

# Research Agenda of the German Federal Institute for Risk Assessment (BfR)

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## 1. The Task and Structure of the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the German Federal Ministry of Food and Agriculture (BMEL). It advises the German government on issues of food, chemical and product safety as well as in the area of laboratory animal protection. The BfR conducts independent research on topics that are closely linked to its assessment tasks. With its work, the BfR makes a decisive contribution towards the protection of consumer health.

The BfR was established in 2002 to strengthen consumer health protection. It is the scientific institution in the Federal Republic of Germany which prepares reports and opinions on questions of food and animal feed safety, as well as on the safety of substances and products and the protection of laboratory animals. The BfR is tasked with assessing existing and identifying new health risks, preparing recommendations on risk limitation and communicating this process to policy makers and the general public.

The BfR assesses health risks from a scientific point of view and outlines possible courses of action to minimize risks. These are converted into protective measures for consumers by risk management on the federal government level ([detailed legal foundations of the BfR](#)). It is the duty of the competent authorities of the German federal states (“Laender”) to monitor compliance with the national and European regulations on consumer health protection. The BfR supports the German federal states (“Laender”) in this task by developing and establishing analysis methods for monitoring, for example, or giving an advisory opinion on current consumer

health protection issues. The BfR is also involved in various registration and approval procedures. The BfR also performs the tasks of the “German Centre for the Protection of Laboratory Animals (Bf3R)”.

In its risk assessment, the BfR is advised by a network of scientific experts from committees, as well as the Scientific Advisory Board. As the national point of contact for the European Food Safety Authority (EFSA) and partner of the European Chemicals Agency (ECHA), the BfR cooperates with more than 50 national, international, governmental and non-governmental institutions. The BfR is independent in its scientific assessments, research and communication activities.

## **2. Research at the BfR**

One of the BfR’s key competences is independent, application-orientated, ad hoc research as required. The research topics are closely related to its assessment tasks. In doing so, BfR cooperates with other institutions, especially with the BMEL and the university sector in addition to the Member States of the European Union and international partner countries. The BfR’s research activities thus also serve to promote national and international networking. The BfR is independent and transparent in the planning, organisation and performance of all its research activities. One aim is to close gaps in knowledge. Another is to constantly expand the Institute’s scientific expertise in risk assessment and risk communication independent of economic, political and social interests. To prevent research from being influenced by economic interests, research is funded exclusively by third-party funds from public national and European institutions. The BfR is actively involved in numerous national and international third-party funded projects.

### **Experimental Infrastructure**

The BfR is equipped with a modern experimental infrastructure in the domains of instrumental analytics, microbial diagnostics, toxicology and food technology. This includes a farm with an animal facility and aquaculture, a facility for performing experimental work on animals, and modern molecular and cell biology laboratories as well as analytical and protein-biochemical laboratories for toxicological research and for developing alternative and replacement methods to animal experiments. Work up to safety level S2/L2 can be performed in the large and small animal laboratory. Microbiological work is possible up to level L3. The laboratory infrastructure is continually adapted to scientific developments and technical possibilities. The instrumental equipment enables interdepartmental and interdisciplinary investigations and assessments along the entire feed and food chain as well as the goods and product chain.

The infrastructure also includes the BfR reference and consultant laboratories, which develop and validate state-of-the-art sensitive detection methods. These are capable of providing rapid and reliable results on the occurrence, spread and characterisation of pathogens, residues, contaminants and undesirable ingredients.

## Study Centres

The study centres serve to set long-term priorities in strategically important areas of the BfR. In this way, the BfR study centres bundle and intensify technical expertise on interdepartmental topics, combined with participation in national and international research projects.

## Promoting Young Scientists

Future-oriented training and support of young scientists represents one of the BfR's strategic tasks. With the BfR doctoral training programme, doctoral candidates obtain overarching knowledge on scientific work in addition to their own research work affiliated with a department. Due to its modular design, the structured programme for continuing and further training enables individual specialisations and thus also reflects the diversity of disciplines represented at the BfR. Junior research groups offer young scientists shortly after their doctorate the opportunity for independent research and scientific qualification on focus topics in the area of consumer health protection at an internationally competitive level. In doing so, the BfR specifically boosts core research areas and junior scientists. In its research, the BfR implements the guidelines of the German Research Foundation (DFG) based on the [principles of good scientific practice](#).

## Quality Assurance

Comprehensive quality assurance forms part of the BfR's strategic focus. The BfR bases its activities on the relevant ISO standards and recognised standards for quality management. In many scientific laboratories, test procedures are accredited on the basis of the DIN EN ISO/IEC 17025\* standard. In addition, all working areas of the BfR – science, assessment, communication, and administration – have been certified in accordance with quality standard DIN EN ISO 9001 since 2010. The Institute thus maintains a quality management system in line with international standards, both in the area of practical laboratory work and in the area of scientific assessment processes and administration.

\* See accreditation certificate and annex of the DAkkS D-PL-18583-02

## Scientific Advisory Board

To promote scientific work, the BfR established a Scientific Advisory Board in 2005. It advises the BfR on setting priorities in research and on strategically developing medium- and long-term goals in the technical-scientific field, as well as on optimising the organisation of the Institute and with regard to its work in the technical-scientific field. The advisory board also supports contacts and cooperation between the BfR and other research institutions in Germany and abroad and provides the Institute with guidance when appointing renowned scientists to the commissions located at the Institute.

## 2.1. Overarching Research Goals

The BfR views assessment, the preparation of expert reports and research as a single unit. The overarching goals of the BfR's research activities include:

- Independent, application-oriented and ad hoc research,
- Competent advice to political decision-makers based on a high scientific level and internationally recognised expertise,
- Ensuring the quality of assessments in certification tasks,
- Strengthening competence in the network of European scientific authorities working in the field of consumer health protection and the protection of laboratory animals,
- Ensuring a high level of technical expertise for the exchange of ideas, concepts and in the implementation of joint research projects at national and international levels,
- Analysis of the risk perception of various stakeholders from the fields of science, industry, politics, media, associations, non-governmental organisations and the consumer community as a foundation for the development and application of suitable participatory instruments of risk communication.

Research activities are carried out in such a way that they are

- independent of political, economic and social interests,
- impartial,
- quality-assured,
- transparent,
- application-oriented and
- need-based.

## 2.2. Digitisation in Research

Digitisation is an everyday process in research. To implement a digital transformation across the entire research process and thus also set new research impulses, digital expertise and infrastructure need to be generated. The foundations for this are research data management, an interoperable system for the structured storage of data and software, and a powerful IT infrastructure for the collection, processing and storage of very large data sets. Developments already underway in data generation, archiving and data access – as well as those in metadata standards, ontologies and quality criteria, and the establishment of high-performance computing pipelines – are being continuously pursued with a view to enabling cutting-edge risk assessment. In addition, the “Digital Innovation” department was set up to develop innovative digital tools for the standardised exchange of data, models and IT procedures between institutions of the BMEL, the German federal states (“Laender”) and industry.

To support the digitisation processes and the BMEL's role as a digital reference ministry, the German Federal Institute for Risk Assessment (BfR) and the Julius Kühn Institute Federal Research Centre for Cultivated Plants (JKI) concluded an agreement on the establishment of a “Digitisation Laboratory for Food, Agriculture and Consumer Health Protection” (Digilab-ELV). The Digitisation Laboratory for Food, Agriculture and Consumer Health Protection bundles the capacities and expertise of current and future IT research and development activities of both institutes and networks research projects related to digitisation of both institutes in the future.

## 2.3. Research in Working Areas

The BfR conducts its own research primarily in subject areas in which risk assessments are required or in which there is an urgent need in the context of consumer health protection. The

resulting data, methods and procedures form the basis for an assessment and policy advice based on the latest findings. The Institute's research also includes work of a non-experimental nature. Research is conducted at an international level with the aim of scientific excellence. The working areas of research are oriented towards its legal mandate. To implement its research agenda, the BfR organises internal research funding on the one hand and acquires public third-party funding on the other ([current third-party funded projects of the BfR](#)). In addition, the BfR has funds available for awarding to third parties and for Bf3R research funding (replacement and reduction of laboratory animals in research; recognition, classification and reduction of pain, suffering or harm in laboratory animals; refinement of housing conditions) so it can involve external expertise to meet research needs. The BfR's research activities can be assigned to the following interdepartmental working areas:

### **Risk Assessment**

Risk assessment is made on the basis of internationally recognised scientific assessment criteria. Research activities include the acquisition of data for exposure assessment (occurrence, distribution and intake of substances and microorganisms), the development of advanced methods for detecting the mechanisms of action of toxic properties of pathogens, substances and products, as well as research on exposure to various substances (e.g. chemicals, cosmetics, textiles, toys, plant protection products and biocides or non-textile care articles) and the further development of exposure assessment methods.

### **Risk Identification, Early Risk Detection and Risk Minimisation**

Scientific risk assessment requires knowledge of the properties, mechanisms of action, functionality and pathogen-host relationships of microorganisms, viruses and substances. Research in this area involves the integration of holistic considerations along the entire food production chain so that, if necessary, the cause of the contamination of food with pathogens or undesirable substances can be traced back seamlessly. This way, risk potentials can be identified and assessed during various stages of production and manufacturing processes. New approaches are being developed for the investigation of food safety, microbiological safety, plant protection products and biocides as well as chemical safety and the safety of consumer products, allowing faster and more accurate findings on toxic properties while replacing animal experiments. This also includes the development of sensitive analytical methods for the detection of actual or potential toxic substances.

### **Risk Communication**

Research on risk communication includes, among other things, the design and implementation of scientific projects to quantify individual, societal and media risk perception and to involve "stakeholders" (interest groups) from the fields of science, business, politics, media, associations, non-governmental organisations and the consumer community at an early stage. Scientific methods for communicating risks including scientific uncertainty are compiled and scientific projects for risk-benefit assessment are carried out.

### **Alternative and complementary methods to animal experiments**

The documentation, assessment, development and validation of alternative methods to animal experiments is carried out with the aim of avoiding (replacement), minimising (reduction) and improving (refinement) animal experiments (the "3R principle"). This also includes experimental research and development of alternative methods for risk assessment in consumer and occupational safety and in basic research without animal experiments. Research and development is complemented by informatics approaches for research into alternative methods to

animal experiments and the (further) development of toxicological test methods with a focus on alternative methods at the regulatory and experimental level.

### **Reference and consultant laboratories**

Reference laboratories are appointed on the basis of joint or national regulations and provided with particular expertise in the respective field. By developing and validating methods (including interlaboratory tests) and carrying out proficiency tests between official control laboratories of the German federal states for quality assurance, the National Reference Laboratories assume a watchdog function for the early detection of occurring risks. They are an important basis for exposure assessments – on a national and, increasingly, on an international level. In addition to their expertise they are characterised by a high degree of political, social and economic independence. The BfR has reference laboratories in the fields of food and feed safety and food hygiene. They are subdivided into two groups: national reference laboratories under Regulation (EU) 2017/625 which are appointed by the Federal Ministry of Food and Agriculture (BMEL), and other BfR laboratories with a reference function.

### 3. Departments at the BfR

Eight specialist departments, 15 National Reference Laboratories and six laboratories with a reference function are responsible for carrying out the technical tasks and implementing the research objectives:

#### 3.1. Risk Communication Department

Consumer health protection involves researching, assessing and communicating risks. According to international standards, risk communication goes well above and beyond the mere dissemination of information, and so do the tasks of the department at the BfR. Here, not only are actual risks important, but also their medial communication and the subjectively shaped perception of risks. Scientific findings must be communicated in a transparent and comprehensible manner to promote the rational handling of risks. In this context, the degree of scientific uncertainty must also be communicated.

The Risk Communication Department has expertise in social science research, particularly in the fields of psychology and communication sciences. Both qualitative and quantitative methods are used to determine the risk perception and communication needs of the various stakeholders and to develop communication formats tailored to specific target groups. Social science research is conducted in cooperation with universities, non-university institutes and external service providers as well as at the BfR itself. The department places emphasis on media analyses, population and stakeholder surveys as well as focus groups and consumer conferences. Social science research is closely interlinked with concrete application in the units of Press and Public Relations and the BfR Academy as scientific event management. This allows early risk detection, risk perception research as well as communication and participation strategies at the BfR to be applied directly in all technical areas of responsibility of consumer health protection such as food, feed, chemical and product safety.

#### Spectrum of Tasks and Competences

The BfR has the legal mandate to communicate risks and informs the public about possible health risks and the research results on which they are based in the field of food, chemical and product safety. In doing so, the BfR enters into an active dialogue with various points of contact from science, industry, politics, the media, associations, non-governmental organisations and the consumer community. In addition to target group-oriented press and public relations work, this communication process includes the active involvement of various interest groups through expert discussions, status seminars, consumer protection forums, stakeholder conferences and public symposia.

One focus of the BfR is crisis prevention and coordination as well as early risk detection. The Risk Communication Department scientifically processes events and crises for this purpose.

The interdisciplinary Risk Communication Department conducts research projects on the perception of risks, the early detection of risks and the assessment of their consequences – projects that cover the areas, for example, of new technologies such as genome editing, changes in the dietary behaviour of consumers following risk communication or the prioritisation of risks by various social interest groups. Representative surveys, consumer conferences, Delphi surveys and focus groups are used as instruments for this purpose.

To implement these special risk communication measures, the department also has the means to involve external expertise.

#### Core Research Areas

The core areas include risk research, risk perception, early risk detection and risk assessment. The main disciplines of social science research applied in these areas are psychology and

communication sciences in addition to sociology and political science.

- Measurement of the risk perception of various stakeholders from the fields of science, business, politics, media, associations, non-governmental organisations and the consumer community, including reputation management
- Collection of data via social science research methods such as focus groups, Delphi surveys, representative surveys, media analyses, consumer conferences and behavioural psychology lab experiments
- Survey of the information needs of the above-mentioned stakeholders and development of target-group-specific communication instruments
- Risk communication about new technologies using participatory methods
- Media transport of risks and its potential consequences for behaviour
- Presentation of the BfR to the public and the media through generally intelligible communication of scientific work results, also taking into account scientific uncertainty, by means of various publication formats
- Visual communication: Presentation of scientific facts using visual methods (videos, video tutorials, graphics) for the BfR homepage and the BfR's social media presence on Instagram, Twitter and YouTube
- Crisis research, evaluation of crises, crisis prevention and coordination
- Development and implementation of methods for early risk detection including risk-benefit assessment
- Scientific and strategic event conception including conference documentation and evaluation
- Issues management and agenda-setting



### 3.2. Exposure Department

Human exposure to potentially hazardous substances is the basis for the assessment of health risks in the areas of food, chemical and product safety. To estimate and assess exposure in these areas, the department carries out supporting research and development activities. In addition, it conducts research on health protection issues related to the transport of dangerous goods and develops methods in the application areas of statistics, epidemiology, exposure modelling and quantitative risk assessment.

For refined exposure assessment, a Total Diet Study (the BfR MEAL study) was implemented for the first time in Germany at the BfR as well as a Germany-wide representative child nutrition study to record food consumption (KiESEL). The Exposure Department also carries out development and research projects on the documentation of cases of poisoning and formulations of products. Here, too, there is a close link to the statutory tasks of the BfR on the one hand and the mandate for research and development projects on the other – with the aim of optimising the usefulness of this data for BfR health assessments. The Exposure Department conducts predictive studies on consumer behaviour to accompany assessment questions.

Quantitative risk models and associated modelling tools are developed in the area of mathematical statistics and modelling. This allows special requirements to be addressed, for example, for the representation of uncertainties. Methods for the evaluation and visualisation of available data or data that will be available in the future in the wake of digitisation are being developed (machine learning, graph theory).

#### Spectrum of Tasks and Competences

The Exposure Department at the BfR is responsible for the methodological standardisation and implementation of exposure assessments in the field of food and product safety and in the enforcement of the REACH regulation. In poisoning and product documentation, population-based information sources are used in close networking with poison information centres in Germany with a view to identifying and assessing acute toxicological risks in particular, and product information is forwarded to poison information centres for emergency advice.

With concepts and applications of epidemiology, statistics and mathematical modelling, the department supports a quality-assured and evidence-based assessment of consumer health risks by the BfR. The department prepares legally required scientific assessments in the field of the transport of dangerous goods and advises the Central Command for Maritime Emergencies (Havariekommando).

#### Core Research Areas

- Collection of high-quality data for exposure assessment in the field of food safety (e.g. MEAL, KiESEL) and participation in the establishment of an international centre of excellence for total-diet studies
- Further development of exposure scenarios under REACH by generating new data (consumer behaviour studies), standardisation of exposure parameters as well as testing and further development of current models and tools
- New methods in risk modelling, including spatio-temporal aspects and risk-benefit considerations
- Refinement of documentation and early detection of poisoning incidents in Germany, development of a national monitoring of poisoning incidents
- Development of models to illustrate the statistical uncertainties in estimating the frequency of illnesses or infections
- Development and application of computer-based evaluation programmes for high-throughput data (e.g. in the field of proteomics)

- Statistical methods for the exploration and analysis of commodity flows
- Validation of diagnostic tests without gold standards
- Health hazards of chemical substances, particularly in the transport of dangerous goods or in maritime applications (e.g. ballast water treatment)
- Toxicokinetic modelling
- Statistical learning to identify and assess risk factors from epidemiological studies
- Further development and digitalisation of data collection methods in the field of food exposure

### 3.3. Biological Safety Department

The detection and prevention of hazards emanating from microorganisms as well as their toxins are of central importance for human health. In its Biological Safety Department, the BfR focuses on the assessment of microbiological risks in and on food-producing animals, food and feed, as well as cosmetics and consumer goods. In particular, the BfR concentrates on the relevant pathogens for food infections and intoxications.

The BfR develops and evaluates new safety concepts in food and product hygiene and prepares qualitative and quantitative risk assessments on microorganisms and the toxins they produce for human health.

To this end, the Institute develops new methods for the detection and characterisation of pathogens and their toxins. At the same time, existing methods are validated and further developed. This ranges from refined culture methods and new culture-independent detection methods, e.g. metagenomic approaches, to combinations of cultural and, for example, molecular biological detection methods.

For hazard characterisation, state-of-the-art molecular biological methods of pathogen characterisation – including whole genome sequencing of bacteria, viruses and other pathogens – are applied in the quality-assured eight National Reference Laboratories and five reference laboratories. New pathogens and pathogen variants that may form in food and feed as a result of horizontal gene transfer or the consequences of climate change are also detected and their formation process is traced.

To refine exposure assessments, biological and technological processes are modelled and the parametrisation of these models is supported by experimental work. With its epidemiological expertise and competence in the IT field, the department develops software tools to record and analyse the entry of pathogens and toxins into food and feed chains and their behaviour – even in complex commodity chains. This makes it possible to assess the sources of pathogens and toxins and their spread in trade networks.

With its central role in monitoring zoonotic pathogens in the food chain, the department specifically closes knowledge gaps on the occurrence of different pathogens in the various food chains from the farm and its environment to the food in the retail industry.

The networking of competences in microbiology and molecular biology, animal facilities and food technology, software development and epidemiology enables the Biological Safety Department to further develop the standards of risk assessment and to react quickly and efficiently to newly identified hazards. The close networking of the units with the European networks of reference laboratories, state testing facilities and the university landscape gives the department a key role in the characterisation of microbiological risks for consumers associated with food and consumer goods.

The following National Reference Laboratories (NRL) and other laboratories with a reference function are situated in the department:

- NRL for the performance of analyses and tests for zoonoses (*Salmonella*)
- NRL for *Escherichia coli* including verotoxin-producing *E. coli*
- NRL for *Trichinella*
- NRL for *Campylobacter*
- NRL for coagulase positive staphylococci including *Staphylococcus aureus*
- NRL for food-borne transmissible viruses
- NRL for antibiotic resistance
- NRL for *Listeria monocytogenes*
- Consultant laboratory for *Yersinia*
- Consultant Laboratory for Leptospire
- Consultant Laboratory for Vibrions
- Laboratory for Clostridia

- Laboratory for Bacillus species

### **Spectrum of Tasks and Competences**

Within the framework of the statutory mandate of risk assessment in the area of food safety and consumer health protection, the Biological Safety Department deals with health risks to humans emanating in particular from microorganisms, the toxins they produce and other microbial metabolites, including antibiotic resistances. In particular, these include bacteria, viruses, parasites and TSE pathogens.

Not only foodstuffs are evaluated for their potential as sources of biological hazards, but also animal feed, cosmetics and commodities (e.g. food processing equipment, food packaging materials, dishes), including the processes by which they are acquired, manufactured, processed and distributed.

The department's tasks include diagnostic procedures for the detection and characterisation of the various pathogens in food, their virulence and resistance properties as well as work on the occurrence of microbiological hazards in food and commodities, including qualitative and quantitative risk assessments.

The Biological Safety Department is involved in the clarification of outbreaks caused by food-borne zoonotic pathogens (legally anchored task in the Protection against Infection Act (Infektionsschutzgesetz)).

### **Core Research Areas**

- Assessment of foodstuffs (fish, milk, plant-based foodstuffs, etc.) and food technology issues with regard to food-borne pathogens of infection and intoxication
- Assessment of microbial toxins and development of detection methods
- Assessment of the microbiological safety of consumer products such as consumer goods, cosmetics or food packaging, product hygiene and disinfection strategies
- Properties and virulence factors of food-associated pathogens and their tenacity and inactivation in foods
- Development and assessment of new methods in food hygiene and safety concepts for pathogen minimisation in foods
- Modelling methods for the behaviour of pathogens in food and their spread along the food chain, food safety along global commodity chains
- Development of tools for analysing commodity flows
- Zoonoses and antibiotic resistance monitoring, epidemiology of food-associated zoonoses, assessment of zoonosis reporting data
- Horizontal gene transfer in food-relevant microorganisms
- Development of molecular biological detection and typing methods including microarrays and genome analysis (next-generation sequencing)
- Bioterrorism with regard to food safety issues and the development of appropriate diagnostic and preventive measures
- Food safety and climate change, One Health aspects

### **3.4. Food Safety Department**

In the context of food law, the term "food" is defined as any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans. This means that foods are usually complex mixtures of substances. These include natural ingredients (proteins, carbohydrates, fats, vitamins, minerals or compounds of (plant) secondary metabolism), but also substances that are intentionally added to the food during its production and substances that unintentionally enter the food as impurities or are produced during manufacturing, storage and production. All these substances, including

the natural components of food, can pose health risks to consumers under certain conditions. On the other hand, any food that is not safe may not be placed on the market within the EU. The assessment focus of the Food Safety Department ranges from foods for general consumption and food supplements with added vitamins, minerals or other substances with a nutritional or physiological effect to foods for special consumer groups (e.g. infant formula, foods for special medical purposes), novel foods, foods made from genetically modified organisms and food additives, technical adjuvants and chemically defined flavouring substances, to impurities in foods. In addition to toxicological aspects, nutritional and nutritional-medical aspects, including allergies, are also investigated.

The assessment work in the department is characterised by its scientific, research-based approach. To support its risk assessments, results from in-house research efforts are also used, for which a wide range of methods are employed. Epidemiological data is also collected for questions of particular relevance.

### **Spectrum of Tasks and Competences**

The Food Safety Department assesses food with regard to its substance-related risks. Its main focus is the formulation of scientific opinions on issues that are directly or indirectly related to food safety with regard to human health and that can serve as a basis for management decisions. Its assessments are based on current scientific knowledge and take into account not only healthy adults but also special population groups with potentially increased sensitivity, such as pregnant women, infants and children, the elderly or people with certain illnesses. Foodstuffs are also assessed by the department according to nutritional or medical criteria. Within the framework of health risk assessment and, where appropriate, benefit assessment under the aspects of nutritional medicine and physiology, the department assesses food supplements and enriched foods in particular, as well as foods for special consumer groups. It also conducts risk assessments of special diets for which a health risk can be assumed due to the restricted choice of foods involved.

Another focus of the department's work is the preparation of statements on novel foods as well as food and feed made from genetically modified organisms.

Another aspect is the traceability and identity of products. In this context, the department develops detection methods as well as strategies and methods for traceability and food product identity, e.g. within the framework of the tasks of the National Reference Laboratory (NRL) for animal protein in feed and the reference laboratory activities of the European Network of GMO Laboratories for the identification and quantification of genetically modified food and feed.

The following National Reference Laboratory (NRL) and one further laboratory with a reference function are situated in the department:

- NRL for animal protein in feed
- Reference laboratory in the Genetically Modified Organisms (GMO) network

### **Core Research Areas**

The department's main focus is the formulation of scientific opinions on issues that are directly or indirectly related to food safety or consumer health protection and that can serve as a basis for management decisions. This forms the basis for its research activities:

- Research grounded on laboratory-based, molecular biological and cell biological methods as well as non-laboratory-based scientific approaches (e.g. scientific evaluation of health-related human data; *in silico* modelling) and animal experimental research approaches to elucidate the toxicological mechanisms of action of food ingredients and

contaminants (e.g. organic and inorganic nanoparticles, marine biotoxins, secondary plant compounds, PFAS, process contaminants)

- Development and validation of analytical methods for the determination of biomarkers
- Further development of test methods and strategies (*in vitro*, *in silico*) to identify the toxicological potential of food-relevant substances
- Performance of kinetic human studies, e.g. to determine oral bioavailability, to identify metabolism pathways in humans and to establish new exposure markers
- Planning and conducting epidemiological studies to obtain missing human data for risk assessment (examples: dioxins, PFAS, energy drinks, plant-based diets)
- Development and validation of modern methods for tracing animal proteins in food and feed as well as food-associated allergens (in particular PCR- and MS-based methods of allergen analysis in food)
- Reference laboratory activities in the European Network of GMO Laboratories (ENGL) to support the testing and validation of detection and identification methods (for GMOs) according to Article 6 para. 1 of Regulation (EC) No. 1981/2006

### 3.5. Pesticides Safety Department

To obtain authorisation for a plant protection product or biocidal product, it must be ensured that human health is consistently protected when used as intended. With this in view, the Pesticides Safety Department is concerned with the health assessment of preparations (plant protection products and biocidal products) as well as their active substances and metabolites.

Elements of the risk assessment include the verification and identification of inherent toxic properties, dose-response relationships and exposure assessment. In addition to classification and labelling, the department's objectives include the derivation of toxicological limit or reference values and maximum residue levels and the determination of risks for professional users and workers in the plant protection sector as well as consumers and uninvolved third parties in the biocide and plant protection product sector. For this purpose, it also reviews analytical monitoring methods and develops and refines regulatory test methods and assessment strategies.

Within the framework of the research necessary for risk assessment and fulfilment of the legally mandated tasks, the department continuously develops methodological and conceptual foundations for risk assessment in the areas of toxicology and exposure assessment. In addition, potentially new risks or those that may have been inadequately addressed are also analysed and investigated within the framework of preventive research. Currently, the focus in this area is on the cumulative toxicity of mixtures, residues and multiple residues of plant protection products and biocidal products as well as endocrine disruptors. The department also focuses on the potential use of new approach methodologies, including computer-based *in silico* predictions and possible toxicities due to effects on and through the microbiome and dermal absorption. In addition, existing approaches are refined through the analysis of exposure models and consumption data.

The assessments produced in the department are used in national, European and worldwide procedures. National and European approval and authorisation procedures and risk minimisation measures are based on them.

#### Spectrum of Tasks and Competences

The department's tasks include the health risk assessment of plant protection products and biocidal products in accordance with legal requirements as well as ad hoc assessments in the field of plant protection and biocides.

The core tasks of the department include the identification of inherent toxic properties and dose-response relationships, the classification and labelling of pesticide agents and products, and the derivation of toxicological reference and limit values. It also determines the exposure of humans, farm animals and domestic animal, from which it derives risk reduction measures and maximum residue levels with the aim of preventing adverse effects on human and animal health. In addition, analytical monitoring methods are reviewed and regulatory testing and assessment strategies and technical guidance documents are developed and refined.

Assessments take the form of scientific statements, contributions or comments to assessment reports as well as international technical discussions in expert panels. Regulations and risk management measures in national, European and worldwide regulatory approval, authorisation and assessment procedures are based on the health risk assessments of active substances and formulated preparations prepared in the department.

In addition, the department provides expert advice to the Federal Government on national and European legislation on pesticide active substances and maximum residue levels, on product authorisation and on plant protection product and biocide applications. Internationally, the department's work is incorporated into the regulation and further development of plant protection products and biocides both at the EU level and at the level of the OECD, the FAO/WHO, the GHS and in partner projects with countries outside the EU.

## Core Research Areas

The identification of potential hazards posed by pesticides and the determination of exposure are key elements of risk assessment. The Pesticides Safety Department therefore focuses its research on conceptual aspects as well as on the development of methods in the field of hazard identification and exposure. New Approach Methods (NAMs) for improved risk assessment ('Next Generation Risk Assessment') are in the foreground.

- Development of strategies and concepts for the assessment of health hazards of pesticide active substances and additives with the derivation of health-based limits
- Development of strategies and concepts for the assessment of health risks associated with the use of plant protection products and biocidal products
- Development of strategies and concepts for the assessment of residue behaviour and consumer risk from pesticide active substances in plant and animal food and feed and for the derivation of maximum residue levels
- Development of strategies and concepts for the assessment of active substances with regard to endocrine-disrupting properties, for the assessment of genotoxicity and non-genotoxic carcinogenicity as well as for the estimation of cumulative exposure and for the cumulative risk assessment of pesticide agents
- Development of alternative test strategies for the assessment of the cumulative toxicity of plant protection products and biocidal products, taking co-formulants into account (including in the third-party funded projects: EuroMix II, Combiomics, MetaPath, etc.)
- Development of test strategies for metabolites using *in silico* methods
- Basic principles and strategies for risk assessment of nanomaterials in plant protection products and biocidal products
- Refinement of knowledge on exposure to residues of plant protection products: Processing of consumption data and further development of consumption models, processing of processing data and further development of data collections on processing factors, processing of residue studies and further development of residue databases
- Refinement of knowledge on the exposure of users and uninvolved third parties to plant protection products: Further development of assessment models for user exposure and drift
- Refinement of toxicological assessment tools: Investigation on dermal absorption of pesticide agents
- Refinement of consumer protection through timely analysis and the addressing of new and potentially relevant aspects of assessment, including unintended mixtures and effects on and through the microbiome
- Conceptual and practical further development of toxicological assessments and applicability of "new approach methodologies", in particular "omics" and *in silico* methods.



### 3.6. Chemical and Product Safety Department

Lastingly safe products and chemicals are essential for the health of the population.

In the Chemical and Product Safety Department, the BfR assesses the health risks of chemicals and consumer-related products. The department focuses on the assessment of chemical substances according to European chemicals legislation (REACH Regulation (EC) 1907/2006 and CLP Regulation (EC) 1272/2008), Regulation (EC) No 1223/2009 on cosmetic products, Directive 2009/48/EC on the toy safety and the Tobacco Products Regulation. In addition, risk assessment is carried out as part of the process of the inclusion of substances in the “BfR Recommendations on Materials in Contact with Food”, which cover materials not regulated in detail in Europe, as well as in the area of printing ink components and as part of its support of the Council of Europe (on paper and metals/alloys in contact with food) and the Federal Environment Agency (on materials in contact with drinking water).

Two aspects are of decisive importance here: whether and to what extent consumers come into contact with substances contained in products, and what health risks these substances may pose. Comprehensive risk assessment requires comprehensive data on the many substances, materials and their processing into a wide variety of products. The work of the BfR focuses on consumer goods with and without food contact, including tableware, textiles, food packaging, toys, cosmetics, tattoo inks and tobacco products.

Its risk assessment work is complemented by in-house interdisciplinary research. Reliable findings on chemicals and products are obtained by combining toxicological and chemical-analytical research approaches. For example, the department develops analytical methods for the detection and quantitative determination of substances and nanoparticles, also making use of complex cell cultures. In addition, material properties and manufacturing processes are included in the assessment of exposure.

Experimental research is directed at investigating the migration of substances, their emission, penetration and absorption, as well as the subsequent effect in the organism. Not only the metabolism and toxicology of substances and nanomaterials are considered, but also the mechanisms relevant to toxicology and the underlying immunology, biochemistry and molecular biology. For example, the department conducts research on the recognition and effect of potential endocrine disruptors and on sensitisation properties.

#### Spectrum of Tasks and Competences

The Chemical and Product Safety Department assesses chemical substances that fall under European chemicals legislation as well as the other legal areas mentioned above. The objectives are toxicological assessment, health risk assessment for consumers as well as identifying and participating in the initiation of necessary risk reduction measures in accordance with the REACH regulation.

The department’s tasks also include the identification of research needs for risk assessments and the initiation and monitoring of internal and external research projects to support risk assessments, as well as the further development of regulatory testing and assessment strategies.

Furthermore, the department works on the identification, research, assessment and prevention of health risks in cosmetics, tobacco products, tattoo inks, consumer products (e.g. tableware and food packaging, toys, clothing, intimate hygiene products, mattresses), as well as other “consumer-related products” (e.g. 3D printers and 3D pens, furniture, carpets, hobby products, thermal paper, tools). This not only addresses existing knowledge gaps in the area of scientifically based risk assessment, but also takes into account the concerns of the population. Experimental projects on the detection, migration, exposure, toxicity and allergenic properties of substances, including nanomaterials in these everyday products, are an integral part of the department’s assessment activities. Chromatographic separation methods (including multi-dimensional methods such as GCxGC), mass spectrometric methods (including high-resolution

variants such as qToF-MS for the identification of unknown substances), elemental analysis, metabolomics, proteomics, transcriptomics and complex cell cultures are used.

The department is home to the National Reference Laboratory (NRL) for substances designed to come into contact with food.

### Core Research Areas

The department's main areas of activity consist primarily of work in the field of chemicals assessment under REACH and CLP, on cosmetic products, nanomaterials and other novel materials, on materials in contact with food and other consumer products, as well as on tobacco products and tattoo inks. This results in the following core research areas:

- Basic principles and strategies for risk assessment of chemicals such as grouping and read-across of nanomaterials (NM)
- Development of a stepwise approach for the health risk assessment of tattoo inks, for this purpose studies on analytics, toxicology and biokinetics
- Development of *in vitro* methods for determining the inhalation toxicity of aerosols of e.g. nanomaterials and tobacco products at the air-liquid interface
- Establishment of grouping approaches for the toxicological assessment of nanomaterials (NMs), the development of screening methods for NMs based on (surface) reactivity and the development of alternative, in particular data-based (*in silico*) methods to improve the predictability of the toxicological potential of NMs, as well as the development of investigation and assessment strategies for novel materials
- Investigation of nanospecific mechanisms of action, including the use of omics techniques (e.g. proteomics, metabolomics) and machine learning methods, as well as investigation of the biokinetics of nanomaterials
- Investigation of possible health risks of micro- and nanoplastics
- Development and validation of chemical-analytical methods of analysis for the determination of migrating substances from food contact materials in the NRL for substances intended to come into contact with foods
- Studies on migration and emission as well as dermal penetration/absorption, metabolism and toxicology of substances from consumer articles (including food contact materials, toys, clothing textiles and in cosmetic products) with special consideration of polymer additives (plasticisers, UV stabilisers, antioxidants, dyes) and their degradation products (*non-intentionally added substances*, NIAS), heavy metals and other elemental species, perfluorinated compounds, contaminants such as polycyclic aromatic hydrocarbons (PAH) or mineral oil hydrocarbons (MOSH/MOAH), as well as other unintentionally introduced substances and nanomaterials; method development and validation for highly sensitive analytical detection and quantification of these compounds and their metabolites in migrates, exposed skin, indoor air, cell and tissue cultures or as a basis for biomonitoring studies in serum or urine
- Development and validation of screening methods for sensitisation, endocrine and genotoxic properties of chemical substances from consumer products (endpoints: sensitisation including T-cell activation, endocrine disruption, epigenetics and genotoxicity)
- Testing of consumer products as well as tattoo inks, tobacco products and novel tobacco products including their ingredients for tissue-specific toxicological properties taking metabolism into account
- Investigation of the influence of container fumigants on the chemical quality of transported goods

### 3.7. Safety in the Food Chain Department

The occurrence of contaminants, residues and other undesirable substances along the entire production chain of food and feed requires the assessment of the risks that may arise for humans from the intake of these substances. To assess the risk, among other things, the exposure level must be analysed. To obtain exposure data, innovative detection methods are being developed in the Safety in the Food Chain Department to better assess the hazard potential and to make assessments based on these data.

The methods for the detection of compounds that have the potential to endanger human and animal health also include their metabolites and their (quantitative) determination in food, feed and biological matrices. The department's focus is on marine biotoxins, mycotoxins and plant toxins, halogenated persistent organic pollutants (POPs) as well as food additives, flavourings and additives in animal feed. To support the risk assessment of novel undesirable substances, the department develops, validates and standardises analytical methods so that the results can also be used as a reliable basis for risk assessment. In addition, concepts are being developed for the determination of analytes that are not (yet) available as standard substances. Other key topics are product identity and traceability to maintain the integrity of food and feed along global commodity chains. For preventive consumer health protection, the development and provision of strategies for verifying the authenticity of food and feed (authenticity testing) and for preventing food fraud are of key importance. In addition to the analytical focal points, the BfR is also involved in developing the basis for setting up databases that can be used jointly by monitoring and testing institutions.

Within the framework of animal experiments on agricultural livestock, studies are carried out on the transfer of undesirable substances from feed to food derived from animals. This allows the entire food chain to be considered, from the field to the plate. In line with the 3R principle (Reduction, Replacement, Refinement), a number of replacement and supplementary methods to animal experiments are utilised.

#### Spectrum of Tasks and Competences

One of the focal points of the department's work is the assessment of risks arising from the intake of contaminants, residues and other undesirable substances from food and feed. This includes not only food and feed produced on farms, but also includes food from landscape areas such as forests, open space and water bodies.

The field of feed safety covers all stages of the feed production chain, starting with primary production, through feed production to the feeding of livestock and pets.

The following National Reference Laboratories (NRL) and one further laboratory with a reference function are situated in the department:

- NRL for Additives for use in Animal Nutrition
- NRL for Mycotoxins and Plant Toxins in Food and Animal Feed
- NRL for Halogenated Persistent Organic Pollutants (POPs) in Food and Feed
- NRL for the Monitoring Of Marine Biotoxins
- NRL for Food Additives and Flavourings
- Senior Expert Office for the Import Control of Wine in accordance with the Wine Monitoring Ordinance

#### Core Research Areas

- Initiation of research projects within the framework of early risk detection for the analysis of substances that can adversely affect the safety of food and feed

- Development of methods for the detection of such potentially toxic substances, including their metabolites in food, feed and biological matrices (also taking into account the applicability, the cost and time involved and the use of reagents that are harmful to health and/or the environment)
- Transfer studies on agricultural livestock for the transfer of undesirable substances from feed into food of animal origin including the application of the developed methods for the analysis of the resulting samples
- Application of supporting *in vitro* methods, such as RUSITEC or USSING chamber methods for better interpretation of such transfer studies or toxicity tests
- Authenticity and traceability of food (especially honey and wine) and feed with regard to their identity, origin and production along the commodity chain (development and standardisation of non-targeted analytical methods for authenticity testing, including data interpretation strategies based on chemometric methods, development of basics for building shareable databases, including conceptual design and development of suitable database structures/platforms)
- Further development of analytical methods and data interpretation for the assessment of wine
- Development, validation and standardisation of (multi-analyte) methods for the quantitative determination of food additives and flavours
- Field studies on food safety issues in landscape areas such as forests, open space and water bodies

### 3.8. Experimental Toxicology and ZEBET Department

The Experimental Toxicology and ZEBET (Center for Documentation and Evaluation of Alternative Methods to Animal Experiments) coordinates the tasks and objectives of the German Centre for the Protection of Laboratory Animals (Bf3R). The Bf3R is committed to ensuring that animal experiments are limited to an indispensable minimum and that laboratory animals are given the best possible protection. To this end, the department promotes the development and advancement of alternative methods to animal experiments according to the 3R principle in basic research and applied science. State-of-the-art scientific and bioinformatics methods are used for this purpose.

The 3R principle aims to achieve the goal of scientific animal welfare. The three Rs stand for Replace (replacing animal experiments wherever possible by using alternative methods), Reduce (reducing the number of laboratory animals to the minimum) and Refine (reducing the suffering of laboratory animals).

Within the framework of the 3R concept, the area of Reduction and Refinement is to be advanced in particular. In this context, the department is also involved in the field of meta-research and information gathering. The department has also developed a focus on animal welfare and laboratory animal science.

The department is also tasked with the “National Committee for the Protection of Animals used for Scientific Purposes” – in short, the National Committee for the German Animal Welfare Act (TierSchG) – for the Federal Republic of Germany. It is actively engaged in legal research in this context.

The department produces animal reference materials for the NRL and breeds or keeps laboratory animals (laboratory animals, livestock, aquaculture) for research projects.

#### Spectrum of Tasks and Competences

The protection of laboratory animals in line with the 3R principle has been an integral part of the scientific work of the BfR since the establishment of the German Federal Institute for Risk Assessment (BfR) in 2002 and the creation of the Center for Documentation and Evaluation of Alternative Methods to Animal Experiments (ZEBET).

With the amendment of the German Animal Welfare Act in 2013, the BfR was appointed additional laboratory animal protection tasks. The increase in requirements led to the opening of the German Centre for the Protection of Laboratory Animals (Bf3R) at the BfR in 2015, into which ZEBET was integrated.

The BfR performs the following new tasks:

- Publication of non-technical project summaries according to Section 8 (6) TierSchG in conjunction with Section 41 TierSchVersV;
- Advising the competent authorities and animal welfare committees on matters related to the acquisition, breeding, housing, care and use of animals in animal experiments in accordance with Article 15a TierSchG in conjunction with Section 45 TierSchVersV;
- Advice to the competent authorities in matters related to alternatives to animal experiments in accordance with Section 46 TierSchVersV;
- Cooperation with the competent authorities of other member states and the European Commission on issues of the regulatory relevance and suitability of the alternative methods proposed for validation according to Article 16g (2) TierSchG
- Compilation of a statistical evaluation of all laboratory animals used in Germany.

The department researches, develops and validates alternative methods to animal experiments according to the 3R principle to ensure the fulfilment of its legal tasks and for continuously improving policy advice. The latest, state-of-the-art methods and evaluation strategies

are developed with the aim of replacing or at least minimising animal experiments not only in approval procedures but also in basic research.

The department is responsible for meeting the special demand for information on alternative methods in toxicology and basic research. The Animal Study Registry (ASR) database established at the BfR is an international study registry for animal experiments, which will not only contribute to the refinement of the quality of scientific studies with animals, but will also increase animal welfare in parallel. The ASR will also create more transparency about animal experiments among scientists and the public.

### **Core Research Areas**

- Research, development and validation of alternative methods that completely replace animal experiments, reduce the number of animals in the experiment and/or reduce the suffering of laboratory animals in the experiment within the framework of the 3R concept
- Development, assessment and validation of non-animal toxicological test methods and assessment strategies
- Use of state-of-the-art scientific and bioinformatics methods for the further development of toxicological test methods as a basis for risk assessments of chemicals and medicinal products
- Publication of generally understandable, non-technical project summaries of approved animal testing projects (“AnimalTestInfo” database)
- Metascience to refine the quality of basic biomedical and applied research in order to strengthen animal welfare
- Scientific advice to competent authorities and animal welfare bodies on issues related to the acquisition, breeding, housing, care and use of vertebrate animals and cephalopods, as well as on matters related to alternatives to animal experimentation, including at the EU level in the PARERE network (Preliminary Assessment of REgulatory RElevance)
- Food safety of aquatic organisms
- Research on the generation and standardisation of animal reference materials for the NRL