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The Science Magazine of the German Federal Institute for Risk Assessment Issue 2/2018

Heat-induced contaminants

Charred – why over-frying is risky



Breastfeeding in public Is it acceptable? _{Caffeine} Makes the heart beats faster High-resolution microscopy Hormone traces in the nano-world

Dear Readers,

Acrylamide was back in the headlines in April. "EU bans extreme deep frying of chips" was the headline on "Spiegel online", for example, while "Merkur.de" asked shortly afterwards: "Will we now only be able to get soft chips?". This speculation was fuelled by the entering into force of a new EU regulation designed to reduce the level of the potentially carcinogenic substance in foods. "Golden, not charred" is the motto of the German Federal Institute for Risk Assessment (BfR) with regard to acrylamide in baked goods, chips, crisps and co.

The BfR has regularly turned its scientific focus to the topic of acrylamide. We were and still are of the opinion that acrylamide poses a risk that must be taken seriously, even if there is still no conclusive proof that it can cause cancer in humans. It's conceivable that not everyone is happy with our efforts in this area. While some view risk assessments as exaggerated, as is the case with acrylamide, for example, others believe they are not critical enough - glyphosate being a case in point. The BfR is sometimes between a rock and a hard place, but this is something an institute whose work is impartial and scientifically based wears like a badge of honour!

Picking up on this topical issue, the new BfR2GO once again takes a closer look at acrylamide and its unpleasant siblings that are created during frying, BBQing, deep frying and baking, and that are scientifically known as "heat-induced contaminants". We also take a look at the future of toxicology, the science of poisons. In an interview, we ask how computers can help to track down potentially hazardous substances in the risk assessment of heat-induced contaminants.

Computer-based *"in silico"* methods certainly have a future in the field of toxicology. And they are one way of replacing animal experiments. This is one of the central goals of the German Centre for the Protection of Laboratory Animals (Bf3R) attached to the BfR. The Bf3R is using modern microscopes to render experiments on animals unnecessary, while also gaining new insights into cancer risks from the environment, as outlined in our BfR2GO report. So, as you can see, the new issue contains a wide range of new information!

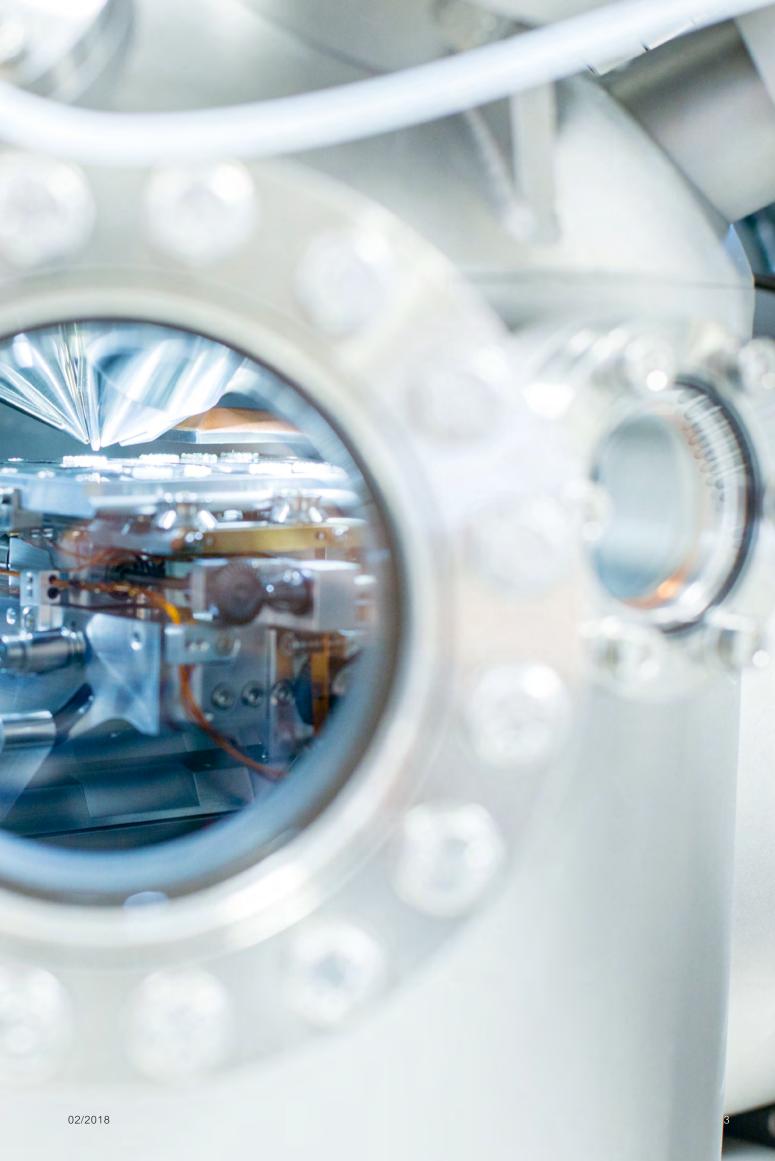
I wish you stimulating reading,

Professor Dr. Dr. Andreas Hensel President of the BfR



10,000 nanometres inside a cell

To fully understand things, we have to get very close to them. This scientific principle also applies to the assessments and research of the BfR. The photo shows the sight glass of an imaging mass spectrometer - a bull's eye like in the Nautilus submarine of Jules Vernes. The BfR uses this special analytical instrument to dive deep down into the microcosm of cell nuclei and membranes in search of the tiniest chemical compounds that might be of significance for human health. In the photo, the instrument is scanning the roe of cod (Gadus morhua). Does it contain microplastics? Into which cell components have the small particles migrated? Have they been altered by the metabolism of the cell? For the BfR, the instrument – which goes by the name of "ToF-SIMS" (stands for Time-of-Flight Secondary Ion Mass Spectrometry) – supplies the central analytical technology needed to track down nanoparticles in cells, tissue or organs. The instrument is being used for a whole series of projects funded by the EU or the Federal Ministry of Education and Research. It can generate three-dimensional images and acts as a kind of chemical microscope by showing inorganic substances in organic matter. The depth resolution is 10,000 nanometres (10 micrometres).





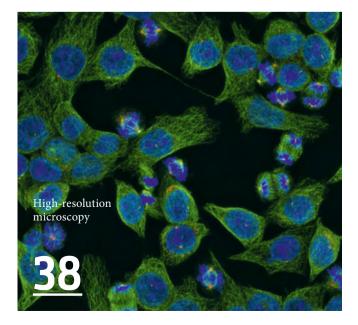
Key Topic: Heat-induced contaminants







Assess. Research. Communicate.



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HEAT-INDUCED CONTAMINANTS

Safe sizzling

Dangerous substances from the pan, the deep fryer and the oven: heating causes changes in unprocessed foods or ingredients. It makes them easier to digest and they taste better. But heating also results in undesirable chemical compounds. Do these compounds pose a problem to health? The first chemical compounds harmful to health that occur when food is prepared at high temperatures were detected in grilled fish and meat in the 1970s. The compounds in question were polycyclic and heterocyclic aromatic hydrocarbons. Since this time, we have made quantum leaps in our knowledge regarding potentially hazardous substances in heated foods, and several hundred of these heat-induced contaminants have meanwhile been identified. The most well-known of them are acrylamide, furan, monochloropropandiol and glycidol. These substances are addressed on the following pages.

Only four out of many

The "fatal four" represent only a small fraction of the undesirable substances that are created when foods are heated. Nothing or only very little is known about the potential risk to health of many of the other substances that may be formed. Scientists at the BfR therefore want to fill these gaps in our knowledge with the help of novel computer-assisted toxicological methods (see the interview on page 12). So that suggestions can be provided to the risk management experts as to which substances should take priority when new regulations are introduced. The aim is to identify further compounds that might give rise to a particularly high or difficult-to-manage health risk. A further focal point of research is to clarify the toxic effect mechanisms of undesirable substances that are already known. Moreover, the BfR scientists intend to develop methods that permit more precise calculation of the actual exposure of humans to these compounds (see info box). These methods will make it possible to further improve assessment of the health risk of these undesirable substances.





What really ends up in the body

What amount of heat-induced contaminants from foods is actually ingested via the intestine? Using the example of glycidyl fatty acid esters, the BfR showed in a research project that the determination of adducts in the blood is a suitable biomarker of measuring the quantity of contaminants that is actually present in the body - the "internal exposure" - more accurately. Adducts are composite molecules. In the body, glycidol is split off from the glycidyl fatty acid esters. Glycidol bonds with the blood protein haemoglobin to form a glycidol adduct. In the BfR study, test persons ate a defined amount of a commercially available palm fat daily with a known concentration of glycidyl fatty acid esters over a period of four weeks. During this time, the glycidol adduct level in the blood of the test persons almost quadrupled compared to the original level based on everyday intake. The data can be used to calculate the current level of this everyday intake.

Acrylamide: the monomer from the kitchen

The discovery of acrylamide in foods was a coincidence. Acrylamide is in fact a building block – a monomer – of the plastic material known as "polyacrylamide". But then researchers in Sweden found acrylamide not only in the blood of workers who had been contaminated with the synthetically produced plastic component due to a work accident, but also found this same chemical compound in the blood of people who had not been involved in the accident. In 2002, the scientists searching for the cause of this contamination made an important discovery, when they found that foods like crispbread, toasted bread, chips, crisps, roast potatoes, roasted cereals and coffee also contained significant amounts of acrylamide. But how did this molecule find its way into potatoes and bread?



Consumer tip

When preparing foods like roast potatoes, biscuits, toast and chips, don't let them get too brown. "Golden not charred" should be the motto in order to minimise acrylamide in the kitchen.

The BfR acrylamide calculator measures how much acrylamide we ingest every day with our food: www.bfr.bund.de/cm/343/acrylamidrechner.xls

Acrylamide is a product of the "Mailliard reaction", a chemical reaction that occurs when we bake, roast, fry or deep fry raw foods – in other words, when we heat them to temperatures in excess of 120 degrees Celsius. Two of the things that happen is that the foods in question become brown and taste different than before. Acrylamide is created during this process when starch, sugar and certain amino acids react with each other in the absence of water. The darker a product becomes during heating, the higher the acrylamide content.

Toxicological tests to determine the effect of this substance in the body showed: acrylamide changes the genetic material (genotoxic effect) and causes cancer in various organs and tissues (carcinogenic effect) when administered to rodents in high doses. These effects are mostly caused by a metabolite of acrylamide, named glycidamide.

Since the chemical compound was first detected, scientists at the BfR have been assessing the health risk of foods containing acrylamide. The problem is that, due to their genotoxic-carcinogenic properties, it is not possible to define a safe intake amount for heat-induced contaminants. This is why there have been efforts for a number of years now to reduce acrylamide levels in foods based on the ALARA principle. The acronym ALARA stands for As Low as Reasonably Achievable. It means that ready-to-eat foods should contain as little acrylamide as is technically achievable with reasonable effort. Based on a BfR risk assessment, the risk management authorities developed a signal value concept in Germany from 2004 onwards, and this resulted in a significant reduction in acrylamide levels in industrially produced foods. In 2018, the Acrylamide Regulation of the European Union stipulated binding guide values for different food groups based on what is achievable in line with the current state of the art. The food and catering industries must comply with these stipulated levels.

Furan: canned foods and co.

Furan is a highly volatile chemical compound and is mainly found in roasted coffee, canned foods, baby food in jars and ready meals. It is created in substantial amounts when carbohydrates, amino acids, ascorbic acid (vitamin C) and unsaturated fatty acids react with each other during roasting and when foods are heated in closed containers.

Animal studies on rats and mice show that furan causes benign tumours and leukaemia as well as liver and testicular cancer in high doses. The underlying mechanisms have not yet been identified. It is therefore not clear whether and to what extent these effects are of relevance to humans. Although the European Food Safety Authority (EFSA) estimates that a massive 90 percent of the furan ingested by adults in Europe comes from coffee, epidemiological studies show that cancer rates among coffee drinkers are no higher than among people who do not drink coffee at all. In view of the major gaps in data on both effects on human health and exposure, it is not possible to definitively assess the health risks of furan.

In view of these uncertainties, it is advisable to minimise the intake of furan to the greatest possible extent. A BfR working group conducted a research project to determine how the way coffee is prepared or the methods by which ready-to-eat foods are heated can reduce the furan level in the meals on our plates. They found that the furan content falls by up to 66 percent if canned soup is heated in open pans or bowls. The furan remained in the foods in the case of ready meals with low water content and a more solid texture. They also found that espresso from the machine contains far more furan than conventional filter coffee – despite the fact that the raw material (ground coffee) had the same furan content in both cases.

Consumer tip

Prepare meals and baby food yourself from fresh raw products. Heat ready meals (canned soups) and jars of baby food in a pan without a lid while stirring. Enjoy coffee in moderation, and preferably drink filter coffee.



Monochloropropandiol and glycidol: Two hazardous by-products of edible oil processing

Until 2007, 3-monochloropropandiol (3-MCPD) had only been detected in soy sauce or bread, but that was the year when tests conducted by the monitoring authorities of Germany's federal states made major waves. It was found that industrially produced infant formulae, the basic foodstuff for babies who aren't breastfed, contained 3-MCPD fatty acid esters. The main source of these heat-induced contaminants are refined oils and fats from the oil palm. These contaminants are formed when the untreated oils from the plant are treated using superheated steam during the refining process in order to remove bitter substances as well as other undesirable aromatics and suspended solids (deodorisation). Long-term studies have shown that 3-MCPD in high doses causes tumours in the kidneys, testicles and mammary glands of male rats. The mechanism behind tumour formation is not yet fully understood, but it is assumed that the compound does not have any mutagenic effects. This means

Confounding of cellular protective mechanisms

In animal experiments, 3 and 2-MCPD were shown to damage kidneys and testicles, and to promote tumours. In a joint project with the Fraunhofer Institute for Toxicology and Experimental Medicine, the BfR has discovered a new mechanism on the molecular level of the cells that relates to this effect. In an animal study, the substances were administered to rats. Modern biochemical methods were used to investigate how the cells in the liver, kidneys and testicles of the animals form, alter and regulate proteins under the influence of 3-MCPD and 2-MCPD ("Proteomics"). It was found that the protein DJ-1, which is known to have an antioxidative effect in the cells, is inactivated by the substances. In the protein formation process, DJ-1 normally suppresses the undesirable influence of readily reactive oxygen molecules that disrupt cellular functions. The BfR showed that 3-MCPD and 2-MCPD permanently change the DJ-1 protein by combining it with oxygen - and that the protein loses its protective function as a result. Consequently, the cells are exposed to oxidative stress; new proteins are incorrectly formed. Current knowledge indicates that oxidative stress is involved in various diseases, including cancer and Parkinson's.

it was possible to determine a value at which no carcinogenic effect is to be expected based on current knowledge. The BfR used this research to derive a tolerable daily intake (TDI) of 2 micrograms 3-MCPD per kilogram bodyweight. This value has meanwhile been confirmed by other authorities like EFSA.

Until recently, it was not clear whether this toxic effect can also be expected in the case of the fatty acid esters of 3-MCPD and the chemically related 2-MCPD. In these compounds, the 2-MCPD or 3-MCPD is firmly bound to fatty acids. Two BfR studies showed that this bond is broken by the process of digestion in the gastrointestinal tract. This results in the formation of free 2-MCPD and 3-MCPD. It is therefore to be assumed that the intake of these fatty acid esters carries the same health risk as intake of the free substances.

Glycidol and glycidyl fatty acid esters are also created during the refining of vegetable oils. This means that they are also contained in the fats and edible oils obtained from these vegetable oils. Unlike MCPDs, free glycidol damages the genetic material. If glycidol is added to the feed of rats in high doses over a lengthy period of time, the animals develop tumours. Due to its genotoxic-carcinogenic properties, it is not possible to derive a safe intake level for glycidol. As is the case with acrylamide, therefore, foods should contain as little as possible of this chemical compound. This also applies to glycidyl fatty acid esters, from which glycidol is released in the gastrointestinal tract and which should therefore be assessed as being equivalent to glycidol from a toxicological point of view.

Consumers cannot influence the level of 2-MCPD and 3-MCPD, glycidol and their fatty acid esters in foods that have already been processed or in food ingredients like oil and fat. This must be done by the producers of refined vegetable fats and oils – by taking suitable measures during the production and processing of palm oils and during the deodorisation process to reduce the levels of these contaminants in their products. At the same time, however, this range of substances can also be formed at home if vegetable oils or fats are heated in the kitchen during frying and come into contact with salted foods.

Consumer tip

Only add salt to vegetables, fish and meat after frying or use or unsalted marinade.



"We can use computer models to find out whether a substance damages our DNA"

Toxicology 4.0: computer-assisted methods are increasingly being used in the field of regulatory toxicology to identify the toxic properties of substances. Professor Dr. Dr. Alfonso Lampen, Head of the Food Safety Department at the BfR, talks about the use of "computer-assisted toxicology" in research into food safety.

Professor Lampen, computer-assisted systems have long been used in pharmacology in the identification of chemical compounds that are suitable for use as active substances in medications. You take the opposite route. What does the BfR do exactly?

We are looking into the benefits of these computer systems known as *in silico* models for the prediction of the health-damaging properties of heat-induced contaminants and other undesirable substances. We intend to use these methods to filter out from the wide range of undesirable substances those substances that might potentially be mutagenic or carcinogenic. The modelling concepts and simulations help us to prioritise experimental investigations.

What is the basis for these in silico models?

We compare chemical structures – or, more precisely, structural activities, in other words the interaction of certain molecule structures with biological systems. In the case of *in silico* models, these kinds of chemical structures that are known from experiments to exhibit certain cell-damaging properties are stored in databases. These include chemical structures that alter genetic material and can therefore have a mutagenic effect or interfere with biochemical processes in the cells in other ways and cause cancer. We compare the known, defined structures with the structures of the individual substances whose effects we currently know little about. The information we obtain about their structure indicates whether they might possess toxic properties.

What is special about the way the *in silico* models are used at the BfR?

There are other research groups working with these methods. What's new about our approach, however, is that we combine the various existing methods and models and then apply them to food-related contaminants in order to arrive at more robust statements regarding the potency of these contaminants. In the case of genotoxicity, in other words changes to genetic material, we have combined five different software tools, and we combined three for the carcinogenicity test.

Which contaminants did you investigate?

In a research project, we first looked at the heat-induced contaminants that have not yet been investigated. There are more than 800 substances that can be created when foods and their raw materials are heated. The project was designed to establish whether and to what extent *in silico* methods are suitable for predicting whether a particular substance has a genotoxic or carcinogenic effect. This was indicated by the software tools on a scale from 0 to 1. Values between 0.66 and 1 signalled a high probability of genotoxic or carcinogenic properties, while values below 0.66 did not provide any clear pointers.

And what were your findings?

From more than 800 heat-induced contaminants, our approach has enabled us to identify 24 that are highly likely to have a genotoxic effect based on their structure or based on components of their structure. These 24 contaminants are right at the top of the priority list for further experimental testing.

Where you surprised by your findings?

There are naturally some substances and structures whose genotoxic effect was already known from experimental analysis – substances such as aldehydes, for example. But there were also substance groups for which no experimental data is currently available – such as thiazoles – that were identified as genotoxic with a high degree of probability. The study showed that the models for the identification of genotoxicity are very suitable, as we were able to conduct follow-up experimental analysis that confirmed the predictions of the models. In other words, computer models can help us to find out whether a substance can damage our genetic material.

And what is the situation with carcinogenicity tests?

The predictive capacity of the models is not yet particularly high in this area, but this is only natural, as the development of cancer is a very complex process. Chemical compounds may play a role in the creation of a tumour; they can promote the growth of a tumour or cause inflammation that changes the properties of the cells, thereby promoting the development of a tumour. This is why it is difficult to model the toxicological endpoint of carcinogenicity. It's not clear whether we will be able to develop suitable *in silico* models for this purpose at all.

What are the next steps in the application of these systems at the BfR?

It is important to consider the conversion of heat-induced contaminants in the body and to incorporate the relevant parameters in the computer models. We know from cell-based and animal experiments that parent substances that are not genotoxic-carcinogenic can be converted in the body into metabolites that can have genotoxic or carcinogenic effects because they possess a specific structure. We can already simulate the creation of new chemical structures in the metabolic process today using *in silico* methods. Our next goal, therefore is to combine these methods with *in silico* methods for toxicological analysis.

Mr. Lampen, many thanks for the interview.

Not on my plate!

People who buy organic food products or follow a vegetarian diet see the health risks of undesirable substances as being greater than people who buy conventionally produced foods or eat meat.



Contaminants are substances that accidentally enter foods during production or transport, for instance heavy metals and dioxins as well as substances like acrylamide which only develop during production or preparation.

Contaminants assessed as posing risks

Communication of health risks from undesirable substances in foods is one of the central tasks of the BfR. One precondition for targeted risk communication is the knowledge of the subjective attitude of the population towards contaminants. The BfR therefore conducted a representative study of more than 1,000 people above the age of 14 to determine awareness of contaminants and opinions on the risk they pose. What was clear is that food contaminants are an important topic from the point of view of consumers, and that the associated health risk is often seen as being high. Moreover, just under one in two (49 %) respondents say they consciously avoid foods that are rumoured to have high contaminant levels.

A further focal point of the BfR study is the question of whether there is any connection between eating habits and risk perception. In order to measure any potential relationships between the two, the study compared statements of people who eat or don't eat meat as well as statements by people who preferably buy ecologically grown foods and people who prefer buying conventionally produced foods. The figures show that people who regularly buy organic foods see the health risk of contaminants as being higher than people who mainly buy conventionally produced foods. Equally, people who follow vegetarian diets say food contaminants pose a higher health risk compared to people who eat meat. People who buy organic foods or have vegetarian diets were also more likely than the population overall (67 % and 57 %) to say that they consciously avoid foods containing contaminants.

Undesirable can mean different things to different people

From a scientific point of view, contaminants are deemed to be particularly undesirable. However, consumers are often also concerned about authorised ingredients in food. The most frequently cited examples of undesirable substances are flavour enhancers, preservatives or artificial flavourings. Many people take a critical view of these substances, although they do not pose any health risk from a scientific perspective based on the actual amounts consumed. In order to allay unjustified fears, one of the jobs of risk communication is therefore also to explain which substances have been assessed as being safe for the consumers' health.

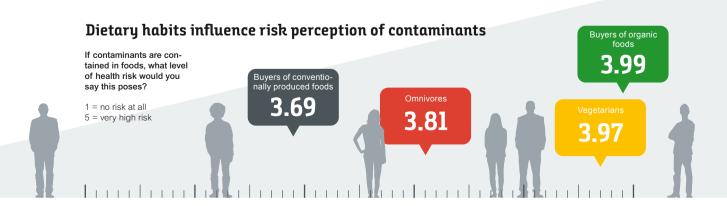
Differing awareness of specific contaminants

The survey on specific contaminants such as dioxin in eggs or milk, arsenic in rice and rice products, acrylamide in chips and toasted bread, benzpyrene in barbecued meat, mercury in fish or pyrrolizidine alkaloids in tea and honey showed that people who buy organic products are more frequently aware of almost all contaminants than people who buy conventionally produced foods. Vegetarians were more frequently aware than omnivores of the contaminants in animal products only. However, these differences in knowledge did not affect assessments of the health risk of these contaminants.

The study showed that vegetarians and buyers of organic foods view the general health risk of contaminants as being higher, but that they assessed the health risk of specific examples of contaminants no differently than people who eat meat or conventionally produced food. Whether it is actually people's eating habits that drive risk perception with regard to contaminants or whether it is the negative attitude towards contaminants that determine why some people decide to adopt a vegetarian or ecological lifestyle are questions that should be addressed by future studies. **■**

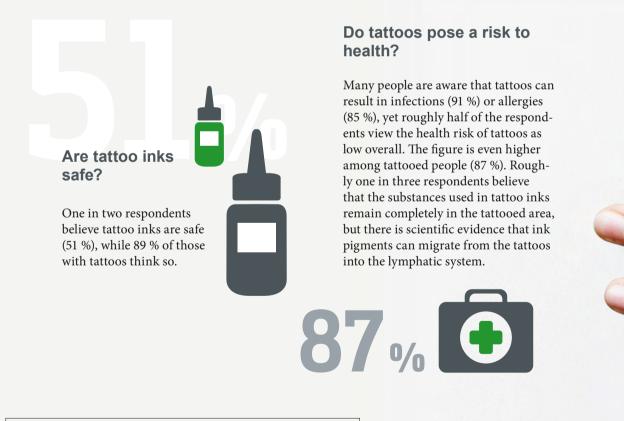
More information:

Koch et al. 2017. Risikowahrnehmung von Kontaminanten in Lebensmitteln. Bundesgesundheitsblatt 60: 7, 774–782 (Open Access, in German)



After the tattoo is before the tattoo

Many people in Germany believe tattoos are safe – as shown by a representative study of the BfR on risk perception with regard to tattoos. This view is shared particularly frequently by people who already have tattoos. However, many tattoo inks have not been researched, and there are increasing signs that some substances may be problematic.



Underlying study: representative telephone survey of 1,009 persons (German speaking population in private households above the age of 14) in July 2018

More information: BfR Consumer Monitor 2018, Special Tattoos www.bfr.bund.de/en > Publications > Brochures > BfR Consumer Monitor



Tattoos - a topic in the media?

44 % say they have heard, seen or read something about tattoos in the media during the last 12 months. In addition to recalling general information, the respondents remember hearing about health risks, cover-up tattoos (new tattoos to cover old tattoos) and tattoos that went wrong ("horror tattoos").

Tattoos are popular

Around one in eight respondents (12 %) already have or used to have a tattoo. Of these respondents, the number of women with tattoos significantly outnumbered the men. People who already have a tattoo are quite willing to have more tattoos: 54 % of the tattooed respondents said they would go under the needle once again. Only 7 % of those without tattoos said they would consider getting one.



Laser removal a risk?

One in three respondents sees no health problems with the removal of tattoos using lasers. Tattooed people are more sceptical, as 47 % of them believe laser removal is unsafe.



"Organic foods have a halo"

How do we perceive risks and how do we assess them? Professor Dr. Michael Siegrist researches the behaviour and preferences of consumers and examines what motivates them.

Professor Siegrist, you recently published a study outlining how experts and laypersons have a different assessment of the health risks in the environment and in foods – something that is also frequently experienced at the BfR. What were the main differences?

Experts and laypersons were asked to say how they would allocate resources that could be used to reduce risks. Among laypersons, the focus was on "synthetic" manmade risks like glyphosate and other pesticides. In contrast, the experts assigned higher risk scores to "natural" risks like bacteria or viruses. Moreover, the number of affected people played little or no role among laypersons. For example, the experts classified the ink used for tattooing as a relatively significant risk, because a lot of people get tattoos. The laypersons considered this to be only a minor problem. They argued that no one is forced to get a tattoo, and that people who take the risk also have to face the consequences.

This was then followed by a second round with additional information and more-in-depth discussion – but it didn't succeed in achieving any change in attitudes. How do you explain this obstinacy?

We humans try to remain consistent in our beliefs. If we believe that pesticides pose a major risk, then we are unable to reverse this opinion without further ado. And strongly held opinions are particularly hard to revise. If this wasn't the case, we would constantly change our opinions every time we read the newspaper.

What should be the consequences of this for scientific risk communication?

There are some risks that are wrongly perceived, and risk communication should do more to focus on these risks. This takes me back to the natural and the manmade risks. We should point out that not everything that comes from nature is free of risk and is always good for us – and that, by the same token, not everything created by humans is harmful. This kind of black-and-white mindset can lead to wrong decisions. It goes without saying that risk communication cannot change these attitudes in the short term, but if we continually remind people of the facts, then this can change some of these attitudes.

Your work is also concerned with "naturalness". Why are we so enthusiastic about everything that we associate with "nature"?

In many areas, nature no longer poses a threat to us here in Europe or to people in other developed regions. The risks that used to exist have been massively reduced. Take bacterial infections, which we have effectively combatted thanks to science and medicine. It's ironic that this success hasn't made people more enthusiastic about research and technology. On the contrary, there is a growing interest in "natural products", which are seen as posing a lesser risk. Ultimately, nature has technological innovation and scientific knowledge to thank for its good image!

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Ultimately, nature has technological innovation and scientific knowledge to thank for its good image.

Do we subconsciously assign things to certain categories and put them in mental compartments like "natural" and "artificial"?

I'd rather put this down to heuristics – simple rules of thumb that help us to make decisions. Unfortunately, there are also heuristics that are misleading, like when we believe that everything that is natural is good and everything made by humans bad. Then there is the "halo effect". If we view a particular property of an object positively, then that also rubs off on other attributes of that object, and a product is given a kind of "halo". Consumers perceive organic foods as being better for the environment, for example, and this in turn leads them to also classify these foods as being healthier and better-tasting.



Negative judgements are also based on information. In the case of things like genetically modified plants and pesticides, which factors determine whether information actually reaches us or whether we simply don't take note of it?

The information in question must have some kind of meaning for consumers. They have little or no benefit from genetic engineering, for example. Genetically modified corn is not cheaper, it doesn't taste better, and doesn't have any other recognisable advantages. It's naturally difficult to accept a new technology if it doesn't supply any benefits – particularly in cases where there are also reservations. The same applies to pesticides; they have a poor image as synthetic chemicals. It's very difficult to convince people that it is in fact quite a good idea to use pesticides in moderation. The situation is different when it comes to the Internet or cars, where the consumer has a noticeable benefit and is willing to accept a certain level of risk.

You're a Swiss national. Is there a typical "Swiss" kind of risk perception?

One conspicuous thing about Switzerland is that we're over-insured in many areas. The general rule should be: if you can rectify some type of damage yourself without any real problem, then you don't need to take out insurance for it. But many Swiss people still have travel insurance which covers them up to a sum of 2,000 Swiss francs. It's not really worth it for most people.

Many thanks for the interview, Mr. Siegrist. **D**

Swiss national **Michael Siegrist** has been Professor for Consumer Behavior at the ETH University of Zurich since 2007. Born in Vordemwald in 1965, Siegrist studied Psychology, Business Management and Journalism at Zurich University, where he also completed a PhD in 1995 and gained a postdoctoral qualification in 2001. His core fields of research are risk perception, risk communication, acceptance of new technologies and decisions under uncertainty. Siegrist advises the BfR as a member of the Scientific Advisory Board. BREASTFEEDING IN PUBLIC

Is it acceptable?

Breastfeeding is best for mother and child. Despite the undisputed benefits of breastfeeding, there has been controversy in the past over breastfeeding in public, an issue which the media have readily picked up on. The general attitude appeared to be: breastfeeding yes, but please do it at home. But is this an accurate reflection of people's opinions? Are Germans against breast-feeding in public? What are the experiences of breastfeeding mothers? In order to ascertain the views of Germans on breastfeeding in public, the BfR conducted a research project in which 1,003 members of the general public above the age of 14 years and 306 mothers with children of breastfeeding age were polled - and the outcomes were, in the main, reassuring. Explicitly negative reactions to breastfeeding in public tend to be rare: only six percent of mothers who breastfeed in public reported mainly negative experiences. 66 percent of the population sample basically think that breastfeeding should be possible at any time and anywhere, compared to 80 percent of the surveyed mothers. The more people knew about the health benefits of breastfeeding, the more positive their attitude towards it. One frequently mentioned reason for critical attitudes towards breastfeeding in public was the visibility of the woman's breast. Breastfeeding in public gives rise to conflict in particular in restaurants and cafés: the polled population sample say that breastfeeding is only partly appropriate in these settings, but women cannot and do not want to avoid breastfeeding their babies in these locations. Suitable measures could be introduced for such settings in order to further boost positive attitudes towards breastfeeding in Germany. Some cities and municipalities have already made a start with voluntary signs in cafés and other public places drawing attention to the fact that they are "breastfeeding-friendly" locations.

More information:

Koch et al. 2018. Ist Stillen in der Öffentlichkeit gesellschaftlich akzeptiert? Erfahrungen und Einstellungen der Bevölkerung und stillender Mütter. Bundesgesundheitsblatt 61: 990–1000 (Open Access, in German)

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Makes the heart beat faster:

Caffeine

500 ml

Energy drinks are especially popular with adolescents, but how do they affect their health? Whether black or with milk, coffee is the most popular drink in Germany, even outperforming beer and water. Other beverages containing caffeine are also in demand. Alongside tea and cola, one of the in vogue beverages among young people are energy drinks. So when is the consumption of caffeine of health concern and who is particularly at risk?



Diane Labombarbe/iStock

The first "study" on the health assessment of caffeine took a surprising turn. Legend has it that, in the 18th century, King Gustav of Sweden pardoned two twins who had been sentenced to death and ordered that they instead be imprisoned for life. He then had one of them drink three cups of tea a day, while the other drank the same amount of coffee. His theory? Both would die within a short period of time – first the coffee drinker, then the tea drinker – and thereby scientifically underline the royal decree on the "abuse and excess of tea and coffee". Fortunately for the prisoners, the dose was relatively moderate. It's said that both men outlived not only the king but also the doctors, and that the first prisoner to die was the tea drinker at the age of 83.

Scientific studies are performed differently today, but the early "toxicologists" weren't completely wrong. Coffee and black tea really can have undesirable effects on health – even if not of the kind that was assumed to be the case back then. Both beverages contain the same active substance, namely caffeine, in differing concentrations. This is why toxicologists are still interested today in the question of how much caffeine humans can tolerate.

High quantities can cause cardiovascular problems

It is undisputed in physiological terms that caffeine has a stimulating effect on the cardiovascular and central nervous system. The intake of caffeine causes people to temporarily be more alert and focused. However, high intake amounts can also cause nervousness, excitability, sleeplessness, outbreaks of sweating and heart palpitations. If caffeine consumption is excessive over long periods of time, this may under certain circumstances lead to cardiovascular problems like elevated blood pressure and can also inhibit the growth of the foetus in pregnant women.

For healthy adults, the European Food Safety Authority (EFSA) has derived a guidance value of 3 milligrams (mg) caffeine per kilogram (kg) bodyweight which can still be considered safe as a single dose. This means that a healthy adult weighing between roughly 60 and 70 kg can consume a caffeine dose of up to around 200 mg caffeine without any expected health impairments. This is approximately equivalent to two mugs of coffee (see graphic page 25). In the case of habitual consumption spread over the course of the day, an amount of up to roughly 400 mg caffeine per day is considered safe for healthy adults.

Children and pregnant women should be particularly cautious

It's important to note that these are maximum amounts that are considered safe and not intake recommendations. "Sensitivity to caffeine can vary widely between individuals", explains Dr. Karen Ildico Hirsch-Ernst, Head of the Nutritional Risks, Allergies and Novel Foods Unit at the BfR. "People who are sensitive to caffeine tolerate less caffeine than others. And children, pregnant women and breastfeeding mothers should exercise particular restraint when it comes to caffeine or should ideally refrain from consuming products with high caffeine content."

Nevertheless, caffeine is popular all over the world – as a stimulant, a pick-me-up and a break beverage. And it's not only coffee that makes the heart beat faster. One thing most people are unaware of is that children mainly consume caffeine through the chocolate they eat. One bar (100 g) of dark chocolate contains roughly the same amount of caffeine as one mug of black tea. Alongside cola and tea, a further source of caffeine has become popular with adolescents in recent decades – namely energy drinks. The caffeinated soft drinks that generally contain not only caffeine but also taurine, glucuronolactone or inositol came into fashion in the 1990s and have been advertised as boosting the ability to concentrate and physical performance.

When does the consumption of energy drinks become a health risk?

One can of energy drink contains about as much caffeine as one mug of coffee. Moderate consumption is therefore unlikely to result in any health impairments in healthy adults. There is little or no data for children, but as children are a particularly sensitive group of people and are often not used to caffeine, they should refrain from consuming these kinds of drinks wherever possible. The same applies to pregnant and breastfeeding women. Health risks can arise particularly if energy drinks are consumed in large quantities, especially together with high amounts of alcohol or during intense physical activity. Some case reports describe serious health impairments such as cardiac arrythmia - that can even result in death in a worst-case scenario - following high-level consumption of energy drinks, often in combination with alcohol. However, causal relationships have not been investigated in this context.

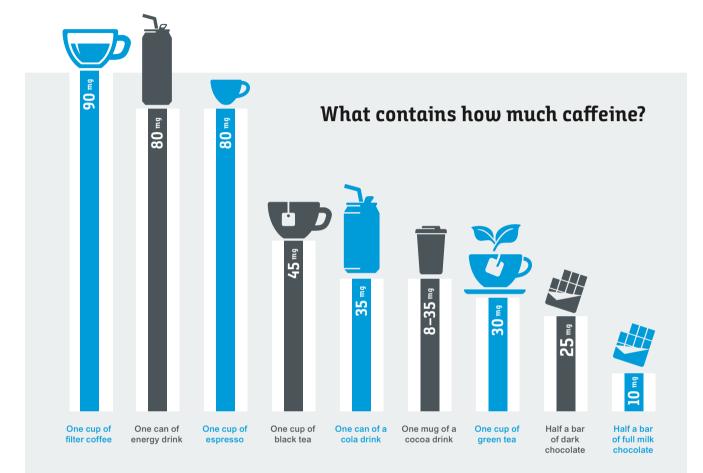


What is caffeine?

Caffeine is a natural alkaloid, a substance that plants form as protection against predators. In addition to being in coffee, caffeine is found in over 60 plants, such as tealeaves, cocca beans, guarana seeds, mate leaves and cola nuts. After being consumed, caffeine is rapidly absorbed by the body and readily crosses the blood-brain barrier and the placenta. The BfR conducted a study in order to establish how many energy drinks are consumed by some of the socalled "high consumers" and under what circumstances this occurs. The theory was that energy drinks are drunk in excessive quantities above all on certain occasions, such as parties and music and sporting events. The BfR therefore performed the surveys in places where it was assumed that the consumption of energy drinks is at its highest.

Up to five litres of energy drinks in individual cases

Accordingly, the interviews took place in discotheques, at festivals, at sporting events and at LAN parties, during which computer games are played on a common network. The participants were first asked if they had drunk more than half a litre of energy drinks during the past 24 hours. Those who answered in the affirmative were then



A healthy adult can tolerate up to roughly the following caffeine intake:

(No intake recommendation, but a maximum safe amount*)



* The figures do not apply to people who are highly sensitive to caffeine, to children or to pregnant or breastfeeding women.

Long waking phases, intensive dancing and high quantities of caffeine and alcohol: this combination can cause serious problems for the heart and the circulatory system.



asked to answer detailed questions on their consumption habits. It was found that high consumers drank an average of roughly one litre of energy drinks at the various events within 24 hours, equivalent to caffeine intake of around 320 mg; the participants who mixed the energy drinks with alcohol had an average intake of 1.5 litres. The behaviour of some extremely high consumers was particularly troubling. In individual cases, they drank up to five litres of energy drinks within 24 hours, often together with alcohol.

It is not only the quantity of energy drinks but also the behaviour of the participants in connection with this intake that can pose health risks. The gamers at LAN parties in particular stayed awake for up to two days and two nights. And at sports and music events, high consumers were often physically active, danced intensively or rode bikes for several hours at a time. The combination of extremely long waking phases or intense sporting activity and high amounts of caffeine can increase the risk of cardiovascular problems.

Risk warnings on drinks

A further finding of the study is that high consumers are hardly aware of the health risks. This means there is a need for more information. But what is the best way to communicate these risks? "The BfR already recommended back in 2008 that labels should be attached advising children, breastfeeding mothers and people who are sensitive to caffeine to refrain from consuming energy drinks", says Hirsch-Ernst.

In 2014, the new labelling regulation of the EU Commission came into force and also outlined labelling obligations for caffeinated foods. Ever since, beverages in the EU containing more than 150 mg caffeine per litre that are not coffee or tea beverages must bear the warning: "High caffeine content. Not recommended for children or pregnant or breastfeeding women".

Still little or no research regarding consequences for children and adolescents

Does this mean that toxicology can now close the chapter on caffeine? By no means. Data on the possible effects on the health of children and adolescents are still rare. What happens, for example, if adolescents regularly consume more than one litre of an energy drink per day over a longer period of time? The BfR convened an expert meeting on this issue in 2017. As no data is currently available in this regard, the question remains for the participants whether chronically high consumption of energy drinks might favour the occurrence of cardiovascular diseases.

The BfR believes that targeted information is important to reduce the risks, particularly in the case of adolescents. One thing the BfR recommends is to explain on the labels of energy drinks, too, that the consumption of large quantities particularly in connection with high-intensity sporting activities or alcohol consumption can have undesirable effects on health.

Competition for improved performance

All the while, more and more caffeinated trend products are coming onto the market. Gyms are a good example: "Certain food supplements for those engaging in sport contain caffeine as an ingredient designed to enhance performance", says Hirsch-Ernst. But especially the combination of excessive caffeine intake and intense exercise can increase the risk of cardiovascular problems.

Ice tea, mate, chai, matcha and guarana also promise to deliver a certain kick and have reached new target groups. Perhaps the hype over caffeine is partly due to the desire for improved performance, the pressure to keep up. A trend towards more calmness and a sense of proportion would certainly be helpful. Or, as people used to say: switch down a gear, take it easy.

More information: www.bfr.bund.de/en > A-Z-Index > Caffeine

Hazardous food supplements from natural sources

They are one of nature's sophisticated weapons. Plants produce pyrrolizidine alkaloids (PAs) to keep herbivores at bay. These secondary plant ingredients can enter the food chain via PAproducing wild herbs growing on areas for cultivated plants. The problem: pyrrolizidine alkaloids can damage the human liver and have been shown to cause genotoxic and carcinogenic effects in animal studies. A further problem are food supplements made from plants like borage, coltsfoot or hemp agrimony – all of which produce PAs. Food supplements containing PA-producing plants or parts of plants significantly contribute to the intake of pyrrolizidine alkaloids. The PA level in some food supplements is so high that toxic effects are possible even after short-term intake. The BfR therefore advises against the use of food supplements that contain PA-producing plants or parts of plants. In contrast, no PAs were found in oil-based extracts of PA-producing plants.

More information: BfR Opinion No. 020/2018 of 14 June 2018



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Health risk from sausage and cold cuts

Anyone who eats raw pork – for example in the form of ground pork or minced meat - may get a gastrointestinal infection due to Yersinia for example. It is still not clear whether popular raw sausage products like salami or sausage meat spread are involved in infections due to Yersinia. As the bacteria also multiply at refrigerator temperatures, it is important that food products are free of these pathogens. The BfR is therefore carrying out a multi-year project to determine whether the standard production methods reliably eliminate Yersinia in raw sausage products. For this purpose, the Food Technology Centre at the BfR produced various types of salami (with and without addition of starter cultures) and smoked sausage spreads ("Teewurst" and "Mettwurst") and deliberately added Yersinia bacteria. The study team then tested whether salting, drying, acidification, maturing or the addition of starter cultures eliminated the bacteria up to the end of the best before date. This was only found to be the case in the salami products with starter cultures, while Yersinia were still detected up to the end of the testing period in salami without starter culture and pork sausage spreads ("Teewurst" and "Mettwurst"). These products could pose a health risk for particularly sensitive groups of people such as small children, pregnant women, senior citizens and people with compromised immune systems.

More information: www.bfr.bund.de/en > A-Z Index: Yersinia

Food supplements during the cold time of the year

Winter is the season of colds, and a time when many people turn to food supplements to provide them with vitamins and minerals, in the hope of preventing colds. At the same time, a balanced diet generally supplies a healthy body with all the nutrients it needs. However, supplemental intake of nutrients via highly dosed food supplements and fortified foods may increase the risk of undesirable health effects due to excessive nutrient intake. The BfR regularly assesses the potential health risk of food supplements and issues recommendations to minimise this risk. The BfR recently updated its recommendations for the maximum amounts of vitamins and minerals in food supplement products that can be considered safe. For healthy people above the age of 15, for example, the maximum dosage recommendation for vitamin D in food supplements is 20 µg per day. Vitamin D in particular only needs to be supplemented if the overall quantity of vitamin D formed by the body itself through sunlight and intake via a person's regular diet is insufficient.

More information:

Weißenborn et al. 2018: Höchstmengen für Vitamine und Mineralstoffe in Nahrungsergänzungsmitteln. J Verbrauch Lebensm. 13 (1): 25–39. (Open Access, German)

SPECTRUM



The pig barn – a playground for pathogens

Cattle, pigs and poultry can all carry bacteria that are resistant to antibiotics. The spread of these bacteria is considered to be a major problem, as it complicates the use of antibiotics in humans and animals – and sometimes renders antibiotics ineffective. It's essential to treat pathogens in livestock facilities as early as possible. But how do these bacteria spread within herds in the first place?

Herds of pigs naturally develop a social structure; they like to interact with herd members and are curious. Pigs live in groups both in nature and in modern livestock barns. In a unique experiment, the BfR has investigated the contact structure of these animals inside their barns in order to gain insights into the potential spread of disease pathogens.

Due to a lack of suitable data, scientists normally model the infection dynamics in livestock on the assumption that microorganisms are spread through random contacts between the animals. Within the framework of the MedVetStaph research network, the BfR for the first time was able to record position data of animals from which the contact structure between individuals could be elucidated under realistic conditions. In addition, the animals were tested for colonisation with MRSA bacteria (methicillin-resistant *Staphylococcus aureus*) when joining and leaving the farming unit.

Movement data reveals social behaviour

In cooperation with the University of Kiel, the research team at the BfR recorded the positions of each individ-

ual animal in the gestation facility/barn at the Training and Research Centre Futterkamp in Schleswig-Holstein – second by second and around the clock. For this purpose, the sows were equipped with ear tags containing a battery-operated transmitter. The location of each individual animal was recorded by triangulation. Every week, some sows left the barn before giving birth to their piglets, with new, pregnant sows joining the group in their place. Roughly 1.1 billion positional data from a total of 330 different animals were recorded over a period of six months. Scientists at the BfR used this data set to develop algorithms for the analysis of the contact dynamics between the sows.

Loners and socialisers

Evaluations to date show that the sows became calmer the longer they stayed in the group. In addition to a daynight rhythm of contact frequency in all animals, the evaluation of movement patterns showed that some sows may have preferred contact with only a few others, but then regularly and for longer times/durations. Contact with most other animals, on the other hand, was short and irregular (see figure). Parallel to this, there were some very sociable sows that stayed in different areas of the barn and had contact with numerous animals. As carriers of antibiotic-resistant bacteria or disease-causing microorganisms, these sows may be more likely to pass those pathogens on to many other animals. On the other hand, bacteria that are hardly communicable may have a higher chance of spreading if the contact time between the animals is extended.

Promoting systematic disease prevention

The investigations on the contact structures show that MRSA bacteria do not necessarily have to spread to the entire herd. Individual MRSA-populated sows did not carry the bacteria permanently; MRSA bacteria were not detected consecutively in any of the repeatedly tested sows. It could therefore be discussed whether, depending on the pathogen, it would be more target-oriented, cost-effective and less invasive for the herd to test or treat only animals with frequent contacts.

Further studies should be conducted in other livestock farms/facilities in order to determine if it is possible to generalise the findings of this study.

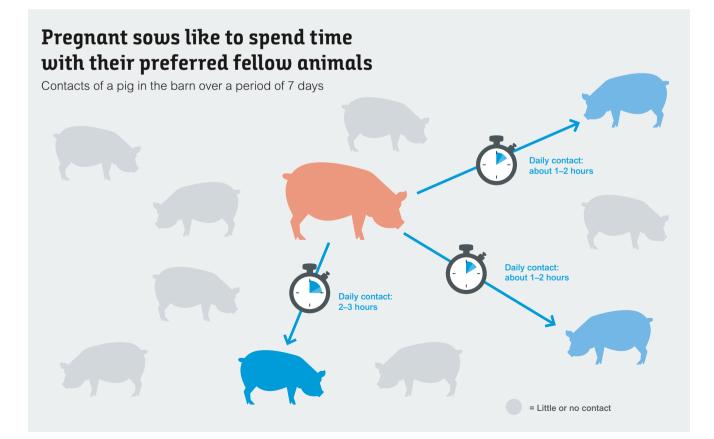
More information:

Will et al. 2017. Accuracy of a real-time location system in static positions under practical conditions: Prospects to track group-housed sows. Comput Electron Agric. 142 (A): 473–484

MedVetStaph



The MedVetStaph research network investigated the relevance of methicillin-resistant *Staphylococcus aureus* bacteria (livestock-associated MRSA) in animals for infections in humans. This interdisciplinary project was funded by the Federal Ministry of Education and Research (BMBF) from 2010 to 2018. The studies conducted at the BfR show that carryover of MRSA can occur between animals and humans on livestock farms and that the pathogen can also be transferred to kitchen utensils, work surfaces and other foods during the preparation of foods of animal origin.





"Safeguarding trust in food safety for the long term"

The European Commission has presented a legislative proposal for more transparency in scientific studies in the field of food safety. Dr. Bernhard Url, Executive Director of the European Food Safety Authority (EFSA), on the background and implications.

Dr. Url, how do you view the initiative of the European Commission?

I see the Commission's proposal as a great opportunity to adapt the EU's General Food Law, which is now 15 years old, to today's needs so that it remains viable for the future. This does not mean that the principles laid down in it, above all the principle of risk assessment, are outdated. On the contrary, the Commission only recently asserted that the regulation, which also created EFSA in 2002, is as relevant as ever. It has achieved its core objectives of ensuring a high level of protection of consumer health and the smooth functioning of the internal market, and our food is safer today than it was 15 years ago.

Where can improvements be made?

We have strict and sometimes unclear confidentiality requirements with regard to the information submitted by companies when it comes to the assessment of risks from applications for regulated products for approval, such as pesticides and GMOs *(genetically modified organisms)*. This aspect, together with EFSA's legal obligation to base its work also on industry studies, leads to a perceived lack of transparency and independence. In addition, there are indications that it could become difficult in the long term with the current panel system to secure the necessary scientific expertise. The Commission's proposal aims to address these issues and to increase transparency and sustainability.

What role has the debate on the plant protection product glyphosate played in this?

The influence of the glyphosate debate on the proposed changes cannot be ignored. The controversy was never solely about renewing the approval of an active substance. It was the expression of wider societal trends: a general loss of trust in politics and science as well as increased expectations regarding transparency and participation. The successful European Citizens' Initiative on glyphosate gave political weight to these ideas, and the Commission responded to them and others with its proposal to strengthen transparency in the scientific evaluations and to increase the reliability and independence of the underlying studies.

What concrete measures should be taken to achieve this?

The proposal provides that, in principle, all studies and documents submitted to EFSA for risk assessment purposes should be made public on our website. EFSA would decide on well-founded, legally precise exceptions. If the proposal is accepted, it would move us a big step forward on our path towards an open EFSA. Other proposed measures in this direction are public consultations on the studies submitted and a register of commissioned studies, which would allow EFSA to verify whether an applicant has transmitted all studies at its disposal. In addition, the Commission would have the possibility, in exceptional cases, to mandate EFSA to commission additional studies for review purposes.

What effect do you foresee these measures will have?

All this would not only increase transparency, but also strengthen public participation and thus help to bridge the perceived gap between risk assessment and society. In addition, the scientific work would be done on a broader basis. Open raw data, access to the latest research results and more minds to deal with them increase the likelihood of identifying potential risks in the food chain and ultimately create more safety for the consumer. Overall, the proposed measures could therefore strengthen public trust in the independence and robustness of our work – but it must also be clear that additional tasks require additional resources.

What does the Commission proposal mean for the Member States?

The proposal suggests stronger involvement of Member States in order to ensure the sustainability of the European risk assessment model also in the future. For example, they would be represented on EFSA's Management Board and be able to propose experts for EFSA's scientific panels. In addition, it may in future be possible for national scientific organisations that work with us to produce preliminary opinions, which would then be submitted to the panels for review and approval. This would ease the burden on EFSA and speed up our work. It would also benefit the Member States, as better financial compensation would be provided for the performance of preparatory work, as well as for the dispatch of experts.

Are there also factors you see critically?

In all these initiatives, we must ensure that EFSA's independence is maintained. This also applies to risk communication, where we welcome the aim for better coordination at EU and national level, but which must not be at the expense of our independence. It will be intriguing to see how the European Parliament and the Council will comment on the Commission's proposals. Personally, I am convinced that a more transparent risk assessment process and even closer cooperation with strong partners such as the BfR are important steps towards safeguarding trust in food safety for the longterm and jointly tackling the challenges of tomorrow.

Thank you for the interview, Mr. Url.



Dr. Bernhard Url, Executive Director of the European Food Safety Authority

General Food Law

Regulation (EC) No 178/2002 lays down the general principles of the EU General Food Law. It was adopted following a series of food crises in the late 1990s. In April 2018, the European Commission presented a proposal for its revision, which is currently under consideration by the European Parliament and the Council. The proposal follows a four-year fitness check, a public consultation and a European citizens' initiative.



Purity is all-important

Cosmetics contain mineral oils. There has been much debate over whether these oils may pose a health risk – above all when lip balm and similar products enter the body not just via the skin but also via the mouth.

In Antiquity, the Egyptian Queen Cleopatra is said to have bathed in donkey's milk to preserve her smooth skin. This level of luxury was the exception rather than the rule; for thousands of years, vegetable oils and beeswax were used as beauty treatments and to care for the skin. Today, however, many cosmetics on the market contain ingredients based on mineral oils. Due to their various positive properties, mineral oils are meanwhile used in creams, lotions, body and facial cleansers, sunscreens, self-tanning lotions, deodorants and antiperspirants, lip balms, make-up, nailcare products, hair gels, Vaseline and baby oil. Depending on the product, the mineral oil content can range from 1 to 99 percent. Vaseline is also used as a base or vehicle in medicinal formulations.

From crude oil to Vaseline

"When they hear mineral oil, some people perhaps think of black crude oil, which contains many harmful substances", says Dr. Bärbel Vieth, who is responsible for the safety of cosmetic products at the BfR. But the mineral oil used in cosmetics has very little in common with the raw material. Unrefined oil, crude oil, is a highly complex mixture containing thousands of constituents. It mainly consists of saturated, unsaturated or aromatic hydrocarbons as well as numerous heterocyclic compounds. It is above all the aromatic compounds that can be carcinogenic. Mineral oils are produced in the various purities required for the different applications by means of fractionated distillation,

MOSHs, MOAHs, mineral oil

MOSHs is the abbreviation for Mineral Oil Saturated Hydrocarbons, which are contained in all mineral oils. In animal studies, MOSHs were shown to have inflammatory effects on the liver. The European Food Safety Authority (EFSA) has therefore only authorised certain waxes and white oils for use as food additives, and they have to meet the defined criteria. MOAHs stands for Mineral Oil Aromatic Hydrocarbons, which include substances that can have mutagenic and carcinogenic effects such as polycyclic aromatic compounds (PACs).



A contaminant in foods

Not cosmetics but foods are the main source of intake of mineral oils. This is mainly due to packaging made of recycled paper that contains mineral oils. These oils originate from inks used for newsprint. The BfR already pointed to this problem back in 2009. This contamination is undesirable, and this is why barrier solutions such as bags or coatings are used in packaging. As one aspect of the BfR MEAL Study "What's in our food", levels of mineral oil components are determined in foods in order to create a data basis for risk assessment purposes. Data on mineral oil contamination in foods is also being collected on EU level, and Germany is involved in this process. The legal basis for these activities is provided by Recommendation (EU) 2017/84 of the European Commission.

vacuum distillation and subsequent multiple, specific extraction steps. "These are multi-stage physico-chemical and chemical refining methods during which a mixture of substances is separated into individual fractions", chemist Vieth explains.

The more purification stages an oil passes through, the greater the extent to which potentially harmful highermolecular constituents are filtered out. The necessary purification steps are adapted to the applications for which the mineral oils are used. Mineral oils with a low or medium degree of refining are used for technical applications, for example – in such things as printing inks or as lubricants. Where mineral oils are used in cosmetics, on the other hand, the aromatic compounds are removed to the greatest possible extent in a multistage refining process and via additional hydration steps. This results in highly pure oils and waxes of the kind that have been used in Vaseline for over a century and are today used in many cosmetic products.

How pure are cosmetics?

It is known that mineral oils that are inadequately purified can lead to cancer if they come into contact with the skin, and this is why mineral oils have become a topic of interest to the BfR. "The question that concerns us is whether in their daily routine consumers absorb mineral oil via cosmetics and are therefore potentially exposed to health risks", explains Bärbel Vieth. The BfR has investigated the risk potential of mineral oil in cosmetics and the possible health risks in a whole series of expert discussions and conferences with scientists, consumer organisations, authorities and industry. The BfR has also analysed the occurrence of mineral oil constituents in cosmetics and has developed and validated a suitable analytical method for this purpose.

"Our risk assessment shows that, based on the current state of scientific knowledge, health risks are unlikely due to the use of highly refined mineral oils in cosmetics applied to the skin", says Vieth. "Moreover, mineral oils used in cosmetics meet the purity criteria for medicine." The stipulations of the EU Cosmetics Regulation ensure that only mineral oils that are safe for human health may be used in cosmetic products. According to the regulation, mineral oils may only be used if they are non-carcinogenic, if the refining history is fully known, or when the distillate has been tested using the IP346 method. This method is an input test for those mineral oils that are subsequently subjected to additional purification stages for use in cosmetic products.

"The available data is extremely robust, as the most important data comes from animal studies and all the studies come to the same conclusions", adds Vieth. "Based on current knowledge, therefore, no health risks to consumers are to be expected due to the uptake of mineral oils in cosmetics via the skin."



Lipstick - a special case

As lipstick and lip care products not only remain on the skin but can also be licked and swallowed – thereby entering the body via the mouth – Cosmetics Europe (the European Association of Cosmetics Producers) advises producers to only use mineral oils that are also approved for use in foods. The Joint Expert Committee for Food Additives (JEFCA) of the WHO and the European Food Safety Authority (EFSA) have derived acceptable daily intakes (ADI values) for these food-approved mineral oils. The BfR risk assessment showed that orally ingested mineral oils from lip care products contribute less than ten percent to the ADI of consumers. In the opinion of the BfR, no health risk is to be expected if producers comply with the recommendations of Cosmetics Europe.

SPECTRUM

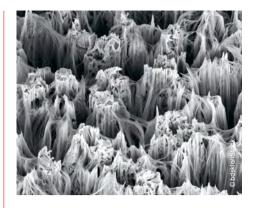
The use of chemicals in everyday life

How much dish-washing liquid do Germans use when cleaning their plates? How long are DIY enthusiasts in contact with filler? Exact data on the way people use these and other products is needed in order to assess the health risks of household chemicals. To date, very few scientific studies have been performed, and there is no standardised methodology. The BfR has tested several different methods in a feasibility study. Telephone interviews, in combination with self-administered protocols, supply reliable data on exposure to consumer chemicals, and the BfR has already collected sample information for some products. The data shows that a maximum four grams of dish-washing liquid is used in half of all washing-up sessions. And filler is used for a maximum 15 minutes during every second DIY task. The BfR is currently using the derived methods to collect representative data on the use of adhesives. In future, this data can be incorporated in the risk assessment and regulation of chemicals.

More information:

Schneider et al. Consumer behaviour survey for assessing exposure from consumer products: a feasibility study. J Expo Sci Environ Epidemiol. 2018; in press:1–12.





Systematic assessment of nanomaterials

The chemical industry uses them, so do the medical and electrical engineering sectors: nanomaterials, extremely tiny particles about the size of viruses, with a maximum size of one hundred billionths of a metre. Making optimum use of these particles and addressing the potential risks in a responsible manner is a major challenge for science, technology and consumer protection authorities. Nanomaterials can be produced in an unlimited number of forms. Even when nanomaterials have the same chemical composition, changes in size, shape or surface structure can result in numerous different variants, and it is practically impossible to analyse each individual variant in detail for regulatory purposes. During the past three years, the BfR has been working with 14 project partners in the "nanoGRAVUR" research project funded by the Federal Ministry for Education and Research (BMBF) to determine how nanomaterials with similar behaviour or comparable effect can be categorised into groups. To this end, the project has defined allocation criteria and tested these criteria using typical examples. This will pave the way for the more rapid analysis of nanomaterials in future. The findings of this project were presented and discussed at the OECD in Paris in September.

More information:

www.nanogravur.info www.bfr.bund.de/en > Research > Third-party projects of the BfR >

Nanotechnology

Chlorinated disinfectants

Water treated with chlorinated biocides for disinfection purposes can, if not prepared in the correct manner, contain chlorate and perchlorate in concentrations that may be harmful to health. These salts of chloric and perchloric acid have also been detected as residues in foods such as fruit and vegetables. If these salts are repeatedly ingested in sufficient amounts, they can inhibit iodine uptake in the body. This can be problematic for people with thyroid diseases or iodine deficiency as well as for newborn babies and children. According to the European Food Safety Authority (EFSA), chlorate can also pose acute health risks following short-term intake; this is unlikely in the case of perchlorate. Efforts should be made to further reduce concentrations in foods and drinking water in future. EFSA and the BfR recommend reducing the entry of chlorate and perchlorate into the food chain. Consumers do not generally need to change their dietary habits, as the health benefits of fruit and vegetables remain undisputed.

More information: BfR Opinions Nos. 006/2018 and 007/2018 of 15 February 2018



The three EU teams: the BfR was represented by six PhD candidates and one jury member.

The Iranian capital was the venue for the final of the 1st International Nanotechnology Olympiad from 10 to 15 April 2018. This competition is designed to help up-and-coming science talents to interconnect with each other. Doctoral candidates from the BfR also qualified and were in Teheran for the event.

TEHRAN 07 24 2018

Nanotechnology is seen as a key technology in Iran, and the Nano-Olympics are just one of the many national and international programmes of the Iranian government geared towards training the future generation of researchers. Universities, research institutes and companies receive high-level funding, and the federal ministries house the competent offices for the assessment and regulation of these tiny particles, which differ not only in size but also in terms of shape and surface composition from larger particles.

The Iranian government also organised a national Nano-Olympics in 2017, and around 30,000 doctoral candidates, students and schoolchildren participated in the event. Several hundred mobile laboratories - known as "nano-trucks" - regularly travel the country and visit the schools. In these mobile labs, participants can make nanomaterials under supervision, and there are many simple applications for these materials. This nanotechnology promotion programme certainly has a positive effect: whereas in 2001 Iran was ranked 57th worldwide based on scientific publications on the topic of nanotechnology, the country now ranks 4th with over 9,000 publications a year. There are currently over 400 different nano-products on the Iranian market, and

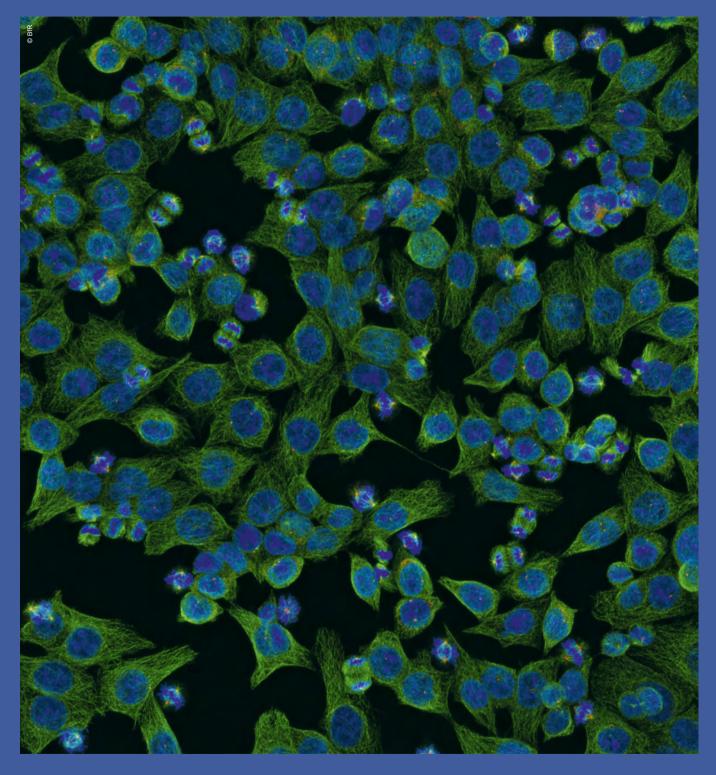
these products are found in the fields of medicine, cosmetics, textiles, dyes or packaging – much as is the case in Europe. Some of these Iranian nano-products are already being exported.

The International Nano-Olympics in 2018 was the next step towards creating a platform via which future scientists can interconnect. Nine teams from Iran, South Korea, Taiwan, Russia and the European Union competed with each other in Teheran to solve real-life tasks in the field of nanotechnology. During the preparations and the competition itself, each team was supported by a mentor, and each of the participating countries posted up to two jury members. The European Union nominated three teams of up-and-coming scientists, and these teams had to take part in a competition to qualify for the final. After a successful European qualifying round, the BfR team went on to the final in Teheran. Each team had to choose a problem from the area of water and waste water, and then search for a solution using nanotechnology, outline this solution in detail and then present it to the international jury.

More information: http://nanoolympiad.org

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"In the run-up to the event, we were slightly concerned about the unusual destination, but these concerns were soon allayed by the friendliness and cordiality of our hosts. The programme comprised workshops, exercises in international teams and the preparation of our final presentation and was tightly scheduled. Nevertheless, there was still time for outings to Golestan Palace and a typical bazaar. Unfortunately, we were not able to bring home any of the prizes. The participants from the Asian region had researched and fine-tuned their ideas for a lot longer and were even able to present prototypes or patents. We made an important contribution to the overall discussion, however. Thanks to all organisers and participants for an exciting week in Iran."



Divided risk: colon cancer cells under the microscope, many of them recorded during cell division.

Cell nuclei are coloured blue; the microtubules ("spindle fibres") involved in cell division as a "spindle apparatus" are coloured green.

Hormone traces in the nano-world

Scientists at the BfR are using high-resolution microscopes to examine how oestrogen-like substances alter the body's cells. This research also serves to replace animal experiments.

G ilbert Schönfelder has a cold and therefore has several packs of paper tissues at the ready. This is quite appropriate, as he can use the tissues to illustrate how breast cancer cells proliferate. The physician and toxicologist at the BfR puts down three packs of tissues close to one another. "The mammary gland cells are in a row like a picket fence", explains Schönfelder. If a cell breaks free from its anchorage, then it has to break off the close contacts with its neighbours." The scientists demonstrates this by pulling the middle pack out of the row. This separation from a group of cells is a fateful step. It can signal the start of a metastasis. "After all, 90 percent of cancer sufferers die from the metastases and not from the original carcinoma itself", says Schönfelder.

People understand by observing

Observing promotes understanding. Humans rely on what they can see. When we see something, we can understand it better. This also applies to processes that take place in the microcosm of the cell and its surroundings. Even in the age of laboratory analysis, bioinformatics and genetic data, therefore, observation is still of great benefit in medical research. Indeed, it is even making a comeback. Together with computer-assisted evaluations, observation in the form of microscopic images constitutes an important source of information for scientists like Schönfelder – when, for example, the job is to determine which chemical substances from the environment can separate the mammary gland cell from its surroundings, resulting in gaps in the picket fence.

"To make the small world large" is the goal of Schönfelder and his team. He set up a microscopy centre at the BfR together with biotechnologist Konrad Gulich. The "BioImagingCenter" is located in a darkened, vibration-protected room with a constant temperature on the ground floor of the BfR complex in Berlin-Marienfelde. The microscopes are high-resolution microscopes that are capable of capturing images and processing them instantly – the computer has been given "eyes".

The research at the BioImagingCenter provides important support for the German Centre for the Protection of Laboratory Animals (Bf3R) at the BfR in the development of novel methods that can replace and supplement animal experiments. This means that researchers who can observe through the microscope how chemicals alter the properties of cells (keyword: cancer) can refrain from conducting one or more animal experiments (or design the experiments in a more meaningful and targeted manner).

A nanoscope for the inside of the cell

The centrepiece of the BioImagingCenter is the PALM/ STORM microscope. It has a room all to itself and is currently the "highest-resolution light microscope in the world", explains Gulich, not without pride. "Its magnification factor is around 20 times higher than that of conventional microscopes". A green-coloured something can be seen on the screen of the "PALM/ STORM" with two closely located blue circles at the centre. It is a cell that is in the process of dividing, and one cell becomes two. The cell is highly sensitive during this division phase: the chromosomes – the carriers of the genetic material – dock on to fine protein fibres, known as the "spindle apparatus". The fibres "pull" the chromosomes in the direction of the newly developing daughter cells.

"Some substances can hinder this process, as can be observed under the microscope", says biologist Ailine Stolz. "We are researching the potential of these substances." Stolz uses the PALM/STORM microscope to study the way in which hormone-like substances act during cell division and can possibly therefore cause or at least promote cancer. The huge level of accuracy of the microscope is based on an invention that won the Nobel Prize for Chemistry in 2014. The new technology turned the microscope into a nanoscope, as the Noble Prize Committee wrote in its reasons for choosing this technology.

The limit of resolution

It was physicist Ernst Abbe from Jena who defined the seemingly unsurmountable limit of resolution way back in 1873. According to Abbe, the microscope can no longer distinguish between two dot-shaped objects if they are less than 0.2 micrometres apart. Generations of researchers who succeeded Abbe were unable to overcome this constraint.

In 2005, American physicist Eric Betzig succeeded in outmanoeuvring nature. His "PALM" method (PALM stands for "photoactivated localisation microscopy") is based on the realisation that molecules that have been previously marked with fluorescence are caused to light up with a small light impulse. This impulse is so weak that only a few molecules flicker in each case. Moreover, they are more than 0.2 micrometres apart in other words, they obey Abbe's Law and are visible independently of one another. The trick is that an overall image with an extremely high resolution down to 10 nanometres (0.01 micrometres) is only achieved after thousands of individual images are combined in the computer. "It's like a night sky in which more and more stars gradually begin to appear until, finally, they're all shining", is how Gulich explains the PALM principle.

The high-throughput microscope in the next room is based on a different approach. The focus is not on small

details in the cell but rather on changes in many cells that are magnified by the microscope. The computer registers the images and evaluates them statistically. "We are developing a test method that will help us to better understand the effects of hormonally active substances", explains biologist Sebastian Dunst. On the screen showing the microscopic image, it is possible to recognise tightly packed and blue-coloured nuclei of breast cancer cells with green-sprinkled boundaries – the cell membranes.

More metastases due to hormones?

The substances that colour green on the cell membrane are adhesion proteins. They connect cells, they glue the cells together, so to speak. Dunst and his colleagues noticed that adhesion proteins can change under the influence of certain substances, strengthening or weakening the bond between the cells as a result. This may mean that the risk of metastases is lower when the connection is stronger – because the cell remains in its "picket fence" structure. The theory behind this is that substances that have a similar effect to that of the female sex hormone estrogen loosen the cell contacts, thereby increasing the risk of metastases. In contrast, substances that block estrogens reduce the risk. This is probably also due to the effect on the adhesion proteins.

When the high-throughput microscope is used to examine cell cultures, it is possible to study exactly what happens when the dose of a substance is increased. If a chemical substance is used to block the hormone estrogen, the cells adhere better to each other and the cell is less mobile. If, on the other hand, estrogen-like substances are dripped onto the cells, the reverse happens. "We have tested more than 20 active substances with estrogen-like effect and succeeded in observing clear effects", Dunst reports.

High-penetration laser for deep insights

Multi-photon microscopy provides deep insights into living organisms and is also used at the "Bio-ImagingCenter". The researchers use long-wave laser light that can penetrate tissue up to a depth of one millimetre. This may not sound a lot but it represents a major step in the microcosm of life –1,000 micrometres no less.

This technique makes it possible to study life processes in complete organisms, such as zebrafish embryos in organ-like microstructures, known as organoids – and to do so cell by cell, so to speak. Organoids are to be used increasingly in future for testing medications or chemicals." With this approach, we are working to reduce the number of animal experiments in basic research", says Schönfelder, as he looks at a hugely magnified organoid. If only microscope pioneer Abbe could look over his shoulder, he would be astounded.

Cell in focus: impressions from the BioImagingCenter



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We want to make the small world large!

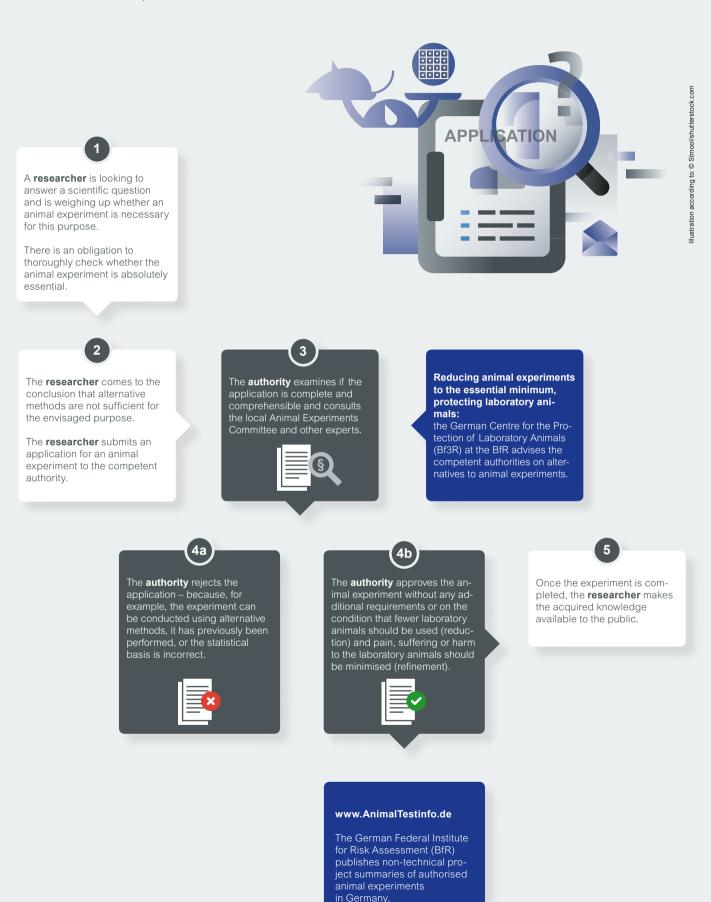
Professor Dr. Gilbert Schönfelder, toxicologist





Strict review process

How an animal experiment is authorised



Less suffering – for humans and animals

The BfR research funding programme supports external projects focusing on the development of innovative alternative methods to animal experiments. Eight projects received funding approval in 2017. Here is an overview.

Better donor organs, fewer laboratory animals

Lung transplants can save lives, but there is always a lack of donor organs. More lungs are being successfully transplanted through the rinsing and respiration of a donor lung outside the body, known as "*ex vivo* lung perfusion". The working group headed by Professor Markus Kamler at Essen University Hospital is investigating whether pigs' lungs from the slaughtering process are just as suitable to improve the procedure as lungs from laboratory animals. If this proves to be the case, fewer laboratory animals would have to be killed in order to obtain their organs in years to come.

Cardiac insufficiency: fruit flies rather than rodents

Persistently weak pumping power of the heart muscle (chronic cardiac insufficiency) is a serious complaint, and the number of patients is constantly increasing. The team under Professor Ulrich Kintscher at the Charité – Universitätsmedizin Berlin is investigating new treatment options in this area. The researchers are combining microscopy and video technology – and using the fruit fly (*Drosophila melanogaster*) as the model organism. This can help to reduce the number of rodents currently used in such experiments.

Rats and mice from the printer

Animal experiments require the safe handling and use of laboratory animals. Most courses focusing on animal experiments still use rats and mice for practice purposes. In order to reduce the burden on laboratory animals, the necessary techniques can be practiced on training models (simulators) that simulate the reaction of the live animal in question. The working groups headed by Professors Johanna Plendl and Christa Thöne-Reinecke (both Freie Universität Berlin) are assessing existing rat and mouse simulators. The objective is to create a model that is as close as possible to reality and that can then be printed out on a 3D printer.

"Mini-organs" for effective research

How do chemical substances affect the embryo? This is one of the main questions for toxicologists. Organoids – organ-like microstructures in the Petri dish – provide a new tool for the investigation of this question. These "mini-organs" can be used to perform toxicological experiments and investigate the effects on the development of the embryo without the need to use laboratory animals for this purpose. The team headed by Dr. Christian Schröter from the Max Planck Institute for Molecular Physiology in Dortmund is developing this kind of organoid system, which simulates the properties of an embryo. This is an alternative to animal experiments with a future.

Why wounds heal - without animals

The healing of a wound is a complex process, the success (or failure) of which can decide on life or death in extreme cases. Together with her team, Professor Sarah Hedtrich from Freie Universität Berlin is developing a wound healing model based on human skin cells. The aim is to improve our understanding of the healing process – including, for example, the inflammation that occurs during healing. The model also represents a further important step towards replacing animal experiments in wound healing research.

Liver under pressure

The liver is essential to survival as our central detoxification and metabolic organ. In order to better understand how the liver works, the working group headed by Professor Jens Kurreck at Technische Universität Berlin is designing three-dimensional models. This involves bringing together living cells to create a kind of "artificial liver" on a small scale with the help of "bioprinting". As an organ model, the "printed liver" represents an alternative to animal experiments.

Less pain for zebrafish

After mice and rats, it is the small, agile zebrafish (*Danio Rerio*) that are used most frequently in animal experiments, and their use is increasing. Zebrafish share more than 80 percent of the genetic dispositions that are involved in the development of diseases in humans. Together with his team at Tübingen University, Junior Professor Aristides Arrenberg is researching methods that can reduce the pain and suffering of zebrafish. This also includes the development of suitable anesthetics for fish.

Sick lung, healthy lung

Chronic diseases can permanently damage the lungs. But how does this respiratory organ still manage to recover? A working group at the Helmholtz Centre in Munich headed by Dr. Claudia Staab-Weijnitz is tasked with investigating this question. At the same time, the group is also trying to identify new techniques that can replace the debilitating animal experiments that use chemicals and are currently employed to address such questions. For this purpose, the researchers are growing human respiratory tract cells that can be used to study the regeneration of the lung.

The next invitation to apply for Bf3R research funding will be announced in the spring of 2019.

More information:

www.bfr.bund.de/en > German Centre for the Protection of Laboratory Animals > Bf3R Research Funding

PERSONNEL



"We discuss things that are part of something bigger"

Dr. Tanja Schwerdtle has been Professor of Food Chemistry at the German Institute of Human Nutrition at the University of Potsdam since 2013, the year she also became a member of the Scientific Advisory Board of the BfR. In August 2017, the members of the Board unanimously elected her to the position of Chairperson.

Ms. Schwerdtle, why does a departmental research establishment like the BfR need a Scientific Advisory Board in the first place?

Our view as members of this body is that an advisory board should be there to externally mirror the performance and the strategy of the BfR. We also advise the BfR on its scientific and specialist focus, in particular with regard to long and medium-term strategy and in connection with cooperation projects with research establishments in Germany and abroad. We can provide support in areas such as joint appointments, for example, or by discussing critical issues with other risk assessment entities.

What are the concrete tasks of the Advisory Board?

The Advisory Board is currently working on the implementation of some of the recommendations of the German Council of Science and Humanities, who evaluated the BfR in 2015. One of the recommendations is to strengthen the BfR's risk communication activities. We are currently discussing various strategies for the effective implementation of this recommendation with the management of the BfR.

Based on your experience to date, how would you say the work of the Advisory Board impacts the development of the BfR?

In both of the terms during which I had the privilege of serving on the Advisory Board, the BfR profited from our support during the inspection by the German Science Council. Professor Schäfer-Korting, the former Chairwoman of the Advisory Board, and I discussed various matters with the members of the Council, and I think this was helpful. Moreover, during the last two periods in office, numerous members of the Advisory Board have provided excellent advice to the BfR on the fostering of young talents and improving research performance.

How do you benefit personally from your involvement?

On the interdisciplinary Advisory Board, I can engage in a very high standard of discussion regarding matters that don't really concern my own work directly but that are part of something bigger. It's fun to see things from different points of view and then to arrive at a common perspective that supports the BfR. It's enjoyable to work on these kinds of things outside my day-to-day job routines.

EVENTS



All fake?

On 15 November 2018, the BfR is hosting a stakeholder conference at the Kaiserin-Friedrich-Hörsaal in Berlin on the topic "Is it fake? Science in the age of multiple truths". Prominent speakers from the world of science, politics, the media and NGOs will be discussing scientific facts and perceived truths. Attendance at the event is free of charge.

More information: on this and other BfR events at the website of the BfR Academy: www.bfr-akademie.de

INTERNATIONAL NEWS

International guests at the BfR

This year, delegations from Japan, Korea, China, Taiwan, Myanmar and Sweden visited the BfR with the objective to promote international cooperation and scientific exchange. With the Japanese Minister for Consumer Protection and Food Safety, Teru Fukui, and his ten-strong delegation, for example, the BfR discussed the application of new Omics methods for the analysis of complex biological samples as well as the use of modern techniques for the tracing of suspicious foods along the product chain.

Science gateway to Africa

In March, a three-day workshop organized by the International Livestock Research Institute (ILRI) in Nairobi, Kenya, attended by the BfR, the Freie Universität Berlin and the Friedrich Loeffler Institute took place to initiate future cooperation between Africa and Europe. The ILRI conducts research on the management of livestock animals with the aims of improving food safety and reducing poverty in Africa. The workshop focused on strategies to deal with foodborne diseases and antimicrobial resistance.

Summer Academy in Uruguay

During a one-week Summer Academy in Montevideo, the BfR informed and trained 40 researchers from Uruguay in the field of official risk assessment in Germany and Europe on behalf of Germany's Federal Ministry of Food and Agriculture (BMEL). Uruguay intends to create structures in the field of risk assessment that closely resemble our system in Germany. The BfR and the Uruguayan Ministry of Agriculture have been cooperation partners since 2014.



Commitment in Portuguese-speaking countries In spring, the BfR organised a two-day workshop in the capital city of Cap Verde (Cabo Verde) for attendees from the island itself, Angola, Brazil, Guinea-Bissau and Mozambique. The workshop focused on approaches dealing with disease outbreaks caused by pathogens in and on food. The BfR has had cooperation agreements with some of the aforementioned countries for a number of years now to intensify scientific exchange. In February, the BfR published an almanac on food safety for the Community of Portuguese Language Countries (CPLP).

More information: www.bfr.bund.de/en> The Institute > Co-operation

UP-AND-COMING TALENTS

Wide-ranging support for doctoral candidates Junior researchers who complete their doctorate at the BfR benefit from a high-quality advancement programme. The doctoral candidates not only conduct research into topical and applied subjects with the help of state-of-the-art technical equipment; they also undergo an accompanying further training and development programme to improve their specialist and non-specialist skills. This doctoral training programme is divided into five modules that can be compiled flexibly. The doctoral training programme at the BfR comprises not just the further training programme but also a supervisory agreement that guarantees specialist assistance during the three-year doctoral phase. Depending on core areas of research and the volume of acquired third-party funding, the BfR advertises around 20 positions for doctoral candidates every year. The dissertation project itself is registered at a university, and the BfR signs the employment contract. You can also find information on vacant doctoral positions on the BfR website.

More information: www.bfr.bund.de > Job advertisements www.bfr.bund.de > Research > Support for junior scientists





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