Annual report of the work of the Central Committee on Biological Safety in the year 2006

(BVL 51/2007/4)

17th report since the Genetic Engineering Act came into force

June 5, 2007

Index

Abbreviations

AAV	adeno-associated virus
BBA	Biological Federal Institute for Agriculture and Forestry
BfN	Federal Office for Nature Conservation
BfR	Federal Institute for Risk Assessment
BMELV	Federal Ministry for Food, Agriculture and Consumer Protection
BVL	Federal Office for Consumer Protection and Food Safety
CAV	canine adenovirus
CMV	cytomegalovirus
E. coli	*Escherichia coli*
EFSA	European Food Safety Agency
EU	European Union
FLI	Friedrich Loeffler Institute, Federal Research Institute for Animal Health
GenTG	Genetic Engineering Act
GenTSV	Genetic Engineering Safety Regulations
GMO	genetically modified organism
HBV	hepatitis B virus
HIV	human immunodeficiency virus
miRNA	micro RNA
PMWS	Postweaning Multisystemic Wasting Syndrome, a disease of pigs
RKI	Robert Koch Institute
SFV	semliki forest virus
SIV	simian immunodeficiency virus
ZKBS	Central Committee on Biological Safety

1 Introduction

1.1 Background to the ZKBS

The Central Committee on Biological Safety (ZKBS) is an expert committee comprising sixteen members and sixteen deputy members. The members are experts from various specialist fields and their deputies are experts from the same specialist background. The ZKBS examines and evaluates questions relevant to safety in genetic engineering according to the regulations of the Genetic Engineering Act (GenTG) and advises the Federal Government and Federal States. It provides position statements for the appropriate authorities, particularly on safety or containment level assignment for genetic engineering operations, required safety measures in genetic engineering facilities and possible risks associated with release or introduction onto the market of genetically modified organisms (GMO). In its recommendations it takes into account international developments in the area of genetic engineering safety. The members of the ZKBS and their deputies perform their activities voluntarily.

The ZKBS is based at the Federal Office for Consumer Protection and Food Safety (BVL), which belongs to the operating area of the Federal Ministry for Food, Agriculture and Consumer Protection (BMELV). The members of the ZKBS and their deputies are appointed for the duration of three years by the BMELV in agreement with the Federal Ministries for Education and Research, for Employment and Social Services, for Health as well as for the Environment, Nature Conservation and Reactor Safety.

The ZKBS has a chairperson, supported by two vice-chairpersons, and reaches its decisions either at a general meeting or by a written procedure. The members of the ZKBS and their deputies are sworn to secrecy. The meetings are not public, but the ZKBS publishes general position statements and reports on its work to the public each year.

1.2 Development of genetic engineering in Germany and other member states of the European Union

Legal development

The work of the ZKBS is based on the Genetic Engineering Act (GenTG), which came into force in 1990 and has been revised many times since then. The Act for reforming the Genetic Engineering Laws from December 21, 2004 came into force on February 4, 2005. Essential changes also affected the structure of the ZKBS, resulting in the ZKBS being divided into two committees: one committee for genetic engineering operations in genetic engineering facilities, which continues to comprise sixteen members; and another committee for release and placing on the market, which comprises twelve members. These new arrangements have not yet been completed. The third Act to change the Genetic Engineering Laws was passed on March 17, 2006. It was stipulated in the transition regulations (§ 41) that until the two committees are formed the relevant tasks should be taken on by a special committee that corresponds to the previous structure of the ZKBS.

This third Act to change the Genetic Engineering Laws is primarily aimed at ensuring the proper implementation and execution of the regulations according to the European Directive 2001/18/EC on release of GMOs. This mainly concerns the stipulations on form and procedure:

- Content of the application documents (environmental risk assessment, submission of a monitoring plan, submission of a summary of the dossier, demand for additional documents, reference to documents from third parties)
- Regulating working deadlines
- Public relations participation

- Instructing the public about monitoring measures

Genetic engineering operations and genetic engineering facilities

The term “genetic engineering operations” primarily covers the creation and handling of GMOs. Depending on the required safety, i.e. containment level, genetic engineering operations must be registered or approved by the appropriate state authorities and carried out in a genetic engineering facility, which also has to be registered or approved depending on the required containment level. Further genetic engineering operations at containment level 1 can then be carried out without further registration, as long as the operating facility is already registered. Genetic engineering facilities can be a laboratory, a productionfacility, a greenhouse or facilities for keeping animals.

Participation of the ZKBS in such notification or approval procedures has changed since the Genetic Engineering Act (GenTG) came into force in 1990. Initially, the ZKBS provided a position statement on all genetic engineering operations that were submitted for registration or approval. Since the amendment of the GenTG at the end of 1993, only genetic engineering operations at containment level 3 and 4 and such genetic engineering operations at containment level 2 that cannot be compared to other operations where the ZKBS has previously provided a position statement, are to be examined and evaluated by the ZKBS.

Since the GenTG came into force in 1990,1559 applications for containment level assignment of genetic engineering operations and evaluation of the required technical safety measures have been submitted to the ZKBS. 32 applications were submitted in the year of this report, and the ZKBS provided 27 position statements; at the end of the year 5 applications were still under review and were completed in 2007. Since 1992, the BVL has been informed by state authorities about 7713 position statements on genetic engineering operations, 510 of these in the year of this report. Table 1 lists the position statements from 2006 based on their containment level.

Table 1: Genetic engineering operations evaluated for safety in Germany in 2006 (as of December 2006)

Position statement provided by	Biosafety level	Number
Federal State Authority	S1	188
Federal State Authority	S2	322
ZKBS	S1	2
ZKBS	S2	11
ZKBS	S3	12
ZKBS	S4	2

In Germany a total of 5445 genetic engineering facilities have obtained operating approval (as of December 2006). In 2006, the BVL was informed about 215 new genetic engineering facilities going into operation by the relevant state authorities. Table 2 lists the genetic engineering facilities according to the kind of operator and level of safety measures for the facilities.

Table 2: Genetic engineering facilities in Germany (as of December 2006)

Operator	Containment level	Number
public	S1	3242
public	S2	1069
public	S3	68
public	S4	2
private	S1	866
private	S2	185
private	S3	13

It is not possible to compare genetic engineering operations or genetic engineering facilities with other EU member states, since no information is available.

Further information about genetic engineering operations and genetic engineering facilities as well as about organisms, cell lines and vectors used in genetic engineering operations is provided on the BVL Internet site: http://www.bvl.bund.de

Deliberate Release

The term “deliberate release” means any intentional introduction of a GMO into the environment, if approval for placing this GMO on the market with the intention of releasing it later into the environment has not yet been granted. According to the Genetic Engineering Act, one must apply for approval for every intentional release. This is then granted if according to current knowledge the planned release will present no hazard, or no preventable hazard in relation to the purpose of the release, to humans and the environment.

Since April 01, 2004, the BVL has been responsible as the overall Federal Authority for approving the release of GMOs in Germany. The BVL reaches its decisions in conjunction with the Federal Office for Nature Conservation (BfN), the Federal Institute for Risk Assessment (BfR) and the Robert Koch Institute (RKI). The ZKBS, the Biological Federal Institute for Agriculture and Forestry (BBA, since January 01, 2008: Julius Kühn-Institute) and the relevant authorities in the Federal States involved provide position statements on the planned release. In the case of release of genetically modified vertebrates or genetically modified microorganisms that are to be used with vertebrates, the Friedrich Loeffler Institute (FLI) is also involved. Other EU member states are informed about the release application and can take a position on it.

Since the Genetic Engineering Act came into force, 186 applications for approval of a release have been made in Germany (as of December 2006). In 2006, nine new applications were submitted to the BVL, and two applications were approved in the same year. In total, thirteen new approvals were granted in 2006, eleven approvals relating to applications made in the previous year. Figure 1 summarizes the annual number of approvals for release since the Genetic Engineering Act came into force in 1990. Additional reports from further locations on approved releases according to the simplified process (decision of the EU Commission from November 4, 1994 on stipulating simplified processes for the intentional release of genetically modified plants according to Article 6 Paragraph 5 of the Directive 90/220/EWG of the council, 94/730/EG) are not taken into account. The decrease in the frequency of approvals after 1999 corresponds to a decrease in applications for approval.

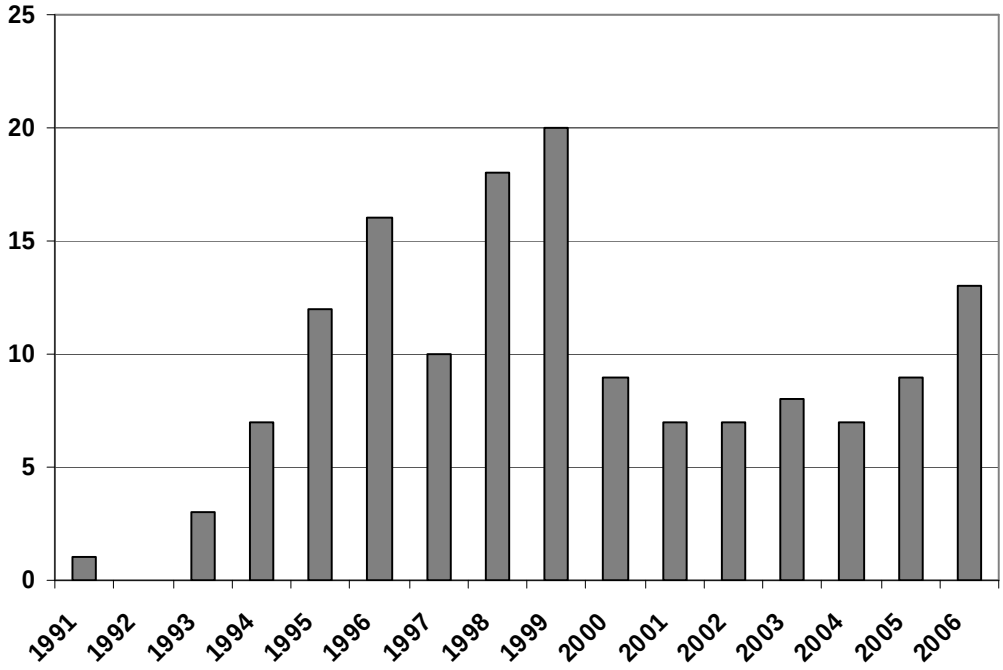

Figure 1: Number of approved releases in Germany since the GenTG came into force in 1990 (as of December 2006).

The BVL has information on damage to areas used for the release of genetically modified plants in Germany between 2003 and 2006. In 2003, two release areas were damaged, in 2004 five areas, while in 2005 only one release area was damaged. In the report year 2006, the BVL was informed about two completely and two partially damaged areas. In April 2006, a field in Bavaria, where release of genetically modified potatoes had been carried out the year before and where soil analysis was to be carried out, was completely destroyed by domestic central heating oil. In June 2006, up to about 20% of a release field with genetically modified barley was destroyed in Hessen. In September 2006, a test field with genetically modified maize was destroyed in Nordrhein-Westfalen, and in October 2006 a test field with genetically modified potatoes was also completely destroyed in Mecklenburg-Vorpommern.

Also within the EU, the frequency of applications for approval of release has decreased since 1999. A comparison of the registered applications from various member states of the EU is given in Figure 2, showing the following selected years: the current report year of 2006, the previous years 2005 and 2004 and the year 1999, when the most applications were submitted and approved in Germany.

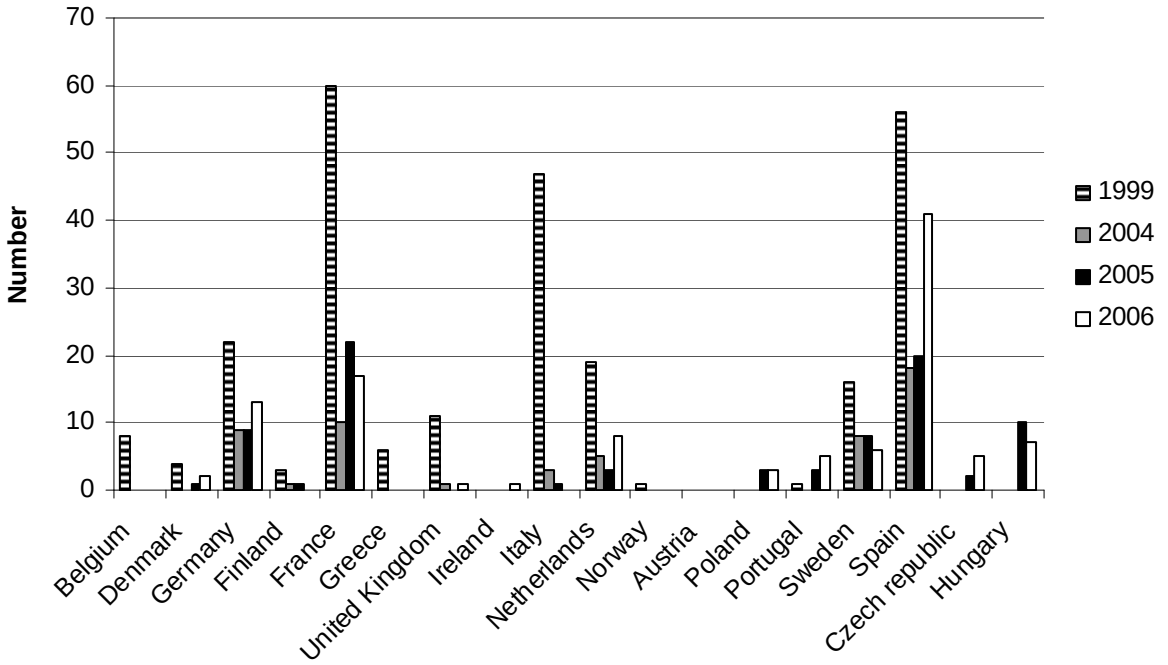

Figure 2: Release approval applications for genetically modified plants in the years 1999, 2004 2005 and 2006 submitted by member states of the EU and Norway. It should be noted when comparing the number of release approval applications between the EU member states that additional reported locations applying the simplified process in Germany are not included here.

The graph shows that not only in Germany, but also generally in the EU, the number of applications for approval of release of genetically modified plants has decreased since 1999. These conclusions cannot be made for Poland, the Czech Republic and Hungary, since they first joined the EU on May 01, 2004 and no information is available either for the year of entry or the period before this. Since the Genetic Engineering Act came into force, a total of 2267 applications for the release of genetically modified plants have been submitted within the EU.

Further information about releases in Germany and the EU are provided on the BVL Internet site: http://www.bvl.bund.de

Placing on the market

The term “placing on the market” of GMOs or products containing GMOs applies to making available these products to third parties. Placing of GMOs on the market requires approval. Since the decision to place a GMO on the market is made through an EU-wide approval procedure, it applies to all member states of the EU. All the relevant authorities of all EU member countries are involved in the approval process. The BVL is the competent German authority, and in conjunction with the BfN, BfR and RKI, provides position statements on applications for placing GMOs on the market. Before this, however, the ZKBS presents the BVL with position statements on applications made in Germany for approval of placing on the market according to the Directive 2001/18/EC, previously 90/220/EEC. The BBA also provides the BVL with a position statement, and in the case of genetically modified vertebrates or genetically modified microorganisms that are to be used with vertebrates, also the FLI and Paul Ehrlich Institute.

Table 3 lists those GMOs that have been approved for introduction onto the market in the EU according to the Directive 90/220/EEC and/or the Directive 2001/18/EC.

Table 3: GMOs approved for placing on the market in the EU according to the Directive 90/220/EWG and/or the Directive 2001/18/EC.

Submitted by member country	Year submitted	Product	Genetically engineered modification	Year approved
Germany	1993	Pseudorabies vaccine against Aujesky's disease in pigs	Reduction in pathogenicity by deletion of genes	1994
France	1993	Rabies vaccine against rabies in foxes	Insertion of a rabies virus gene in vaccinia virus	1994
France	1993	Tobacco	Herbicide tolerance	1994
UK	1994	Rape seed plants	Male sterility and herbicide tolerance	1996
France	1994	Maize	Resistance to insect pests and herbicide tolerance	1997
Netherlands	1994	Radishes	Male sterility and herbicide tolerance	1996
UK	1994	Soya beans	Herbicide tolerance	1996
UK	1995	Rape seed plants	Herbicide tolerance	1998
France	1995	Maize	Herbicide tolerance	1998
France	1995	Maize	Resistance to insect pests	1998
Finland	1996	Test kit for antibiotics	*Streptococcus thermophilus* strain with a luciferase gene	1997
UK	1996	Maize	Resistance to insect pests	1998
Netherlands	1996	Cloves	Altering the flower color	1997
Netherlands	1997	Cloves	Longer shelf-life	1998
Netherlands	1997	Cloves	Altering the flower color	1998
Spain	2001	Maize	Herbicide tolerance	2004

The EU-wide procedure distinguishes between whether the GMO is to be used as food or feed (since 1997, Regulation (EC) No. 258/97 for food; since 2004, Regulation (EC) No. 1829/2003) or not (Directive 90/220/EEC; since 2001, Directive 2001/18/EC). Products from GMOs that are not used as food or feed and contain no organisms capable of replicating (e.g. clothing made of cotton) require no approval for placing on the market.

In contrast to release experiments limited to a particular location and time, the agricultural cultivation of genetically modified plants is not limited to a particular location or experimental year. Agricultural cultivation of genetically modified plants can only take place if approval has been granted for the genetically modified seeds' placing on the market of for the purpose of placing them on the market. Approval for placing on the market is initially limited to ten years.

After an interruption of six years (1998-2004) GMOs and food or feed derived from them are once more being approved in the EU. Approval of the insecticide and herbicide resistant sweet corn (maize) Bt11 was given in 2004 according to the Regulation (EG) No. 258/97 on novel foods and food additives. Similarly in 2004, the use of the herbicide resistant maize NK603 and its processed products was approved by the European Commission as a food and food additive according to the above Regulation. No further approvals were granted in either 2004 or 2005.

Since 2004, strict rules apply in the EU for the approval and labeling of genetically modified food and feed. The newly established European Food Safety Authority, EFSA, is responsible for the scientific evaluation. Genetically modified food and fodder that were on the market in the EU before 2004 are permitted to remain on the market for a transitional period of time. Subsequently, reapplication for their introduction onto the market must be made. In addition, a standardized certification process for each GMO must be available.

A further 44 applications for approval of genetically modified food or feed according to Regulation (EG) No. 1829/2003 have currently been submitted to the EU, but no approvals have been awarded as yet.

Further information about the approved and submitted applications for GMOs in the EU is provided on the BLV Internet site. http://www.bvl.bund.de

2 Structure of the ZKBS

The ZKBS brings together experts from various specialist fields. The specialist fields represented are defined in the Genetic Engineering Act (GenTG) and must be covered by the structure of the ZKBS. This makes it possible to institutionalize and access a broad range of factual knowledge for the tasks performed by the ZKBS as defined by the GenTG, namely the evaluation of microorganisms as donor and recipient organisms in genetic engineering operations, containment assignment for genetic engineering operations, the evaluation of technical safety measures in genetic engineering facilities as well as the evaluation of release and introduction onto the market of GMOs. The members of the ZKBS are listed in Table 4.

The chairperson of the ZKBS is Prof. Dr. Klaus Peter Schaal; vice-chairpersons are Prof. Dr. Angelika Vallbracht and Prof. Dr. Alfred Pühler. In 2006, the members Prof. Christine Gatz (area of genetics), Prof. Dr. Wolfgang Friedt (genetics), Prof. Dr. Michael Treuber (microbiology) and Prof. Dr. Herbert Sukopp (ecology) stepped down. New appointments were Dr. Siegfried Throm (business), Prof. Dr. Klaus Überla (virology), Jutta Jaksche (consumer protection), Prof. Dr. J. Wienands (genetics), Prof. Dr. G. Wenzel (genetics) and Prof. Dr. Marcus Koch (ecology). The structure of the ZKBS presented here corresponds to the previously valid version of the GenTG. When the Act for reforming the Genetic Engineering Laws came into force on February 4, 2005, the ZKBS was divided into two committees, but this new arrangement has not yet been completed. In the structure given here, as in the past, the ZKBS has taken into account the functions of both new committees yet to be established.

Table 4: Specialist areas and members of the ZKBS (as of December 2006)

Specialist area	Member	Representative member
Microbiology	N.N.	Prof. Dr. Klaus Lingelbach University of Marburg
Cell biology	Prof. Dr. Bernd Gänsbacher TU Munich	N.N.
Virology	Prof. Dr. Herbert Pfister University of Cologne	Prof. Dr. Edgar Maiß University of Hannover
Virology	Prof. Dr. Angelika Vallbracht University of Bremen	Prof. Dr. Klaus Überla University of Bochum
Genetics	Prof. Dr. Jürgen Wienands University of Göttingen	Prof. Dr. Gerhard Wenzel TU Munich
Genetics	Prof. Dr. Alfred Pühler University of Bielefeld	Prof. Dr. Uwe Sonnewald University of Erlangen-Nürnberg
Hygiene	Prof. Dr. Klaus-Peter Schaal University of Bonn	Prof. Dr. Uwe Groß University of Göttingen
Ecology	Prof. Dr. Marcus Koch University of Heidelberg	Prof. Dr. Stefan Vidal University of Göttingen
Ecology	Prof. Dr. Wolfgang Dott RWTH Aachen	N.N.
Technical safety	Dr. Jürgen Wahl Roche diagnostics GmbH Penzberg	Dr. Uwe Bücheler Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach a.d. Riß
Trade Unions	Prof. Dr. Dr. h.c. Wilfried Wackernagel University of Oldenburg	Dr. Manfred Keilert Berlin
Business	Dr. Siegfried Throm Association of Research Drug Manufacturers (Verban Forschender Arzeneimittelhersteller) Berlin	Dr. Anja Matzk KWS SAAT AG, Einbeck
Employment protection	Frank Gerschke State Authority for Employment Protection, Potsdam	Dr. Hans-Josef Riegel Professional Trade Union of the Chemical Industry, Cologne
Research funding organizations	Dr. Ingrid Ohlert DFG, Bonn	Prof. Dr. Bernd Müller-Röber University of Potsdam
Environmental protection	Dr. Gerd Neemann BlaU Environmental Studies Göttingen	Prof. Dr. Thomas Eikmann University of Gießen
Consumer protection	Sigrid Lewe-Esch Work Association of the Evangelical Household Management Force of the German Evangelical Woman's Federation e.V., Duisburg	Jutta Jaksche Consumer Center Federal Association e.V., Berlin

3 Advisory activities of the ZKBS in 2006

3.1 Working methods

In 2006, six meetings of the ZKBS took place at the BVL in Berlin. Position statements of the ZKBS were usually adopted at these meetings. In addition, decisions were also made in written procedures if simpler questions, not requiring detailed discussions between all the members, were submitted.

3.2 Working groups

In the year of this report two new working groups were set up that were primarily concerned with the evaluation of technical safety measures in genetic engineering facilities. They comprised ZKBS representatives from the specialist areas of technical safety, employment protection, ecology and, depending on the planned genetic engineering operations, the fields of virology or microbiology. In addition, these working groups included representatives from the operating location, the competent federal state authorities, the operators and the engineers commissioned with the planning. They dealt with:

- Extension of the Friedrich Loeffler Institute on Riems Island and
- Extension of the Robert Koch Institute in Berlin.

Furthermore, a working group of the ZKBS has existed for many years to deal with preparing position statements of the ZKBS on applications for approval of release before these are presented to the plenum for passing a resolution.

The detailed examinations and discussions of the working groups are presented to the entire ZKBS and are integrated into a position statement of the ZKBS for the competent authorities.

3.3 Advising the federal state authorities in cooperation between authorities

In the context of cooperation between authorities, state authorities have asked the ZKBS for position statements on the following themes:

- Classifying microorganisms that are to be used as donor or recipient organisms in genetic engineering operations (see Table 5).
- Safety requirements for an S2 greenhouse
- Waste water disposal from *E. coli* B production processes without specific pretreatment
- Evaluation of AAV or other adenoviral vectors expressing miRNAs
- Classifying genetic engineering operations with the genome from HBV
- Classifying genetic engineering operations with the SFV helper system (expression of rasGRP)
- Evaluating laboratory strains for transformation
- Checking the classification of Marek’s disease virus BAC20
- Carrying out checks on the airtight seals for an S4 area
- Classifying recombinant type 5 adenoviruses whose E1 and E4 genes are under the control of the CMV immediate-early promoter or an SV40 promoter
- Use of the FACS analyzer Canto in a containment level 3 genetic engineering installation

- Extensive alterations in the structure and operations of the animal house at the German Primate Center GmbH, Göttingen
- Use of Berner FlowSafe ventilation filter boxes in a containment level 3 genetic engineering installation

3.4 Risk assessment of donor and recipient organisms

The following microorganisms used as donor and recipient organisms in genetic engineering operations were assigned to a risk group in 2006 according to § 5 in conjunction with Appendix 1 of the Genetic Engineering Safety Regulations (GenTSV):

Table 5: Newly assigned microorganisms

Organism	**Risk group**
Viruses	
Mycobacteriophage λ TM4	1
Bacteriophages from bacteria in risk group 2: *Burkholderia, Campylobacter, Citrobacter, Clostridium, Enterobacter, Enterococcus, Klebsiella, Listeria, Proteus, Pseudomonas, Salmonella, Serratia, Shigella, Staphylococcus, Vibrio, Plesiomonas*, *Yersinia* and *Escherichia coli*	*2*
Deformed wing virus	2
Thailandvirus	2
Thottapalayamvirus	2
Tobacco rattle virus	2
Trichomonas vaginalis virus (TVV)	2
Tulavirus	2
Tupaia paramyxovirus (TPMV)	2
Australian bat lyssavirus (ABLV)	3**
Nipah virus	4
Bacteria	
Salmonella enterica enterica serovar enteriditis 318 metabolic mutant from the vaccine TAD salmonella vacE [(a)]	1
Salmonella enterica enterica serovar enteriditis 6403 PT4 from the vaccine Salmovac SE [(a)]	1
Brucella abortus S19	2
Francisella philomiragia (syn.: *Yersinia philomiragia*)	2
Paenibacillus larvae ssp. *larvae*	2
Salmonella enterica enterica serovar Gallinarum 9R from the vaccine Nobilis SG9R	2
Staphylococcus lugdunensis	2

Staphylococcus pseudintermedius	2
Tetrathiobacter kashmirensis[(b)]	2
Tetrathiobacter mimigardefordensis [(b)]	2
Fungi	
Aspergillus amstelodami (anamorphic form of *Eurotium amstelodami*)	1
Bremia lactucae	1
Cladosporium fulvum (syn. *Passalora fulva* or *Fulvia fulva*)	1
Colletotrichum graminicola [(c)]	1
Neosartorya fischeri (anamorph of *Aspergillus fischerianus*) [(d)]	1
Penicillium commune	1
Piriformospora indica [(e)]	1
Plasmopara viticola	1
Fusarium proliferatum (anamorphic form from the *Gibberella fujikuroi* complex)	2
Plasmopara halstedii (syn. *Plasmopara helianti*)	2
Parasites	
Besnoitia besnoiti (tachyzoites)	2
Trichomonas vaginalis	2
Cell lines	
Jukat-1G5	1
LUSIV	1
Phoenix E	1
BEAS-2B	2

(a) It should be noted that the mutant could be complemented to a wild type form by the cloning of foreign DNA that may exist in a mixture of DNA sequences (e.g. gene banks). In individual cases, higher allocation of the GMOs to **risk group 2** is then necessary. Genetic engineering operations where bacterial nucleic acid sequences are introduced into the mutants that increase the survival capacity of the bacteria or code for the virulence factor of other pathogenic bacteria are to be submitted to the ZKBS for classification.

(b) To date, the investigated properties of these bacteria allow no statement to be made about a pathogenic potential. However, based on the analyzed growth conditions and physiological properties it cannot be excluded that this is not a pathogenic organism (general position statement of the ZKBS 6790-10-43).

(c) Genetic engineering operations with *Colletotrichum graminicola* as the recipient organism where nucleic acid sequences are transferred that can increase the survival capacity or code for virulence factors should be submitted to the ZKBS in individual cases.

(d) Genetic engineering operations with *Neosartorya fischeri* as the recipient organism should be submitted to the ZKBS for individual case assessment.

(e) The phytopathogenic fungus *Piniformospora indica* was down-graded from risk group 2 to risk group 1.

3.5 Containment level assignment for genetic engineering operations

In 2006, the ZKBS provided 25 position statements on safety and containment level assignment for genetic engineering operations. Twelve of the assessed operations were addressing themes in virology and cell biology and ten were concerned with bacteriology. One of these operations came from the area of mycology and two from the area of parasitology. The evaluated genetic engineering operations addressed the following questions and were classified as follows:

Containment level 1

Genetic engineering operations

- to modulate the translation of transcription factors by RNA interference-mediated "gene knock-down" using AAV-based expression systems
- with recombinant *Neosatorya fischeri*

Containment level 2

Genetic engineering operations

- to express presynaptic and postsynaptic proteins of the rat or mouse using CAV-2 derived vectors
- with recombinant *B. abortus* S19
- with recombinant *Besnoitia besnoiti* (tachyzoites)
- to identify phage genes from bacteria of risk group 2
- investigating the influence of the R-region on SIV replication
- with recombinant *Trichomonas vaginalis*
- on genetic characterization of a plasmid from *Paenibacillus larvae*
- on immortalizing human fibroblast cell lines with the help of human telomerase using retroviral transformation
- on the identification and characterization of genes for cleaving dipthiodipropionic acid
- on the transfer of genes using pseudo-type lentiviruses to immortalize cells
- to produce recombinant influenza viruses for the *in vivo* synthesis of viral RNA molecules

Containment level 3

Genetic engineering operations

- to characterize a type III effector from enterohemorrhagic *E. coli*
- on the ecological behavior of enterohemorrhagic *E. coli* strains in the commercial food chain
- to produce new inhibitors of HIV replication *in vitro*
- on functional analyses of the HIV 1 integrase protein
- to establish a hepatitis C virus replicon with the entire genome and analyze its biological properties in a cell culture system
- with recombinant *Mycobacterium tuberculosis*
- on interactions of viral coat proteins with cellular attachment factors and receptors
- investigating the energy, substrate and cell wall metabolism of *Mycobacterium tuberculosis*

- investigating the translation and replication of hepatitis C virus
- on differentiating between sub-species of *Francisella tularensis*
- to analyze “knock-out” mutants of enterohemorrhagic *E. coli*

Containment level 4

Genetic operations

- to produce recombinant arenaviruses

3.6 Assessing technical safety measures in genetic engineering facilities

In addition to stipulating safety measures for the evaluated genetic engineering operations according to the categories in the Appendices of the Genetic Engineering Safety Regulations (GenTSV), in 2006 the ZKBS thoroughly examined the technical and building safety measures in individual genetic engineering facilities and produced position statements on:

- technical safety measures for the S1 to S4 containment level areas for the partial approval of setting up genetic engineering facilities as part of the complete renovation of the Friedrich Loeffler Institute, Riems Island
- technical safety measures of a containment level 3 genetic engineering facility at AiCuris GmbH and Co. KG, Wuppertal
- to assess the equivalent quality of the WIBObarrier vertical plus system to a class 2 microbiological safety workbench
- on the use of a WIBObarrier Sampling Cabin, model VBL/1500-S in a containment level 2 genetic engineering facility
- setting up a second emergency exit in genetic engineering laboratories of containment level 3

3.7 Publication of general position statements

The ZKBS passed the following general position statements, which were published in the Federal Legal Gazette:

- Risk assessment of Tat fusion protein expression (Ref.: 6790-10-88; May 2006)

3.8 Position statements on releases

In 2006, the ZKBS provided position statements for the BVL on the eleven applications for approval of release of GMOs listed in Table 6. The Table lists the applicants, plants, major genetic modifications with their expected effects and the time period for the planned release. Ten of these applications were already submitted in 2005, and the last application listed in the Table was submitted in 2006. All eleven applications were supported by the ZKBS and approved by the BVL.

3.9 Placing on the market

No position statements were provided on applications for approval of placing on the market since no applications for approval were submitted from Germany according to the Directive 2001/18/EC of the EU.

Table 6: Applications for approval of release of genetically modified plants for which the ZKBS provided a position statement in 2006

Applicant	Plant	Major genetically engineered modifications	Time period
Max Planck Institute for Molecular Plant Physiology, Golm	Potato	Water management: fragment of the *SDD1* gene from potatoes in the sense orientation; pyruvate orthophosphate dikinase intron from *Flaveria trinervia*; fragment of the *SDD1* gene from potatoes in the antisense orientation; chimeric gene of the *nptI* and *nos* genes	2006 – 2009
Justus Liebig University, Gießen	Barley	Symbiotic interaction: *cThEn42(GC)* gene from *Trichoderma harzianum* or the gene of a (1,3-1,4)-ß-glucanase*; sGFP* gene; *bar* gene from *Streptomyces hygroscopicus*	2006 – 2008
Monsanto Agrar Deutschland GmbH	Maize	Herbicide tolerance, insect resistance: *epsps* gene; Bt toxin gene; glyphosphate oxido-reductase gene from *Ochrobactrum anthropi*; gene for the CrylA(b) protein product; *nptI* gene	2006 – 2010
Bavarian Federal State Office for Agriculture, Freising	Potato	Amylopektin biosynthase: fragment of the *gbss* gene from *Solanum tuberosum* (potato); *aadA* gene	2006 – 2015
Association to Promote Innovative and Sustainable Agrobiotechnology MV – FINAB e.V.	Summer rape seed	Resveratrol synthetase: reducing the sinapin content; stilben synthetase VST I gene from *Vitis vinifera*; partial sequence of the gene for UDP-glucose; sinapat glucosyl-transferase from *Brassica napus* in the antisense orientation, a partial sequence from the GUS gene from *E. coli*; *npt II* gene, *bar* gene	2006 – 2007
BASF Plant Science GmbH	Potato	Composition of starch: fragment of the coding region of the *be1* and *be2* genes; *be2* promoter sequence; stGH1 gene; *ahas* gene	2006 – 2010
BASF Plant Science GmbH	Potato	Carbohydrate metabolism: fragment of the coding region of the GBSS gene from potato in the antisense orientation; *ahas* gene	2006 – 2010
BASF Plant Science GmbH	Potato	Fungus resistance: *Rpi-bib 1* and *Rpi-bib2* from *Solanum bulbocastanum*; *ahas* gene	2006 – 2010
University of Cologne	Potato	Starch content, tuber yield: *gpt* gene from *Pisum sativum*; *hph* gene from *Streptomyces hygroscopicus*, *ntt* gene from *Arabidopsis thaliana*; part of the *ocd* gene from *A. tumefaciens*; *npt II* gene from *E. coli*	2006 – 2007
University of Rostock	Potato	Biopolymer synthetase, antigen synthetase: *vp60* gene, viral capsid protein of RHDV (rabbit haemorraghic disease virus), *cyel* gene from the cyanobacterium *Thermosynechococcus elongatus*; *ctxB* gene for cholera toxin, subunit B from *Vibrio cholerae*; *nplt* gene from *E. coli*	2006 – 2008
Leibniz Institute for Plant Genetics and Cultured Plant Research, Gatersleben	Winter wheat	Carbohydrate content, protein content: saccharose transporter gene from barley and the *bar* gene from *Streptomyces hygroscopicus* (line HOSUT) or an amino acid permease gene from beans and the *bar* gene from *Streptomyces hygroscopicus* (lines XAP, SUTAP 78, 69, 60)	2006 – 2008