paper describes the methodology that was adopted during the revision of these classification lists. The strength of the chosen methodology lies in the peer-review process, supported by a multidisciplinary panel of scientists. As the methodology is based on unanimously accepted criteria, this will greatly facilitate future revisions and extensions of classification lists (for example, to take into account pathogenic organisms causing emerging diseases). The revision of such classification lists needs to be undertaken regularly, not only with respect to taxonomy, but also in response to new scientific knowledge

and environmental changes in the broadest sense, with a particular emphasis on emerging infectious diseases.

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Table I

Revision form

<div style="text-align:center">

Annex nr

Rationale for the revision of the risk class

</div>

1. Identification of the biological agent

- Name :
- Type (virus, parasite, bacteria,...) :
- Family :
- Underfamily :
- Gender :
- Species :

2. Class of risk

- Risk class as referred in the classification lists
    human :
    animal :
- Proposal for revised risk class
    animal :

3. Rationale

- Pathogenicity (importance of the disease or severity of the infection) :
- Infectivity:
    - virulence of the strain (the ability or degree to cause pathogenicity) :
    - mode of transmission (e.g. airborne, vector) :
    - natural route of infection (e.g. inhalation, fecal-oral, etc.) :
- Host range (e.g. reservoir):
- Spectrum of specificity of target-species (age, sex):
- Potential of survival outside host (e.g. ability to form spores):
- Dissemination in the community or the environment (e.g. zoonosis, presence of vectors , reservoir):
- Production of allergens or toxins:
- Availability and effectiveness of prophylactic or therapeutic measures (vaccination or antisera, antibiotics, chemotherapeutic agents, taking into consideration the possibility of emergence of resistant strains):
- Control or eradication programs active for the disease in Belgium :
- Remarks :

4. References

Table II

Belgian criteria for classification of micro-organisms

Risk class 1 : Micro-organisms known as **non pathogenic** for humans, animals and plants and harmless for the environment or presenting a negligible risk for humans and the environment at the laboratory scale. This class includes, beside organisms whose harmlessness was proven, strains, which can be allergens and opportunistic pathogens.

With respect to animal pathogens, classification is made according to the following criteria:

Risk class 2: Micro-organisms that can cause disease in animals and present, at different levels, one or other of the following characteristics: limited geographical importance, no or weak interspecies transmission, no vectors or carriers. The economic and or veterinary significance is limited. There is usually effective prophylaxis or treatment available.

Risk class 3: Micro-organisms that can cause serious disease or epizootics in animals. Interspecies diffusion can be important. Some of these pathogenic agents require the installation of sanitary regulations for species indexed by the authorities of each country concerned. Medical and/or sanitary prophylactic measures are available.

Risk class 4: Micro-organisms that cause extremely serious panzootics or epizootics in animals with a very high mortality rate or dramatic economic consequences in the affected farming-regions. Either no medical prophylaxis is available or only one exclusive sanitary prophylaxis is possible or obligatory.

Table III: List of revised animal pathogens

Bacteria	Former risk class	Revised risk class
Bordetella bronchiseptica	3	2
Campylobacter fetus	3	2
Clostridium chauvoei	3	2
Clostridium septicum	3	2
Francisella tularensis type B [a]	3	3
Leptospira interrogans (all serotypes)	3	2
Mannheimia haemolytica	3	2
Mycoplasma gallisepticum	3	2
Mycoplasma hyopneumoniae	3	2
Mycoplasma mycoides subsp. Mycoides	4	3
Mycoplasma suis	3	2
Pasteurella multocida [a]	3	3
*Salmonella (*other serological varieties*)*	3	2
Streptococcus equi subspecies zooepidemicus	3	2
Taylorella equigenitalis	3	2

Viruses	Former risk class	Revised risk class
Avian leukosis viruses (ALV)	3	2
Avian sarcoma viruses (Rous sarcoma virus (RSV))	3	2
Bluetongue virus (BTV)	4	3
Border disease virus	3	2
Bovine viral diarrhoea virus (BVDV)	3	2
Duck enteritis virus (DEV)	3	2
Duck hepatitis B virus	3	2
Equid herpesvirus 1	3	2
Equine arteritis virus	3	2
Feline infectious peritonitis virus (FIPV)	3	2
Fowlpox virus	3	2
Haemagglutinating encephalomyelitis virus	3	2
Infectious bronchitis virus (IBV)	3	2
Infectious bursal disease virus (IBDV)	3	2
Marek's disease virus (MDV)	3	2
Orf virus (Contagious ecthyma of sheep)	3	2
Porcine epidemic diarrhoea virus	3	2
Pseudocowpox viruses (bovine papular stomatitis, milker's nodes, paravaccinia)	3	2
Transmissible gastroenteritis virus	3	2

Parasites	Former risk class	Revised risk class
Ancylostomatidae (family) [a]	2	2
Anisakidae [c]	2	-
Ascarididae (family)	2	2
Argas spp. [b]	-	2
Babesia gibsoni [b]	-	3
Calliphoridae (family) [a]	3	3
Cryptosporidium spp. [b]	-	2
Dermanyssus gallinae [b]	-	2
Dipylidium caninum [b]	-	2
Dirophilaria immitis [b]	-	2
Eimeria spp.	3	2
Giardia duodenalis [b]	-	2
Giardia spp [b]	-	2
Histomonas meleagridis [b]	-	2
Oestridae (family) [b]	-	2
Oxyuridae (family) [b]	-	2
Neospora caninum [b]	-	2
Psoroptidae (family) [b]	-	2
Sarcoptidae (family)	3	2
Strongylidae (family) [b]	-	2
Taenia saginata	3	2
Trichostrongylidae (family)	2	2
Wohlfahrtia (gender of the Sarcophagidae family) [b]	-	3

[a] proposal for lowering the risk class was not validated by the expert group or risk class remained unchanged
[b] added to the list
[c] removed from the list

Table IV:

Conclusive criteria for revising the classification of animal pathogens

Risk Class (RC)	Criteria corresponding to Belgian definitions (in order of decreasing frequency)	Additional criteria
Bacteria		
RC 3 => RC 2	- no control or eradication programs active in Belgium (e.g. *Mannheima haemolytica*) - no severe disease (e.g. *Mycoplasma hyopneumonia* - no epizootics (e.g. *Salmonella*) - enzootics (part of normal microbiota) (e.g. *Bordetella bronchiseptica*) - no interspecies transmission (e.g. *Mycoplasma hyopneumonia*) - limited economic impact (e.g. *Taylorella equigenitalis*)	- similarity to other species of same genus with comparable biological risks (e.g. *Clostridium septicum*) - poor persistence (survival) in the environment (e.g. *Mycoplasma gallisepticum*)
Viruses		
RC 4 => RC 3	dependence on multiple factors and the dissemination characteristics such as the serotypes and exclusively transmitted by an insect vector (e.g. BTV)	
RC 3 => RC 2	- no severe disease (e.g. fowlpox virus- - no epizootics (e.g. ALV) - no interspecies transmission (e.g. Duck hepatitis B virus) - prophylactic or therapeutic measures (vaccines available), controlled by isolation or eradication, quarantine (e.g. IBV) - limited economic impact - no control or eradication programs active in Belgium (e.g.TGV) - enzootics (e.g. BVDV, Marek's disease virus) - worldwide distribution (e.g. BDV) (latent) carriers (e.g. FIPV)	- no reservoir (e.g. IBV) - low (or limited) concentration of host in Belgium (e.g. DEV) - sporadic occurrence of the disease
Parasites		
Added to the list: assignment of RC 3 (for the parasite alone or family of parasites)	- severe illness and discomfort (e.g. *Babesia gibsoni, Wohlfahrtia*)	
Added to the list: assignment of RC 2 (for the parasite alone or family of parasites)	- illness and serious discomfort - economic impact by loss of productivity (e.g. Psoroptidae, *Demanyssus gallinae*) or due to reduced growth (e.g. Ascarididae) - Widespread (e.g. Trichostrongylidae, *Giardia duodenalis*)	- only a threat for young or immunocompromised animals (e.g. *Cryptosporidium spp. Giardia spp.*) - abortions (e.g. *Neospora caninum*)
RC 3 => RC 2	- illness and serious discomfort - economic impact by loss of productivity (e.g. Sarcoptidae)	- asymptomatic disease (e.g. *Taenia saginata*) - only a threat for young or immunocompromised animals (*Eimeria* spp.)
Withdrawn from the list	- no symptoms in the host (e.g. Anisakidae)	