German Federal Office of Consumer Protection and Food Safety

Annual report of the work of the Central Committee on Biological Safety in the year 2008

(BVL 80/2009/4)

19th report after the Genetic Engineering Act came into force

April 7, 2009

The report of the work of the Central Committee on Biological Safety in the year 2008 will be announced in the following.

Berlin, April 8, 2009

German Federal Office

of Consumer Protection and Food Safety

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Abbreviations

AIDS	Acquired immunodeficiency syndrome
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
EC	European Community
EFSA	European Food Safety Authority
EU	European Union
FLI	Friedrich Löffler Institute, Federal Research Institute for Animal Health
GenTG	Genetic Engineering Act
GenTSV	Genetic Engineering Safety Regulations
GMO	genetically modified organism
JKI	Julius Kühn Institute
PEI	Paul Ehrlich Institute
RKI	Robert Koch Institute
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 twenty members and twenty 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 (Bundesländer). 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 placing on 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), passed in 1990, and has been revised many times since then. The Act for reforming the Genetic Engineering Laws from April 1, 2008 came into force on April 5, 2008. Essential changes also affected the structure of the ZKBS, resulting in the reversion of the former division of the ZKBS into two committees. At the same time the ZKBS was extended by yet to be appointed experts in the specialist fields of agriculture, nature conservation, plant protection and toxicology.

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. Genetic engineering facilities can be a laboratory, a production plant, 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, 1614 applications for containment level assignment of genetic engineering operations and evaluation of the required technical safety measures have been submitted to the ZKBS. 29 applications were submitted in the year of this report, and the ZKBS provided 33 position statements; at the end of the year 2 applications were still under review and were completed in 2009. Additionally, the BVL has been informed by state authorities about 750 position statements on genetic engineering operations in the year of this report. Table 1 lists the position statements from 2008 based on their containment level.

Table 1: Safety evaluated genetic engineering operations in Germany in 2008 (as of December 2008).

Position statement provided by	Containment level	Number
State Authority	S1	291
State Authority	S2	459
ZKBS	S1	2
ZKBS	S2	9
ZKBS	S3	22
ZKBS	S4	0

In Germany, a total of 5747 genetic engineering facilities have operating approval (as of December 2008). The BVL was informed by the relevant state authorities about 271 new genetic engineering facilities going into operation in 2008. 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 2008).

Operator	Containment level	Number
Public	S1	3432
Public	S2	1181
Public	S3	82
Public	S4	4
Private	S1	865
Private	S2	171
Private	S3	12

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 website: http://www.bvl.bund.de.

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

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 intended 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 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.

In 2008, seven new applications were submitted to the BVL, and two applications were approved in the same year. In total, six new approvals were granted in 2008, four 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. Subsequent notifications of further locations on approved releases according to the simplified procedure (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/EC) are not taken into account. The decrease in the frequency of approvals after 1999 corresponds to a decrease in applications for approval.

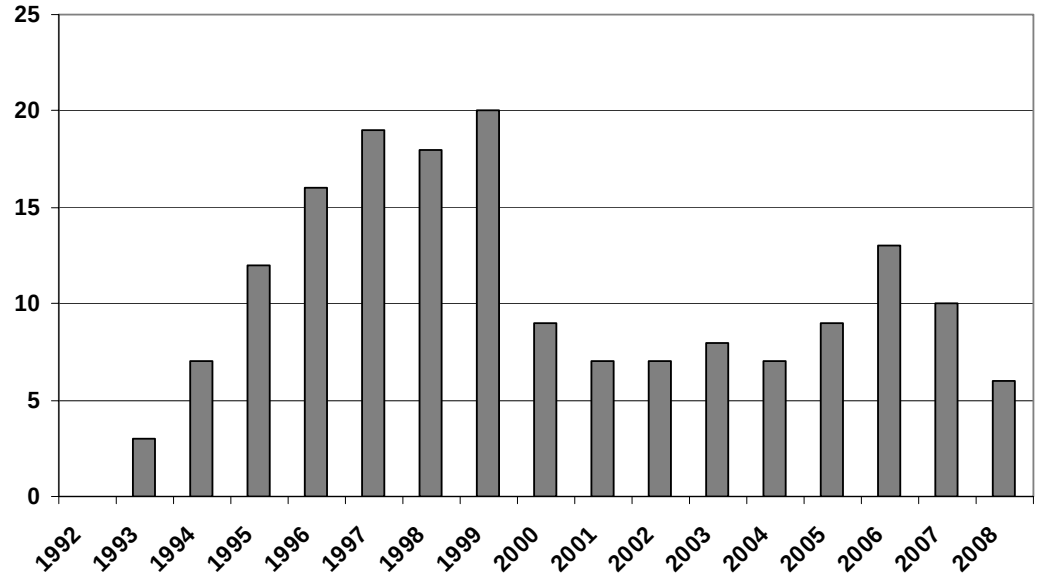

Figure 1: Number of approved releases in Germany since the GenTG came into force in 1990 (as of December 2008).

Figure 2 shows the annual number of notifications of further locations on approved releases according to the simplified procedure.

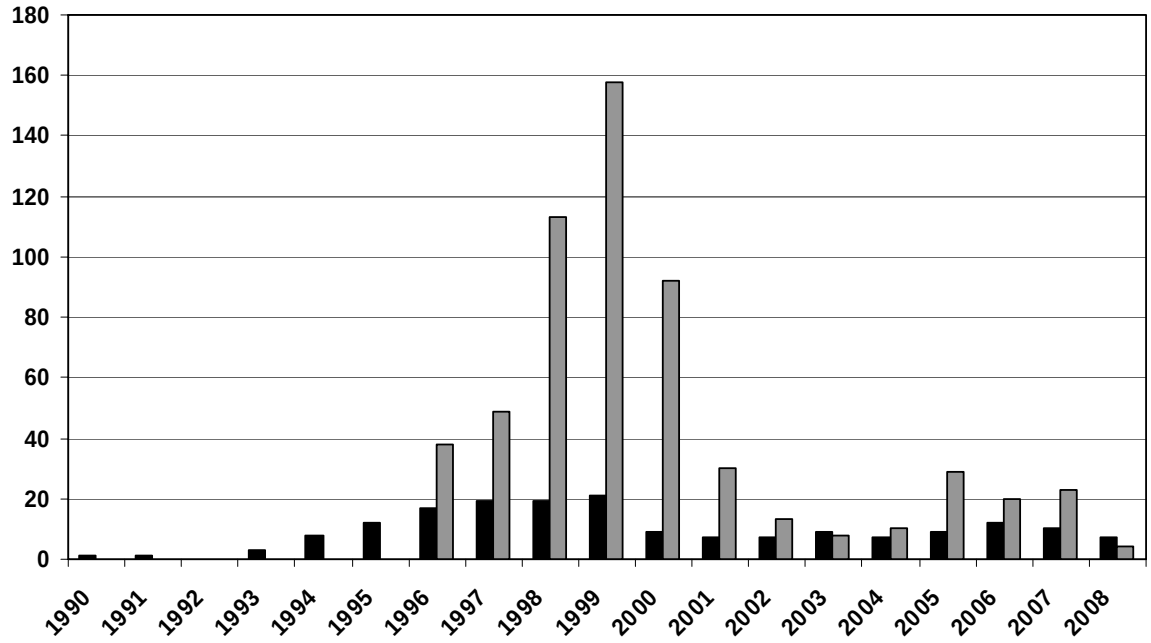

Figure 2: Number of approved deliberate releases (■) and subsequent notifications of further locations according to the simplified procedure (■) in Germany since the GenTG came into force in 1990 (as of December 2008).

For the year under report, the demolition of seven deliberate release areas for genetically modified crops in Germany was reported to the BVL:

April 2008 post-release control of an experiment on biosafety of genetically modified barley in Hesse was impeded due to damage to property caused by field occupation

April 2008 a deliberate release field in Saxony-Anhalt with genetically modified wheat

June 2008 a deliberate release field in North Rhine-Westphalia with genetically modified maize

June 2008 a deliberate release field in Rhineland-Palatinate with genetically modified potatoes

June 2008 a deliberate release field in Mecklenburg-Western Pomerania with genetically modified maize

July 2008 a deliberate release field in Saxony with genetically modified maize

July 2008 a deliberate release field in Baden-Wuerttemberg with genetically modified maize

Due to this, the deliberate release experiments could not be analyzed any longer.

A comparison of the registered applications from various member states of the EU is given in Table 3, showing the following selected years: the current report year of 2008, the previous years 2007, 2006 and 2005 and the year 1999, when the highest number of applications was submitted and approved in Germany.

Table 3: Applications for approval of deliberate release of genetically modified crops by the member states of the EU in the years 1999, 2005, 2006, 2007 and 2008 (as of December 2008).

State	1999	2005	2006	2007	2008
Belgium	8	-	-	-	1
Czech Republic	-	2	5	5	3
Denmark	4	1	2	5	2
Finland	3	1	-	-	1
France	60	22	17	16	-
Germany	22	9	13	9	6
Great-Britain	11	-	1	2	1
Greece	6	-	-	-	-
Hungary	-	10	7	9	3
Ireland	-	-	1	-	-
Italy	47	1	-	-	-
Lithuania	-	-	-	2	-
Poland	-	3	3	-	3
Portugal	1	3	5	1	2
Rumania	-	-	-	14	9
Slovakia	-	-	-	-	4
Spain	56	20	41	45	45
Sweden	16	8	6	4	4
The Netherlands	19	3	8	5	2

The table shows that the number of applications for approval of deliberate release of genetically modified crops has decreased since 1999 not only in Germany, but generally in the EU (except for Spain). This conclusion cannot be drawn for Poland, the Czech Republic, Hungary, Bulgaria, Rumania and Slovakia, since they joined the EU only in 2004 (Rumania only in 2007) and no information is available for the period before.

Since the Genetic Engineering Act came into force, a total of 2471 applications for the release of genetically modified plants have been submitted within the EU. No information has been submitted by the EU member states not included in Table 3.

Placing on the market

The term “placing on the market” of GMOs or products containing GMOs applies to making these products available to third parties. Placing 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 JKI 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 (PEI).

In the EU-wide processes it is distinguished whether the GMO may be used as feed or food [since 1997 regulation (EC) No. 258/97 for food, since 2004 regulation (EC) No. 1829/2003 for food and feed] or not. Products derived from GMOs that are not used as feed or food and that do not contain organisms capable of replicating (e.g. clothing made of cotton) require no approval for placing on the market. Table 4 lists those GMOs that have been approved for placing on the market in the EU according to the Directive 90/220/EEC and/or the Directive 2001/18/EC.

Table 4: GMOs approved by the EU (as of 2008).

Product	genetic modification	Purpose
Cotton MON1445	herbicide resistance	FF
Cotton MON531	insect resistance	FF
Cotton MON531xMON1445	herbicide and insect resistance	FF
Cotton MON15985	insect resistance	FF
Cotton MON15985xMON1445	herbicide and insect resistance	FF
Cotton LLCotton25	herbicide resistance	FF
Carnation Moonlite	modified flower colour	IP
Carnation Moonshadow 1	modified flower colour	C
Carnation Moonshadow 2	increased shelf life	C
Maize DAS1507	herbicide and insect resistance	FF
Maize DAS59122	herbicide and insect resistance	FF
Maize DAS1507xMON630	herbicide and insect resistance	FF
Maize 59122 „Herculex“	herbicide and insect resistance	IP, FF
Maize 1507xNK603	herbicide and insect resistance	IP, FF
Maize NK602xMON810	herbicide and insect resistance	FF
Maize T25	herbicide resistance	IP, FF, C
Maize MON810	insect resistance	IP, FF, C
Maize MON863	insect resistance	IP, FF
Maize 1507	herbicide and insect resistance	FF
Maize GA21	herbicide resistance	IP, FF
Maize Bt11	insect resistance	FF
Maize MON863xMON810	insect resistance	FF
Maize MON863xNK603	herbicide and insect resistance	FF
Maize NK603	herbicide resistance	FF
Canola GT 73	herbicide resistance	IP, FF
Canola T54	herbicide resistance	FF
Canola MS8xRF3	herbicide resistance, male sterility	IP, FF
Soy MON40-3-2	herbicide resistance	FF
Soy A2704-12	herbicide resistance	IP, FF
Soy MON89788	herbicide resistance	IP, FF
Sugar beet H7-1	herbicide resistance	FF

Abbreviations:
IP: import as replication-competent GMO and processing
FF: feed and food
C: cultivation in the EU

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. Cultivation of genetically modified plants can only take place if placing genetically modified seeds on the market for the purpose of introducing them into

the environment has been approved. Approval for placing on the market is initially limited to ten years.

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 feed that were placed 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 placing on the market must be made. In addition, a standardized certification process for each GMO must be available.

Further information about the approved and submitted applications for GMOs in the EU is provided on the following websites:

http://www.bvl.bund.de

http://ec.europa.eu/food/dyna/gm_register/index_en.cfm

http://www.transgen.de/zulassung/gvo/

Exchange of experiences with the Committees on Biological Safety of other member states of the European Union

In September 2008, the BVL hosted the "3rd Meeting of European Advisory Committees in the Field of Deliberate Release of GMOs". The four sessions held addressed the subjects "Horizontal gene transfer and its influence on risk assessment", "Molecular characterization of and methods for detecting GMOs", "Long-term effects of GMOs" and "Cooperation between the EFSA and national committees on biosafety". First results of the European biosafety research projects "Sigmea" and "Transcontainer" were reported, and the German concept of a molecular register for GMOs was presented. Additionally, the meeting provided an opportunity to become acquainted with the structure and the functions of the different national committees in the EU.

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 placing on the market of GMOs. The members of the ZKBS are listed in Table 5.

Table 5: Specialist areas and members of the ZKBS (as of December 19, 2008).

Specialist area	Member	Representative member
	Experts	
Microbiology	Prof. Dr. Regine Hakenbeck TU Kaiserslautern	Prof. Dr. Klaus Lingelbach University of Marburg
Cell biology	Prof. Dr. Bernd Gänsbacher TU München	Prof. Dr. Achim Leutz Max Delbrück Center for Molecular Medicine, Berlin-Buch
Virology	Prof. Dr. Dr. h.c. Herbert Pfister University of Köln	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 München
Genetics	Prof. Dr. Alfred Pühler University of Bielefeld	Prof. Dr. Uwe Sonnewald University of Erlangen-Nürnberg
Hygiene	Prof. Dr. Uwe Groß University of Göttingen	Prof. Dr. Dr. Andreas Podbielski University of Rostock
Ecology	Prof. Dr. Marcus Koch University of Heidelberg	Prof. Dr. François Buscot Helmholtz Center for Environmental Research GmbH, Halle
Ecology	Prof. Dr. Stefan Vidal University of Göttingen	Dr. Walter Durka Helmholtz Center for Environmental Research GmbH, Halle
Plant protection	tba	tba
Technical safety	Dr. Jürgen Wahl Roche-Diagnostics GmbH, Penzberg	Dr. Uwe Bücheler Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach a.d. Riß
Toxicology	tba	tba
	Specialists	
Employment protection	Frank Gerschke State Authority for Employment Protection, Potsdam	Dr. Hans-Josef Riegel Professional Trade Union of the Chemical Industry, Köln
Trade unions	Prof. Dr. Dr. h.c. Wilfried Wackernagel University of Oldenburg	Dr. Manfred Keilert, Berlin
Agriculture	tba	tba
Nature conservation	tba	tba
Research-funding organisations	Dr. Ingrid Ohlert DFG, Bonn	Prof. Dr. Elisabeth Knust Max Planck Institute for Molecular Cell Biology and Genetics, Dresden
Environmental protection	Dr. Gerd Neemann BLaU Environmental Studies Göttingen	Prof. Dr. Thomas Eikmann University of Gießen

Consumer protection	Sigrid Lewe-Esch Working Group of Protestant Housekeeping Managers of the German Protestant Women's Federation e.V., Duisburg	Jutta Jaksche Federation of German Consumer Organisations e.V., Berlin
Business	Dr. Siegfried Throm Association of Research-based Pharmaceutical Companies, Berlin	Dr. Anja Matzk KWS SAAT AG, Einbeck

Abbreviations: tba: to be assigned

Since July 2007, Prof. Dr. Dr. h.c. Herbert Pfister is the chairperson of the ZKBS. Vice-chairpersons are Prof. Dr. Angelika Vallbracht and Prof. Dr. Alfred Pühler.

Dr. Walter Durka was newly appointed representative member for the specialist field of 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 April 5, 2008 the former division of the ZKBS into two committees was reversed and the ZKBS was extended by two experts in the specialist fields of plant protection and toxicology and two specialists for nature conservation and agriculture. For none of the four new specialist areas a member has been appointed yet.

3 Advisory activities of the ZKBS in 2008

3.1 Working methods

In 2008, 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 had been submitted.

3.2 Working groups

In the year of this report the working group "Antibiotic Resistance Genes in Genetically Modified Plants" worked out a new position statement on antibiotic resistance genes in the genome of genetically modified plants that was adopted by the ZKBS in December 2008. This working group comprises ZKBS representatives from the specialist areas of microbiology, hygiene, trade unions and business as well as representatives from the secretary of the ZKBS. The representative member of the specialist field of hygiene was newly affiliated to this working group.

Moreover, the BMELV asked the ZKBS to delegate an expert to the EU working group "New Technologies". Prof. Dr. Dr. h.c. Wilfried Wackernagel was chosen as the ZKBS representative for this working group.

Furthermore, a working group of the ZKBS has existed for many years to deal with preparing position statements of the ZKBS on applications for deliberate release approvals 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 appropriate competent authority.

3.3 Advising the Federal Government

Within the scope of administrative assistance, the Federal Government has asked the ZKBS for position statements on the following themes:

- Draft of a regulation on law simplification and enhancement of occupational medicine precautions
- Application EFSA/GMO/UK/2005/19 of the company Syngenta for approval of placing on the market of the genetically modified maize GA21 as genetically modified food or feed according to the regulation (EC) No. 1829/2003

3.4 Advising competent authorities of the Bundesländer

Within the scope of administrative assistance, state authorities have asked the ZKBS for position statements on the following themes:

- Classification of genetic engineering operations with *Treponema pallidum*
- Evaluation of the oncogenic potential of the genes for HIFα proteins, prolyl-4-hydrolases (PHDs), Creb binding proteins (CBPs), E3 ligases, aryl hydrocarbon receptor nuclear translocator (ARNT/HIF1β), Fog-2, MKL-1 and ATF4
- Evaluation of the oncogenic potential of the Neuregulin-1 encoding gene
- Safety evaluation of genetic engineering work with *Streptococcus pyogenes*
- Revision of the safety evaluation of genetic engineering work with retroviral vectors encoding the NANOG gene
- Risk assessment of recombinant BVDV (*Bovine viral diarrhea virus*) strains as vaccine candidates
- Assessment of a chemical-thermal inactivation procedure for a containment level 1 genetic engineering facility
- Safety-related equipment of a projected containment level 3 genetic engineering facility
- Use of disinfectants of the IHO list

3.5 Risk assessment of donor or recipient organisms

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

Table 6: Newly classified assigned microorganisms.

Organism	Risk group
Viruses	
Cassava brown streak virus (CBSV)	1
Emiliania huxleyi virus [(a)]	1
Yellow fever virus (YFV), vaccine strain 17D	1
Hepatitis B virus (HBV)	2
Hepatitis D virus (HDV)	2
Hepatitis G virus (HGV)	1
Measles virus (MeV), strain NSE (attenuated)	1
Merkel cell polyomavirus (MCV or MCPyV)	2
Modoc virus (MODV)	2
Rice yellow mottle virus (RYMV) [(a)]	1
Simian immunodeficiency virus (SIV)	2
Watermelon chlorotic stunt virus (WmCSV)	2
Bacteria	
Arcanobacterium bonasi	2
Arcanobacterium bialowiezense	2
Rickettsia honei	2
Streptococcus equi subsp. *ruminatorium*	2
Streptococcus pseudoporcinus	2
Staphylococcus simiae sp. nov.	2
Weissella confusa	2
Fungi	
Fusarium avenaceum [(a) (b)]	1
Fusarium poae [(a) (b)]	1
Fusarium tricinctum [(a) (b)]	1
Glomus intraradices	1
Hyaloperonospora parasitica (formerly *Peronospora parasitica*)	1
Magnaporthe oryzae (anamorphous *Pyricularia oryzae*)	1
Magnaporthe grisea (anamorphous *Pyricularia grisea*)	1
Parasites and eukaryotic protozoans	
Herpetomonas muscarum	1
Trypanosoma theileri	1
Leptomonas costaricensis	*2*
Phytomonas spp. [(a)]	*2*
Sergeia podlipaevi	*2*

Trypanosoma avium	*2*
Trypanosoma benneti	*2*
Trypanosoma boissoni	*2*
Trypanosoma carassii	*2*
Trypanosoma chattoni	*2*
Trypanosoma equiperdum	*2*
Trypanosoma evansi	*2*
Trypanosoma mega	*2*
Trypanosoma rangeli	*2*
Trypanosoma rotatorium	*2*
Trypanosoma therezieni	*2*
Trypanosoma triglae	*2*
Trypanosoma vivax	*2*

[(a)] For handling phytopathogenic organisms the ZKBS refers to the Plant Protection Act (PflSchG) and its regulations, in particular to the Plant Inspection Ordinance (PflBeschauV), and to the Plant Quarantine Directive 2000/29/EC.

[(b)] Fusaria are the most frequent mycological cause of keratitis in contact lens users. Due to uncertainty of classification it is recommended to contact lens users or persons with ophthalmological diseases to wear safety goggles.

Risk assessments regarding the organisms listed above can be looked up on the BVL website under the heading “Genetic Engineering” (http://www.bvl.bund.de/cln_007/nn_491798/DE/06_Gentechnik/093_ZKBS/zkbs_node.html_nnn=true).

3.6 Containment level assignment for genetic engineering operations

In 2008, the ZKBS provided 33 position statements on safety and containment level assignment for genetic engineering operations. 24 of the assessed operations were addressing questions in the area of virology or cell biology and seven dealt with bacteriology. Two of these operations came from the area of parasitology. No genetic engineering operation from the specialist field of mycology was filed with the ZKBS. The evaluated genetic engineering operations addressed the following questions and were assigned as follows:

Containment level 1

Genetic engineering operations

- to induce an immune response against heterologous antigens that are recombinantly expressed in commensal, apathogenic *Escherichia coli*
- to clone the C-terminal fragment of the *Pasteurella multocida* toxin in *Drosophila*

Containment level 2

Genetic engineering operations

- to generate and characterize recombinant *Measles viruses* (MeV) that are derived from *Measles virus* strains used for vaccination
- to examine the genetics, cell biology and evolution of kinetoplastid protozoans
- to generate epitope-marked *Yellow fever virus* (YFV)
- to transduce cell lines with subgenomic *Hepatitis C virus* (HCV) replicons using HCV-like particles (HCVtcp)
- to characterize virulence factors of *Arcanobacterium bonasi* and *Arcanobacterium bialowiezense*
- to clone PCR fragments of the causative organisms of anthrax, brucellosis, melioidosis, Q fever and glanders as well as to heterologously express immunogenic proteins of *Brucella* spp.
- to identify genes and receptor proteins involved in circular transmission of *Watermelon chlorotic stunt virus* (WmCSV) by whiteflies
- to investigate the replication of *Torque teno virus* (TTV)
- to produce inactivated influenza vaccine using recombinant influenza viruses

Containment level 3

Genetic engineering operations

- to examine viral and host-specific factors with respect to infectivity and evolution of *Hepatitis C virus* (HCV)
- to transform *E. coli* K12 strains with the proviral full length genome of *Human immunodeficiency virus-1* (HIV-1)
- to study the immunogenicity and pathogenicity of *Mycobacterium tuberculosis* mutants as well as to identify and heterologously express potential porin genes of *Mycobacterium tuberculosis*
- to examine all gene products of containment level 3 influenza viruses
- on the influence of *cis*- or *trans*-acting regulatory factors on replication of *Human immunodeficiency virus-1* (HIV-1)
- to gain insight into the pathogenesis of AIDS and to analyze the *Hepatitis C virus* (HCV) replication cycle in hepatocytes
- to investigate the interactions between *Tick-borne encephalitis virus* (TBEV) and the interferon system
- to analyze highly pathogenic avian influenza viruses of the H5 and H7 subtype
- to analyze genetic reassortment between influenza viruses of different species
- on gene expression and gene suppression using lentiviral vectors and inhibition of *Human T-cell leukemia virus* (HTLV), *Human immunodeficiency virus* (HIV) and *Simian immunodeficiency virus* (SIV) by gene expression and gene suppression

- to characterize *env* variants of *Human immunodeficiency virus* (HIV)
- to investigate replication, immunology and virology of *Chikungunya virus* (CHIKV)
- to investigate oncolysis by modified *Measles viruses* (MeV)
- to test genetic regions of *Human immunodeficiency virus-1* (HIV-1) that are relevant for therapy with regard to resistance against Maraviroc
- on the influence of *Lassa virus* (LASV) glycoproteins on endothelial permeability
- to study the function of the avian influenza virus NS1 protein in chickens
- on the regulation of type III effector gene expression in Shiga toxin-producing *E.coli*
- to analyze chimeras between *Yellow fever virus* (YFV) and *Modoc virus* (MODV)
- to identify metabolic pathways in *Mycobacterium tuberculosis* that are essential for survival in primary human macrophages
- to express green fluorescent protein (GFP) in *Rickettsia honei* and *Orientia tsutsugamushi*
- to establish the complete *Plasmodium falciparum* life cycle under avoidance of infection of humans
- to examine all gene products of highly pathogenic avian influenza viruses of the H2, H5 and H7 subtype in different cell types and animal models

3.7 Assessing technical safety measures in genetic engineering facilities

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

- Disposal of downstream HEPA filters of class 2 microbiological safety cabinets in containment level 3 facilities
- Extension of the already operating genetic engineering facility of the Sächsisches Serumwerk in order to double capacity

3.8 Publication of general position statements

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

- Update of the general position statement of the ZKBS on safety measures for handling risk group 3** retroviruses, Ref. No. 6790-10-80
- General position statement of the ZKBS on risk assessment of *E. coli* K12 containing a complete retroviral genome, Ref. No. 6790-10-89

3.9 Position statements on releases

In 2008, the ZKBS provided position statements for the BVL on the six applications for approval of release of GMOs listed in Table 7. The table specifies applicants, plants, major genetic modifications with their expected effects and the time period for the planned release. Four of these applications were already submitted in 2007, and the two applications listed last in the table were submitted in 2008. All six were supported by the ZKBS and approved by the BVL.

3.10 Position statements on placing on the market

In 2008, the ZKBS provided a position statement on an application for placing on the market of GMOs according to the Directive 2001/18/EC. The application EFSA-GMO-NL-2005-24 for the soybean 40-3-2 of the company Monsanto was filed with the competent authority of the Netherlands and was forwarded to the EFSA on November 4, 2005. In the corresponding position statement the ZKBS reasons that harmful effects on the subjects of protection according to §1 No. 1 of the Genetic Engineering Act (GenTG) due to cultivation of the soybean 40-3-2 are not to be expected.

No applications for approval were submitted through Germany according to the Directive 2001/18/EC of the EU.

Table 7: Applications for approval of release of genetically modified plants on which the ZKBS provided a position statement in 2008.

Applicant	Plant	Major genetically engineered modifications	Time period
Pioneer Hi-Breed	Maize	Maize line 98140; resistance to herbicide; contains the *Bacillus licheniformis gat4621* gene (glyphosate-4-acetyltransferase) and the modified acetolactate synthase of maize	2008 - 2011
Rheinisch-Westfälische Technische Hochschule Aachen	Maize	Maize hybrid MON89034xMON88017; Bt toxin and herbicide tolerance; contains the synthetic Bt toxin gene *cry1A.105* of *Bacillus thuringiensis*, a synthetic variant of the *Bacillus thuringiensis* subsp. *kurstaki* gene *cry2Ab2* and a synthetic variant of the *Bacillus thuringiensis* subsp. *kumamotoensis* gene *cry3Bb1*	2008 - 2010
BASF Plant Science	Potato	Potato (*Solanum tuberosum*) line EH92-527-1; carbohydrate metabolism; contains a fragment of the *gbss* (granule bound starch synthase) gene in antisense orientation and the *E. coli npt*II gene	2009 - 2010
University of Rostock	Potato	Resistance to frost and special rotting characteristics; contains the *Thermosynechococcus elongatus psbY-cph*A_{Te} gene and the *E. coli npt*II gene	2008 - 2009
University of Rostock	Spring wheat	Wheat lines KP4-Greina 16 and KP4-Golin 5; resistance to fungi; contains the *Ustilago maydis virus-4* (UmV-4) *kp-4* (killer protein 4) gene, the *Streptomyces hygroscopicus bar* gene and the *bla* gene (only in KP4-Greina 16)	2008 - 2010
Max Planck Institute for Chemical Ecology	Black Nightshade	Reduction of insect resistance; 307 bp fragment of the *Solanum nigrum* lipoxygenase-3 gene in antisense orientation; 307 bp fragment of the *Solanum nigrum* lipoxygenase-3 gene in sense orientation (complementary to the above-named fragment), intron 3 of the pyruvate-ortho-phosphate-dikinase gene (*pdk* i3) of *Flaveria trinervia* (Asteraceae), *E. coli* hygromycin resistance gene *hpt*II	2008 - 2010

Berlin, April 2009