BfR 2 GO

The Science Magazine
of the German Federal Institute for Risk Assessment
Issue 2/2019

Microplastics in food

Small parts – big impact?

Food
A closer look at additives

Textiles
Fewer risks to the skin

Animal experiments
Transparency through study registry

Dear Readers!


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German scientists are rather cautious when it comes to public debates. This often leads to volume prevailing over reason. If you keep quiet, you'll be pushed aside. I can think of a couple of typical provocative subjects like animal experiments or pesticides.

Someone who won't be silenced is German Nobel laureate for medicine Christiane Nüsslein-Vollhard. She is always advocating freedom of research. In her BfR2GO interview, she takes a clear stance on the latest genome editing, the most well-known of which is CRISPR/Cas9. The BfR also hosted a consumer conference on this highly topical issue in August and September 2019.

Mind you, this doesn't mean that science always gets it right. To err is human. Scientists certainly also make mistakes. It is more a question of their voice being heard and being taken into account in political decision-making. This is all the more the case in a knowledge-based society like ours and even truer when it concerns issues that directly affect scientists in their work.

What actually is the role of science in society? In his interview with BfR2GO, Reiner Wittkowski, BfR Vice-President until September 2019, takes a not entirely unclouded look at the future. The political dispute over the health assessment of glyphosate has resulted in people losing confidence in science, therefore ultimately damaging consumer health protection. Nevertheless, the model of impartial scientific policy consultation, as embodied by the BfR, has proved its worth from Wittkowski's point of view. This, in turn, has also been confirmed by independent bodies such as the German Council of Science and Humanities.

Incidentally, what do glyphosate and copper have in common? The answer might surprise many of you: both are substances used as pesticides. But while phasing out glyphosate in Germany (and soon Europe?) is a done deal, the use of the heavy metal copper was extended for a further seven years without much public involvement at the end of 2018. The prospect of phasing out copper lies in the distant future – reason enough for an overall assessment by the BfR. More on this – and, of course, many other exciting topics – in this issue.

I wish you a stimulating read.

Professor Dr. Dr. Andreas Hensel
BfR President


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Discovery tour through the giant chicken

In August and September 2019, several thousand people in Berlin explored the world's largest chicken made from plants. School children, nursery groups and families discovered fun facts about the chicken and the egg at the "Ei-Land" (Egg Land) of the BfR. In the labyrinth of corn, sunflowers and other plants, which looks like a chicken from above, they explored topics such as: what makes a good egg? How does the egg get from the coop to our plates? And what needs to be taken into account when handling food like eggs and poultry? The 1.5km long path offered stations to get involved in, such as a mobile chicken coop, a barefoot path and a "smellodrome". This is the fourth time that the BfR has hosted a didactic plant labyrinth. The project partner was the University of Kassel.

More information:
www.bfr.bund.de > Presse > Mediathek

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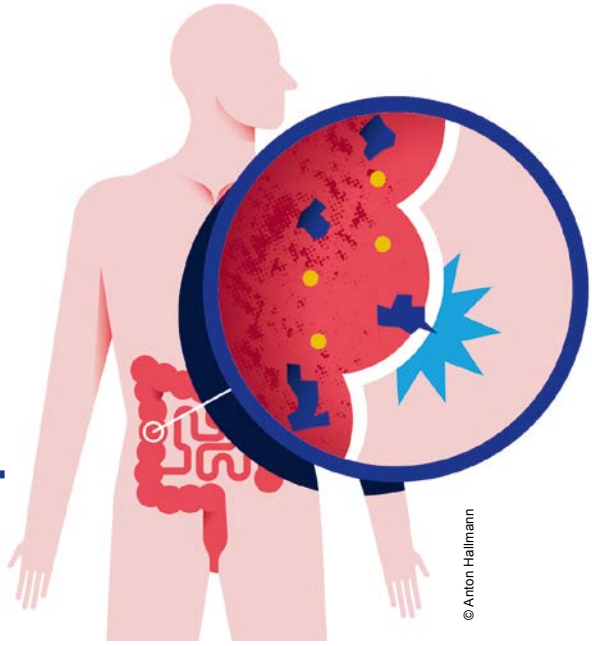

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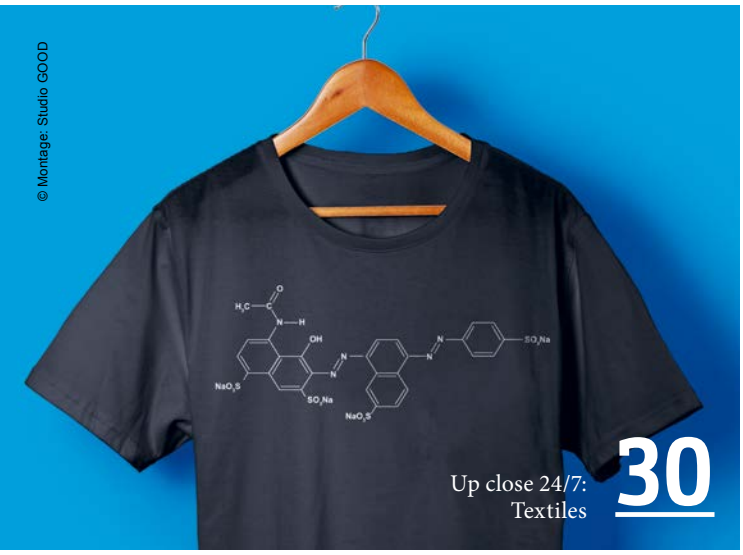

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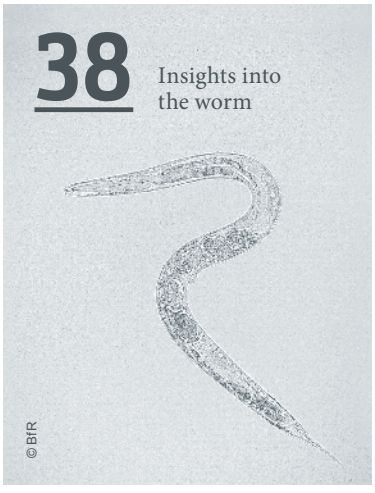
Asssess.
Research.
Communicate.



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Small parts – big impact?

We live in a world full of plastic. It breaks down into tiny particles through chemical and physical processes to form microplastics. There is no doubt that microplastics are found in food. However, research is still very much incomplete. The first studies at the BfR have begun.

Research can be unappetising. For instance, when it concerns microplastics in humans; more specifically, microplastics in our intestines. In a 2018 pilot study, a research team from the Austrian Federal Environment Agency and the Medical University of Vienna examined stool samples from test subjects from Europe and Japan for the first time. The test subjects wrote a nutrition diary for one week and sent a stool sample to Vienna. Every sample contained microplastics. The media response was huge – even at the BfR. Because it was proof: microplastics do not stay in the environment. They have also reached humans.

Plastics age and break down

Today, plastics are present almost everywhere in the human environment. Global production is growing, and more and more plastic is entering the environment. Microplastics are therefore being detected more and more frequently. The difficulties start with the definition itself. The term is used for small plastic particles of different origin, size, shape, and chemical composition. Size specifications are not uniformly defined and usual vary between 0.0001 millimetres (mm) and less than 5 mm. Science distinguishes between intentionally manufactured microplastics and microplastics that are the result of the decomposition process (see box).

Like many other research institutions, the BfR is also tackling this topic. Focus is on the risks to human health when food or drink contains microplastics and is then consumed. For the BfR, there are still major uncertainties and data gaps in many areas of research.
"The first investigations into microplastics began just a short time ago. We therefore lack the basis for a comprehensive health risk assessment," says Professor Alfonso Lampen. The biochemist and veterinarian is Head of the Department of Food Safety at the BfR. Data regarding intake, analysis and the effects of microplastics on people were notably lacking.

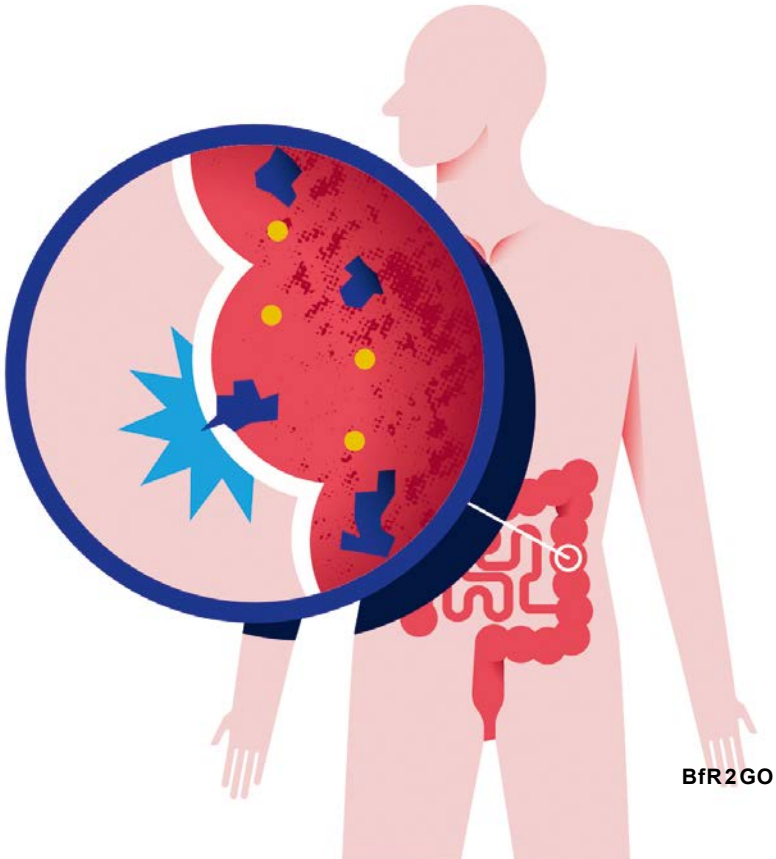
Microplastics in food – yes, but how much?

Microplastics are everywhere, This is scientifically well documented, according to Lampen. It can generally end up in food through the air, seawater, freshwater and groundwater. However, it is uncertain how much really ends up in our food. Furthermore, there is no reliable data about the types of plastic that people ingest as microplastics in food. There are always reports about detection in honey, mussels or even salt. However, information on the quantity and types of plastic is almost always lacking. Fish, for example: here the particles are mainly found in the gastrointestinal tract of the fish, which most people do not eat. Whether they also migrate to other edible parts and accumulate there, science simply does not yet know. Mineral water, for example: The Bavarian State Office for Health and Food Safety has detected microplastics in mineral water – not only in water from plastic bottles but also from glass bottles. Microplastics could therefore also get into the bottle through cleaning processes, colour pigments from the paper label, the plastic cap or even from the air.

Microplastics can enter our food during cooking and eating. This is because the smallest fibres from textiles (regarded as microplastics), such as fleece or nylon, break away when we wear them and, in doing so, end up in our food.

Cosmetic products might also contribute to intake: This includes use in things such as shower gels or peeling products. However, based on the current state of

Microplastics are everywhere and reach our food through the air and water – and in this way enter the human body.



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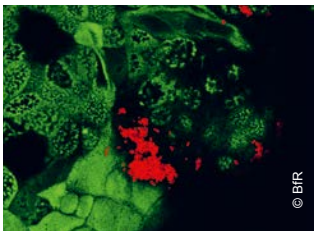


There are countless types of plastic. They are difficult to analytically detect in the micrometre range.

research, it is unlikely that the particles enter the body via the skin. "Intake via respiration seems to be more significant," says Lampen. Car tyre wear, for example, is a significant source of microplastics in the environment. It enters our lungs through the air. "We lack valid data about what we really absorb from all of these microplastics and how long they stay in our body," summarises Lampen.

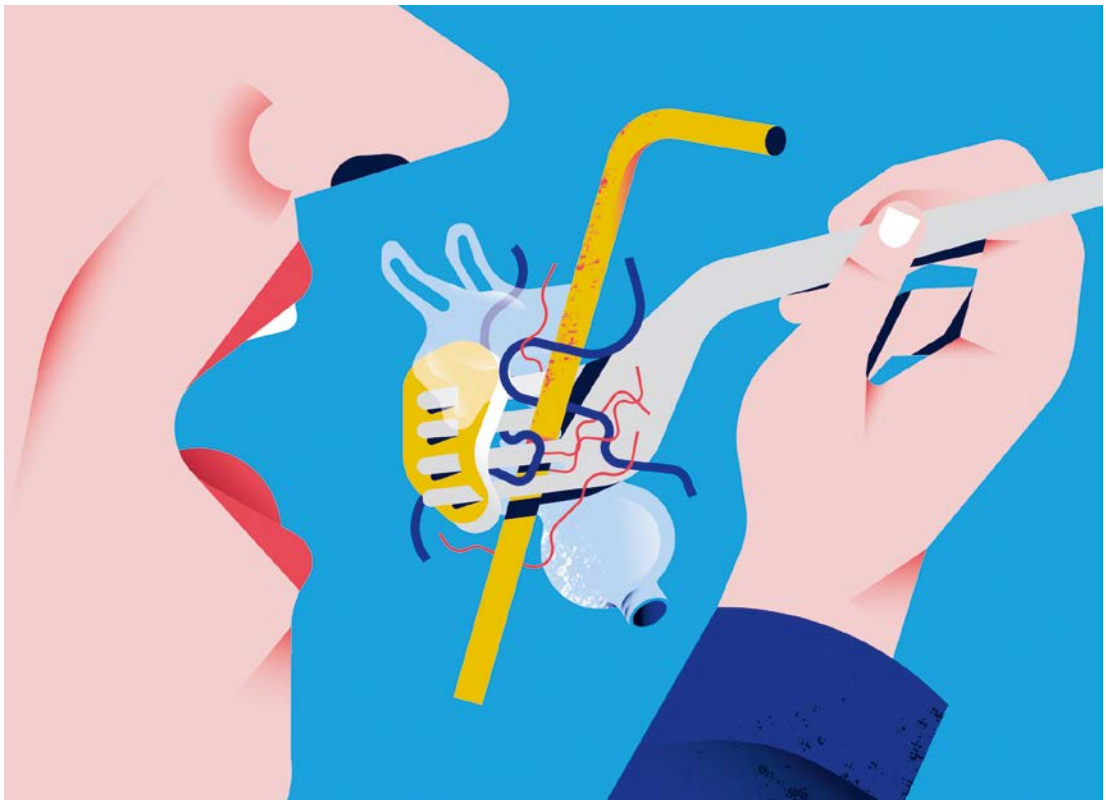
The analytical challenge

If intake is already difficult to research, this is all the more true for the analysis. There are imaging and spectroscopic methods for determining microplastics in food. However, generally recognised and validated methods for identification and quantitative analysis are lacking. One reason for this is that there are countless types of plastic. Another is that sample preparation poses a great challenge for science, according to Dr. Harald Jungnickel. The chemist is an expert in the field of product analysis at the BfR. "In the case of mineral water, it is still relatively manageable, since it is not a compound food. It gets really complicated with soil or animal samples, which are complex mixtures of many different substances." To do this, analyses must distinguish plant-based organic material from microplastics. "And it gets very difficult in the micrometre range." Various analytical approaches for determining and quantifying microplastics are currently being discussed in scientific circles. To this end, the BfR is cooperating with other institutions, such as the Max Rubner Institute, the sister authorities in Denmark (DTU) and France (ANSES), the University of Leipzig, the German Environment Agency and the Federal Institute for Materials Research and Testing. The BfR is discussing current developments with them and coordinating further joint action.

The formation of microplastics

Primary microplastics are produced industrially in the form of plastic-based granules or pellets. Different plastics such as polyethylene (PE), polypropylene (PP), polystyrene (PS), polyethylene terephthalate (PET), polyvinyl chloride (PVC), polyamide (nylon) and ethylene vinyl acetate (EVA) are used.

Secondary microplastics are created by chemical and physical ageing and decomposition processes from plastic bags, bottles or tyre wear. They can also come from washing textile fibres that contain plastic, such as fleece. Based on current knowledge, microplastics found in the environment mainly originate in this way.



Many open questions about the effects

There are hardly any reliable figures on the health effects of microplastics. A lack of studies means little data for risk assessment. One of just a few studies was carried out by the BfR in 2018 (see box). Biochemist and toxicologist Albert Braeuning's unit investigated the effect of microplastics on mice and human intestinal cells. "We found that polystyrene particles are unlikely to cause intestinal damage. However, we cannot prove this for other types of plastic, such as PVC, polypropylene or polyamide. To do this, we need experimental data." Various particles, different in structure, size or shape, must be investigated accordingly. According to private lecturer Dr. Braeuning, particles that are even smaller than microplastics must also be looked at: plastic nanoparticles.

In 2017, a junior research group was founded in the Department of Food Safety at the BfR to deal with both micro- and nano-scale plastic particles (see interview on page 12). Open questions include the effects of additives that make plastics soft, strong and colourful or that protect them from UV radiation. Some of them pose a danger to health. Another area of research: substances from the environment, such as polychlorinated biphenyls or polycyclic aromatic hydrocarbons, could become attached to microplastics. These could also be a threat to our health. In addition, data on microorganisms, such as bacteria or viruses, which "cover" microplastics in the environment as a biofilm, is lacking. Some of these may pose a danger to health.

Concern increases with awareness

Research into microplastics is only just beginning. The goal over the next few years is to obtain reliable data and better assess the health risk. Nevertheless, the topic is currently very much present in the media and population. For Dr. Mark Lohmann, Head of the Sociology of Risk and Risk Benefit Appraisal Unit, the interest in the research results on microplastics is no surprise. "For several years in our surveys, we have seen that the topic is becoming more and more important to consumers. That is what the media is picking up on and looking for answers." The BfR publishes the Consumer Monitor every six months under Lohmann. As a representative population survey, it provides answers to the questions about what the public thinks about topics in the field of consumer health protection.

The results clearly show that the awareness of microplastics as a consumer issue is increasing. And concern increases with awareness. While in February 2017

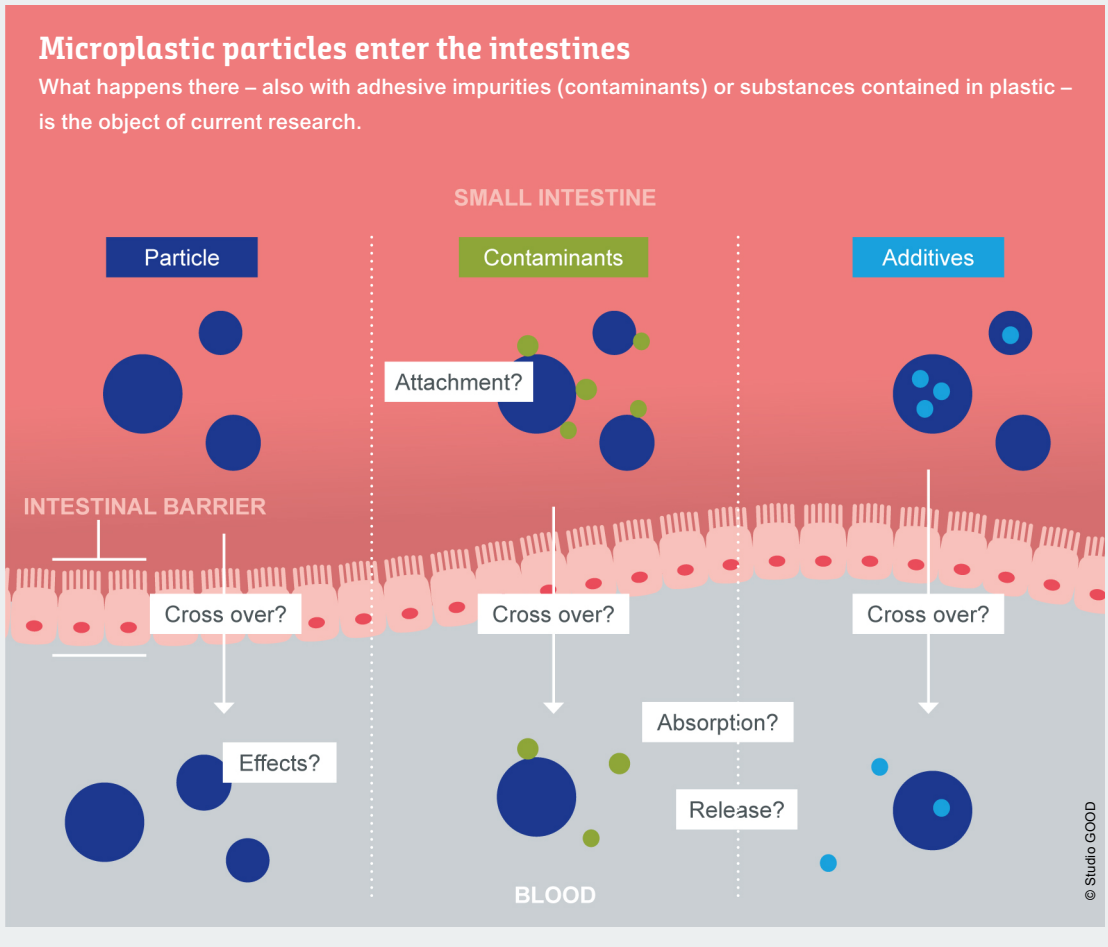
44 percent of respondents were concerned about microplastics, it had increased by twelve percentage points to more than half of respondents in February 2019.

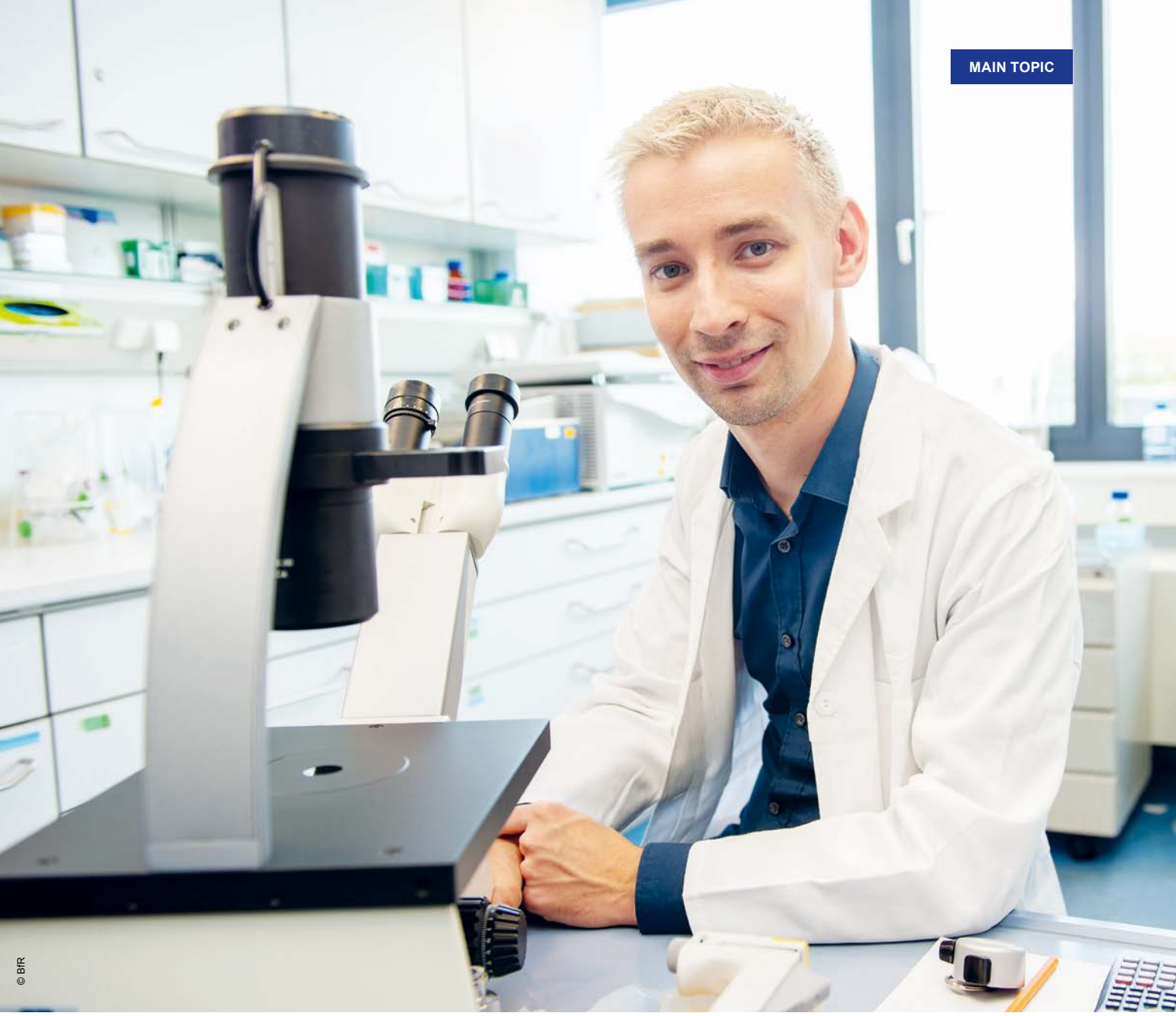
Despite all scientific uncertainties, the BfR assumes that microplastics in food are unlikely to pose any health risks to humans based on the current state of knowledge. The World Health Organization (WHO) shares a similar view with regard to drinking water. Based on previous information, it assumes that microplastics in water pose no health risk. The organization, which observes and scientifically assesses health conditions worldwide on behalf of the United Nations, also calls for even more research and more reliable data. ◘

More information:
www.bfr.bund.de > A-Z-Index: Microplastics

Experiments on microplastics in the laboratory

The BfR has investigated the effect of microplastics from polystyrene, one of the most frequently used plastics in the world. It is used, among other things, for the production of styrofoam, food packaging and everyday items such as bicycle helmets. BfR scientists used two methods: On the one hand, they used cultures of human intestinal epithelial cells (in vitro) to investigate whether polystyrene particles of different sizes might be taken up into the cells. In addition, mice were fed the particles for 28 days. “We have no clear idea of what the particles could do,” says Albert Braeuning, who is researching food safety with his unit. “An inflammatory response? Oxidative stress? There are still fundamental questions here that need investigating.” The study results showed that the polystyrene particles are generally absorbed into the intestinal cells. However, in the mice it was found that, despite the very large amounts administered, they could only be detected occasionally in the intestinal epithelial cells examined. The levels were far above those that appear to be realistic for humans.





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"Nanoplastics will keep us busy for a long time"

Mr Sieg, why is it so difficult to detect microplastics in food?
Foods are very complex mixtures. Investigating the different types of microplastics and quantifying them in food is very difficult in terms of analysis. The difference in density between plastic particles and the surrounding food material is small. Standard methods, such as spectroscopic methods, are unsuitable. This is simply because the usual measuring principles do not work. The studies currently being discussed have therefore only been carried out with very simple foods, such as mineral water or table salt.

It is safe to assume that microplastics are found in many foods.

Microplastics are in the air, water and soil – all parts of the environment. The question is, how much? And: does it enter the food chain? Studies have shown that microplastics are mainly found in mussels and seafood. This might have something to do with the fact that microplastics from the environment accumulate in the sea. As long as they remain in the intestine of the fish and other sea creatures, they will not enter the food chain. Animal intestines are not usually eaten.

Which research approaches are promising to detect microplastics in food?
There is no universal method. Thermoanalytical methods are used to vaporise and analyse samples using heat. However, only the amount of plastic can be de-

Biochemist **Dr. Holger Sieg** has been working at the BfR since 2014. As Head of the Junior Research Group for Nanotoxicology and Microplastics Work Group, he is investigating whether tiny plastic particles pose a health risk.

termined in this way. Spectroscopic methods can be used to characterise particles in terms of size, shape and structure.
Examples are micro Raman spectroscopy and micro-FTIR spectroscopy – both infrared methods that can also display very small particles.

Spectroscopy is based on light scattering.
When a beam of light hits a material, such as food, cell layers or even plastic particles, something happens to it: it is absorbed, bent or reflected away. The resulting scattered light can be measured and conclusions can be drawn about the properties of this material. Light waves that can be seen are referred to as optical spectroscopy. Infrared spectroscopy uses infrared light. X-ray spectroscopy also exists. Different measurements can be made using each wavelength.

Do you carry out the measurements yourself?
We work more in terms of toxicology than analysis: our junior research group is investigating the effects that plastics might cause in the body. We mainly experiment with cell-based systems, for example, simulating the human small intestine. This tells us whether plastic particles are absorbed by the cells, alter them or make their way from there into the blood – and are therefore distributed systemically.

Even smaller particles exist: nanoplastics. Are these particles more problematic than microplastics?
Nanoparticles are smaller than 100 nanometres. Very little is known about these particles. The fear is that nanoplastics might be in the position to overcome cellular barriers and spread throughout the body. But we still don't know anything about the possible effects. Nanoplastics pose a problem for research itself.

In which way?
It is hard to get results. For one thing, the particles cannot be detected with optical microscopes; they are simply too small. Furthermore, we cannot experiment with them yet. To do this, we would need standardised particles; reference particles. These are particles that are always the same size and have the same chemical properties. Nano reference particles are even more difficult to produce and process in the laboratory than microplastic particles. We are currently trying to get hold of this material. The German Federal Institute for Materials Research and Testing is able to synthesise nanoplastics.

What is this process like?
Quite futuristic: a polymer shell is synthesised around a very tiny core. A lot of chemical development work is required to achieve this. There are already core-shell particles made from a material similar to plexiglas. We want to use these to test whether our methods can be applied to nanoparticles.

What do we know about nanoparticles?
We know very little about them because they are so hard to examine. Nano-polystyrene is the most widely known substance to date. We have determined the viability of cells in cell experiments with particles of 20 and 100 nanometres in size, which is just about in the nano range. The particles have a toxic effect in overload situations in which the cells are overwhelmed and eventually collapse. These amounts are significantly higher than any expected human exposure.

So nano-polystyrene means no problem?
Little can be expected from the material itself. It is considered to be relatively unreactive. It could be more problematic that additives are released or environmental contaminants stick to the polystyrene – and then enter the body together with the particles. Projects are being planned to examine this. Many research groups have only just started investigating microplastics, and now we're talking about nanoplastics. We will be looking at this for even longer. ◘

How many people are worried about these food-based issues?

61 %
Antibiotic, hormone or steroid residues in meat

39 %
43 %
Pesticide residues in food

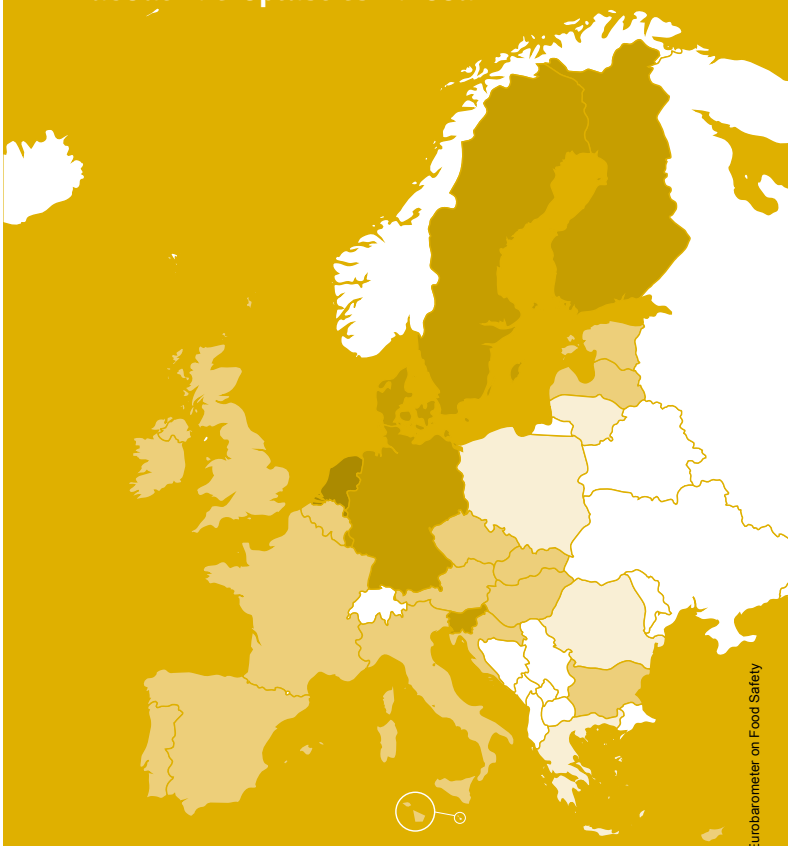
37 %
42 %
Environmental pollutants in fish, meat and other foods

21 %
34 %
Microplastics found in food

Europe (n=27,655)
Germany (n=1,539)

Source: 2019 Eurobarometer on Food Safety

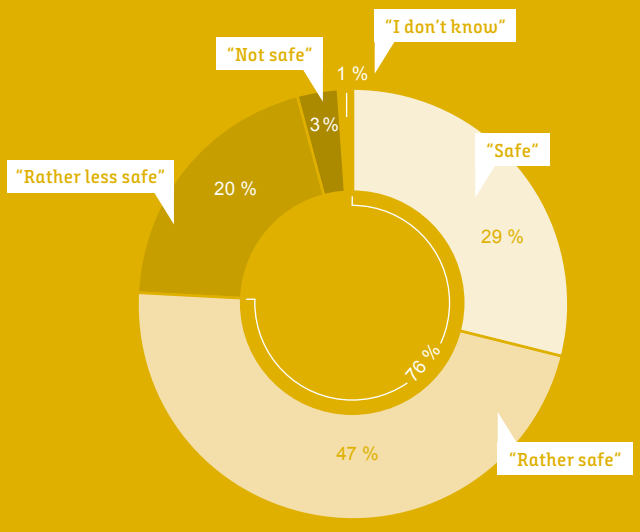
How great is the concern in Europe about microplastics in food?



Source: 2019 Eurobarometer on Food Safety

It's all a question of risk

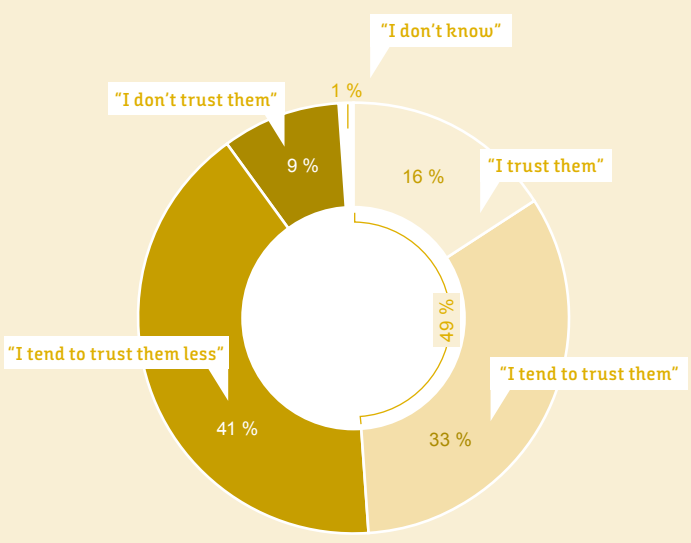
How do you assess the safety of food on offer in Germany?



n=1,016

Source: BfR Consumer Monitor 8/2019

Do you trust state authorities in matters of health protection?



n=1,016

Source: BfR Consumer Monitor 8/2019

What are consumers afraid of? What health risks do they see? The BfR and other scientific institutions are researching risk perception across Europe to ensure that consumers are well-informed and consumer health protection is effective.

Antibiotic, hormone or steroid residues in meat. Artificial additives and questionable environmental substances in food. Substances that are transferred from packaging to food. The range of topics that make up the general term "food safety" is wide and complex. Following the BSE crisis, national authorities, such as the BfR and, at EU level, the European Food Safety Authority (EFSA), were set up in 2002 to deal with these issues. In addition to the scientific assessment of health risks, communication about these risks is one of the main tasks of these institutions. Their approach: in order to communicate effectively, they first explore the attitudes and perceptions of target groups.

No sign of "German angst"

On behalf of EFSA, the EU Commission conducted a representative population survey in the EU member states for the first time since 2010. A total of 27,655 EU citizens were interviewed in person in the spring of 2019; 1,539 of them in Germany. This resulted in the special barometer "Food Safety in the EU".

The national analysis for Germany revealed that Germans are, on average, more interested and informed compared to the rest of Europe. Their greater openness runs through all levels of education and society. They are more familiar than the EU average – in some cases markedly so – with almost all the food risks mentioned in the survey. It is worth noting that the price is not the first thing that Germans pay attention to when shopping for food. The origin of the products is much more important to them. Whether food bears scrutiny of personal and ethical convictions, meaning whether the purchase is tenable in terms of animal welfare, environmental protection or religious aspects, is also a criterion of above-average relevance.

Resting on consumer information levels and quality control?

The German population is also more open to drawing personal conclusions from the information obtained. For example, 38 percent of the respondents stated that they had permanently changed their consumption behaviour (e.g. diet, cooking behaviour or the way they store food) at least once in their lives on the basis of information they obtain. They are more likely to find food safety information "very technical and complex", but this does not mean a greater loss of confidence in the source of the information.

Compared to the EU average, Germans place a higher degree of trust in Europe-wide food safety monitoring. They are more often convinced that this is ensured by authorities taking into account scientific research. That is perhaps one reason why this issue is not regarded as the biggest concern when selecting food in this country. The German population even considers it a matter of course that food is safe.

Public perception as an indicator for communication

This development is also due to the successful risk communication of the institutions, and their research on perception. The BfR also researches the values, attitudes and knowledge about health risks of the German population in relation to specific topics in consumer health protection. The BfR Consumer Monitor has been published every six months since 2017. In addition to food safety, the BfR addresses other topics falling within its jurisdiction, such as the safety of consumer products like cosmetics, textiles and toys. Special editions have already focused on topics such as antimicrobial resistance, plant protection products, tattoos and microplastics. PD Dr. Gaby-Fleur Böl, Head of the Risk Communication Department at the BfR, emphasises the importance of regular data collection: "Our target group is almost 83 million citizens. An up-to-date understanding of their knowledge, interests and concerns about health risks is essential to our mandate of communication." ◘

More information:
www.efsa.europa.eu > About > Documents > Corporate Publications > EU-Food-Safety-Barometer (English)

www.bfr.bund.de > Publications > Brochures > BfR Consumer Monitor

"Fear due to a lack of knowledge"

Genome editing dispute: in this interview, Prof. Dr. Dr. Christiane Nüsslein-Volhard takes a stand in the risk debate on new biotechnological methods. At her laboratory at the Max Planck Institute for Developmental Biology in Tübingen, the Nobel laureate is studying zebrafish and how their colour patterns form.

Ms Nüsslein-Volhard, why are Germans being driven by fear when it comes to genetic engineering?
Well, I'm not concerned! This fear is essentially based on a lack of knowledge. People don't know anything about genetics and only listen to what is wrong. The same goes for politicians. They would rather believe Greenpeace than scientists, and all sorts of long-disproved stories are told which stoke fears.

More knowledge – in this case about biology – is this not also an educational mission?
Yes, actually it is. But pupils at school already have to endure so many subjects. And we must not forget that living beings are incredibly complex. More complicated than a computer or a car; and nobody understands even them. But there is a need. It is shocking how little people know about where their food comes from, how species are cultivated or how the soil is prepared so that anything grows at all. Resistance to the herbicide glyphosate is also based on a blatant lack of knowledge. Glyphosate results in a weed-free field much more gently than any ploughing and harrowing does. But no one knows this.

Science doesn't have a particularly good reputation in Germany at the moment.
In fact, we often see distinct hostility towards science. "Alternatives" are very popular, such as alternative medicine or organic farming, which is being pushed tremendously. People who buy organic produce simply feel better. But this generally isn't justified at all. Organic food is neither healthier nor more environmentally friendly or more energy-saving.

Must science provide more information?
Germany does not have a long tradition of scientific institutions consulting lawmakers on policy, unlike the USA, for example, where the "National Academy of Sciences" plays a leading role. I have high hopes for the German National Academy of Sciences Leopoldina. It has, for example, published opinions on genetically modified plants and genome surgery using CRISPR. The facts of the matter are summarised well and in a scientifically reliable way. It would be nice if politicians would simply trust Leopoldina.

Genome editing, such as that with CRISPR/Cas9, allows for precise interventions into genetic material and is causing a sensation. How do you rate this method?
I think it's marvellous. CRISPR/Cas9 is beneficial for research. We get better and more accurate results faster and with less effort.

Do you use genome editing yourself?
We use it to investigate the biodiversity and evolution of organisms. There has been progress that was previously unthinkable.

Do you see any risks involved with CRISPR/Cas9?
If we follow all the relevant laws, of which there are plenty in this country, then there is no risk whatsoever. Of course, there are people who do not want nature to be genetically modified and, therefore, generally reject these kinds of tools. And there is the fear surrounding the genetic manipulation of people, which is a theme in many science fiction novels.

A scientist in China has already done this.
That was an isolated case without far-reaching significance.

In June 2018, the European Court of Justice classified CRISPR/Cas9 as genetic engineering and subjected it to existing legal regulations.

Totally wrong! It would have been better to relax genetic engineering legislation so that these methods could be applied more easily in agriculture. This is so difficult in Germany today, and because of that there isn't a single genetically modified plant in the field.

Professorin Dr. Dr. Christiane Nüsslein-Volhard in the fish house at the Max Planck Institute for Developmental Biology in Tübingen. Here, the biologist is researching embryonic development in animals, particularly the zebrafish.

According to surveys, Germans do not have much sympathy for "green" plant bioengineering. Your suggestions would probably be met with a divided opinion.

The law is so strict because politicians believe the population wants it to be that way. But this blocks overall development. This should really be reconsidered because genetic engineering methods are incredibly successful in cultivating new species that are more environmentally friendly, more productive, and more economical. It would be desirable for us, too.

Would you agree that CRISPR is synonymous with conventional genetic engineering as the European Court of Justice says?

I simply cannot understand this logic because you can achieve the same results with the CRISPR method as with conventional cultivation. There is no difference. It is therefore wrong to legally classify a product according to how it has been produced. Especially since conventional cultivation is so much more brutal. Plants are well and truly blasted with ionising radiation or chemicals to produce genetic changes, haphazardly and randomly. ◘

> **In Germany, we see distinct hostility towards science.**

Knocked out by CO

Carbon monoxide (CO) emitted by faulty tiled stoves and gas boilers can cause fatal poisoning if it accumulates in a room and is inhaled. A recent BfR survey shows how well known this risk is to the population.

99 %
know about blocked tiled stove vents or chimney flues

Risk situations

Most were aware of situations in which carbon monoxide poisoning could occur. There are gaps in knowledge when it comes to smoking shisha pipes and storing wood pellets.

89 %
know about defective gas-operated devices

20 %
know about incorrectly storing wood pellets

59 %
know about smoking shisha pipes in enclosed spaces

Underlying study:
Representative telephone survey of 1,012 people (German-speaking population in Germany aged 14 and above) from February to March 2019

More information:
Jungnickel, K. et al. 2019. Carbon monoxide - an underestimated risk? Awareness, perception, knowledge and prevention behaviour. Bundesgesundheitsbl. 62: 11, 1324–1331

How do you notice CO?

Almost everyone knows that carbon monoxide emissions can be detected through the alarm of a carbon monoxide detector as well as through headaches, dizziness or nausea. However, more than a third of respondents were under some misapprehensions:

44 %

believe you can smell carbon monoxide

41 %

believe smoke detectors sound the alarm when carbon monoxide is present in the surrounding air

Icon made by Smashicons (nose) and Freepik (smoke detector) from www.flaticon.com

Smoke: © Vagengeim/shutterstock.com

Familiar problem

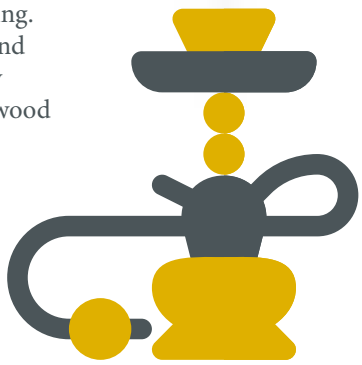
Eighty-two percent of respondents have heard of carbon monoxide poisoning before.

Little knowledge about prevention

Only **9 percent** named installing a carbon monoxide detector, and only **8 percent** named the regular inspection of heating units, tiled stoves or fireplaces as protective measures. A fresh air supply was mentioned most frequently. **Thirteen percent** of respondents did not know any protective measures.

Vulnerable groups

Those who own "risky devices" usually know about the risk of carbon monoxide poisoning. The exception are owners of shisha pipes and respondents with wood pellet heaters; only 38 percent know that CO emissions from wood pellets can lead to poisoning.



33 %

of respondents who own a shisha pipe do not know the risk of smoking shisha pipes in enclosed spaces.

Icon (Shisha) made by Freepik from www.flaticon.com

“Science faces a loss of confidence”

As Vice President, food chemist Professor Reiner Wittkowski played a crucial role in the development of the BfR. In this interview, the food authentication expert and wine specialist talks about the BfR’s achievements and challenges, and consumer health protection.


© BfR

Professor Wittkowski, you have been at the BfR from the very beginning, since 2002; and you are a wine connoisseur. Here's an idea: imagine that the BfR has matured like a good wine over the last 17 years. How does it taste? We'll call it "BfR wine".

There are definitely parallels between wine and science. For good wine you need high-quality grapes and a good must. And suitable tools to ultimately produce a quality product. It's very similar at the BfR. First of all, the areas essential for its tasks were extracted from its predecessor institutions. By appointing an external president, something was achieved that is rare with wine: a symbiosis of presidential spontaneous fermentation and institutional selected yeast. The tools included quality assurance, clearing, cost accounting, and elements such as impartiality and transparency. It was then necessary to let all of these components mature together and form a harmonious whole. No doubt about it, the BfR wine would certainly win great gold at a tasting!

A wine connoisseur possesses not only knowledge, but also intuition. Doesn't something similar apply to risk assessment? Doesn't this also require a gut feeling, a kind of risk instinct in addition to factual knowledge?

Actually, it's the other way around; our risk assessment is based on scientific studies and facts and not on political, social or personal preferences. It has nothing to do with intuition. The risks that we assess are a result of new substances, technologies, microbiological conditions, diets and much more. I would even consider it harmful to connect a personal or institutional gut feeling with a risk assessment.

With its risk assessments, the BfR has considerable influence on politics, consumers and the economy. We therefore hold a great deal of responsibility. How do you manage the balancing act between letting loose and practising restraint?

First of all, the BfR's presence in the media and also in political and social debates proves the relevance of our work, and also that we bear a considerable amount of responsibility. We are, of course, aware of this and try to take it into account. But I don't see the balancing act that you're talking about. The BfR cannot "let loose", and it doesn't have to practice restraint.

What do you see as the BfR's greatest achievement?

When the BfR was founded, as in the case of its European sister authority EFSA, the intention was to keep science-based risk assessment away from social, political and economic influences in order to have an objective basis for decisions. Today, you can see that this has proved successful. The BfR is a model for science-based policy consultation. Providing orientational knowledge is the Institute's great achievement. It does not represent its own interests and does not turn its coat. That is valuable for policy because it helps to make debates more objective. But it is, of course, also the reason why we are criticised – our findings sometimes contrast with ideological, political or personal goals and ideas about life.

You're alluding to glyphosate. The Institute's risk assessment has caused the BfR a great deal of criticism.

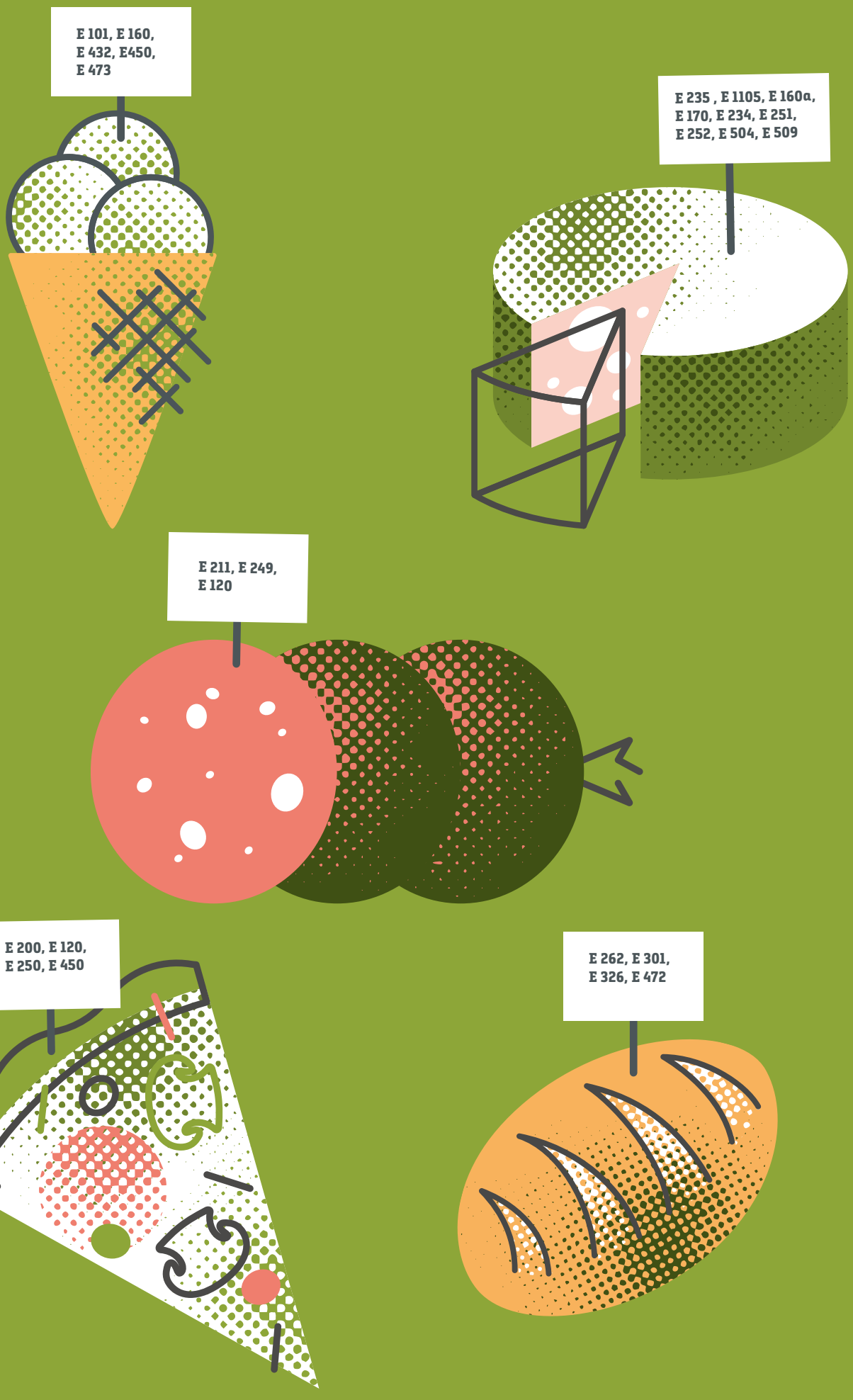
Glyphosate was and is a special case, and at the same time a Fall of Man. It was the first time that massive political pressure was exerted on an independent scientific assessment process. The scientific assessment process was effectively democratised and opened up to society while it was still in the phase of scientific discourse. This led to disputes right up to the European Parliament. As a result, we saw people lose confidence in science.

Democratising science – that sounds good at first.

There is nothing wrong with democratisation when it is about transparency, for example, the disclosure of our scientific approach. But science is also about expertise. Imagine someone bursting into a Berlin Philharmonic orchestra rehearsal and saying: "Hey everyone, I had music lessons once; from now on, I'll set the tone!" That would be unthinkable. It's only when it comes to science that suddenly everyone wants to have a say. Institutions, such as the BfR or EFSA, face a difficult future. Scientific and professional societies are also in demand here.

Where must the BfR improve even further?

The BfR already works pretty well. But we still find it difficult to prepare scientific findings in such a way that the public understands them. We're obviously still doing so in too complicated a manner. But our goal must be to reach as many social circles as possible. It is a considerable challenge to have to communicate highly complex facts in a very simple way. But people want simple messages, as you can see in politics. ◘



Additives in food: harmless?

Food additives are used to colour, sweeten and shape food or prolong its shelf life. The substances are found in many industrially produced foods. Although only additives that pose no risk to our health may be used, they have a bad reputation.

"Chinese restaurant syndrome": many have heard of it, but this phenomenon has not been scientifically proven. It describes complaints such as headaches and itching after a meal at a restaurant. Asian restaurants in particular are suspected by the public of serving dishes with too much of the flavour enhancer glutamate. This is supposed to trigger the symptoms – and is therefore controversial. Some companies now advertise getting by without glutamate. "Yeast extract is now often used instead. It naturally contains glutamic acid and other ingredients that have a taste-enhancing effect," says food toxicologist Dr. Rainer Gürtler, who assesses the safety of food ingredients at the BfR.

Approved substances get E-numbers

Food additives give food certain properties. For example, they are intended to improve the taste and appearance of food or prolong its shelf life. In other words, they fulfil a technological function. This is how thickening agents make pudding firmer. Emulsifiers are used in margarine to mix ingredients containing water and oil, which would not be mixable without emulsifiers. Many additives are used for colouring or to make food production and processing or handling easier. Examples of this are baking agents in dough or foaming agents in cream. Other frequently used additives are stabilisers, gelling and thickening agents, as well as preservatives and sweeteners.

Whether foaming agents in cream or emulsifiers in margarine; food additives serve a technological function.

Flavourings and enzymes are not considered to be food additives and are regulated separately by law. Processing aids are also not considered to be food additives. They are used in processing raw materials, food or its ingredients, and may result in unintentional and technologically unavoidable residues in the end product, which must be harmless and have no technological effect on the end product. Processing aids include, for example, flocculants, filtration aids and release agents. Unlike food additives, flavourings and food enzymes, processing aids are not subject to authorisation. Therefore, food business operators are solely responsible for their use.

Food additives may only be used in the European Union if the intended use has been authorised. Health safety must be proven, as must the technological need of using the substance in the first place. Both are examined in the approval procedure, which the EU Commission carries out together with the member states. The safety of food additives is assessed by the European Food Safety Authority (EFSA) (see interview). If an additive is approved by the EU Commission, it is given a three-to-four-digit number: the E-number. The food categories – for example, meat products, bakery products or ice cream – for which the substance is authorised and the maximum quantities are also specified.

Scrutinising from a risk assessment perspective

Before new substances are included in Regulation (EC) No. 1333/2008, the German Federal Ministry of Food and Agriculture (BMEL) usually requests the BfR to scientifically examine the relevant draft of the EU Commission. As a federal institute, the BfR in Germany is responsible for assessing the health risks of food additives.

"We review and assess the draft regulation from a national point of view, in particular the question of how much of the substance would consumers in Germany ingest under the intended conditions of use," says Gürtler. "We compare this amount with the acceptable daily intake." This "ADI" value is the quantity of a substance that, according to current knowledge, can be ingested daily throughout one's life without appreciable health risk. If the BfR comes to the conclusion that the ADI value would be exceeded, the BMEL informs the EU Commission.

The BfR also acts on its own initiative

In a different way, a consumer question on sucralose (E 955) triggered an assessment of a particular use of the sweetener. Scientists at the BfR found that if foods with sucralose, which may be contained in canned vegetables, for example, are heated to temperatures higher than 120 degrees Celsius in the oven, chlorinated organic compounds may be formed which could potentially be harmful, such as polychlorinated dibenzo-p-dioxins/dibenzofurans or chloropropanols. For a final risk assessment, additional data are still required. "Nevertheless, we made EFSA, which is currently re-assessing the approved sweeteners, aware of the issue," recalls Gürtler. For the time being, the BfR recommends not baking, deep-frying or roasting any food with the sweetener.

Aspartame in focus

While many of the approximately 320 food additives are barely known to the public, individual substances are all the more the centre of attention. This also has an impact on research. Gürtler gives one example: "Aspartame is one of the most investigated additives at all." The reason: the sweetener, found in coke or chewing gum, has long been supposed to be carcinogenic, which is why new studies have always been performed. According to the food toxicologist, none of them have confirmed the presumed harmful effect.

Are there good and bad additives?

For the expert, the safety of food additives is beyond dispute. Ultimately, only additives that do not, on the basis of the scientific evidence available, pose a safety concern at the proposed level of use may be authorised. And: "The EFSA assessments belong to those that have the highest standards in the world." Gürtler suspects that doubts about food additives could be related to false assumptions. "Many believe that artificial substances are harmful to health and natural substances are healthy." This is wrong because there are also natural poisons. "Whether a substance is natural or synthetic says nothing about its hazard potential," says Gürtler. Citric acid, for example, can be produced by squeezing lemons. However, industry produces the substance as an additive with the number E 330 mainly with microbiological (fermentative) processes, because enormous quantities of it are required. "However, the manufacturing process is taken into account in the risk assessment of additives because it may provide indications of possible impurities."

Nevertheless, anyone who wants to avoid food additives can do so. The use of additives is subject to labelling, meaning they must be indicated in the list of ingredients of packaged foods. There are also foods produced on an industrial scale that do not contain food additives, such as honey. And: untreated food is generally free of additives. ◘

Frequently used additive groups

Preservatives impede the growth of bacteria or moulds, therefore extending the shelf life of food. Examples: sulphur dioxide in dried fruit, acetic acid in marinades.

Antioxidants delay the reaction of food ingredients, such as vitamins, with atmospheric oxygen. Examples: ascorbic acid in canned fruit, tocopherol in cooking oils.

Flavour enhancers enhance the flavour of processed foods. Examples: glutamate in seasonings.

Sweeteners replace sugar for sweetening. Examples: aspartame in sugar-free chewing gum, sucralose in sugar-reduced jams.

Colours improve the appearance of food. Examples: beta-carotene in margarine, curcumin in potato flakes.

Thickeners change the consistency of food and make aqueous solutions creamy or viscous. Examples: modified starch in pudding, pectin in sauces.

More information:
www.bfr.bund.de > A-Z-Index: Food additives

BfR Opinion No. 012/2019 of 9 April 2019

“Sweeteners are a controversially debated topic with the public”

Professor Maged Younes is Head of the Panel on Food Additives and Flavourings at the European Food Safety Authority (EFSA). The committee assesses the health risks of food additives for all EU countries. These include controversial substances like titanium dioxide or phosphates.

© private

Professor Maged Younes is a chemist and toxicologist. In 2018, he was elected Chairman of the EFSA Panel on Food Additives and Flavourings. He is also a member of the EFSA's Scientific Committee.

Mr Younes, a food additive requires authorisation if it is going to be used in the EU. 316 substances are currently authorised. How does the approval procedure work?
First, the manufacturer must submit an application to the EU Commission, which then is forwarded to EFSA. Our panel assesses exposure and health risks using the scientific toxicity data provided. On the basis of our assessment, the EU Commission decides whether a substance is authorised and whether there are any restrictions on its use. For example, we can propose an acceptable daily intake – the ADI value – which should not be exceeded.

The panel also deals with substances that have already been authorised and that need to be reassessed by 2020. Why is that?
The authorisation for some food additives dates back decades. Therefore, the EU decided in 2008 that all additives approved before 20 January 2009 must be re-tested. Since then, the substances have been tested in accordance with the latest scientific findings. We examine whether there is still a scientific basis for using these substances or whether there may be a risk. We have reassessed around 60 percent of food additives. We must reassess the remaining 40 percent by 2020. I hope we succeed. The sweeteners group is important to me because these substances are a controversially debated topic with the public.

Phosphates, which the panel reassessed recently, are also under discussion. An ADI value was determined for the first time. How did this come about?
Evaluating phosphates was difficult. Phosphates are found in the human body. They are a natural component of foods such as cheese, sausage and fish. And they are also additives for technological applications in coke, milk powder or meat products, for example. The problem: a phosphate deficiency is detrimental to our health; an excess may be just as harmful. The committee finally managed to calculate an acceptable daily intake. This takes into account ingesting phosphate via additives and via food.

Titanium dioxide – a white colour pigment for baked goods and chewing gum – is also the subject of controversial debate. In the EU it is authorised as E171. The substance is suspected of being carcinogenic. Is there anything to worry about?
In our reassessment in 2016, we concluded that the toxicological data did not include any health concerns. However, there are slight uncertainties as to how the substance affects the reproductive system. We have therefore recommended further studies to close the data gaps. Titanium dioxide is an interesting substance for research because it also comes in the form of tiny nanoparticles. New data indicates that the number of nanoparticles is significantly higher than expected. ◘

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Beautiful and dangerous at the same time

Round, colourful, exotic – because of their attractive appearance, plant seeds are used in some countries to produce jewellery or for the decoration of musical instruments. The problem: the "natural beads" of plants like the castor oil plant or the jequirity bean (see picture) contain toxic substances. Severe diseases are possible if chewed or damaged seeds are consumed. Abrin, for example, is one of the most potent phytotoxins and is contained in the seeds of the jequirity bean, which has even accidentally appeared in spice mixtures at bazaars. Ricin is contained in the seeds of the castor oil plant, which is often to be found in parks or gardens as ornamental plant. Even low doses of abrin and ricin cause severe poisoning. A single seed of the jequirity bean may contain doses of abrin lethal to infants. The BfR advises to pay special attention when buying products made from or decorated with these kinds of plant seeds in exotic countries.

More information:
Communication No. 024/2019 by the BfR dated 3 July 2019

Bacteria in cookie dough

Raw cookie dough is a topic on everyone's lips right now. We have always gladly eaten cookie dough before putting it in the oven. But raw dough has health risks – even without eggs. Flour may contain pathogens such as shiga toxin-producing Escherichia coli, or STEC for short. It is a slightly processed natural product that should be heated before consumption. This is why professional cookie dough manufacturers use specially treated flour suitable for raw consumption. In North America, several outbreaks have already been reported, which can be ascribed to STEC in flour. STEC was also found in flour during routine checks in Germany. The BfR is investigating these kinds of isolates and, in doing so, came across STEC, which is associated with various illnesses. These STECs are currently being analysed in more detail at the BfR and genetically characterised. This should clarify where the STECs in the flour come from and how contamination can be prevented.

More information:
Mäde, D. et al. 2017. Detection and isolation of Shiga-toxin producing Escherichia coli in flour in Germany between 2014 and 2017. J Verbrauch Lebensm 12, 245–253

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© Dewald Kirsten/shutterstock.com

Targeting adulterated feed

Feed fat contaminated with dioxins in Belgium in 1999 and in Germany in 2010; simulated high feed quality by addition of melamine in China in 2007: manipulated feed can have potentially harmful consequences for the health within the food chain. Detecting adulterations is therefore all the more important. Non-targeted analytical methods are suitable for detecting unknown additives that may be harmful to health. In this context, a team from the BfR department "Safety in the Food Chain" is working on a project establishing the conditions for a database. It is founded on data describing the "normal" composition of feed using spectral information. In case of an incident, this reference data can be used to identify anomalies and possible entry pathways for adulterations or contaminations. The goal is an expandable instrument for the German federal states' ("Laender") monitoring authorities to determine possible risks.

Forests, game and parasites

Game meat is becoming more and more popular. Few people know that it could also contain parasites. The BfR is investigating the spread of pathogens in roe deer, red deer and wild boar.

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Game studies are a core research area at the BfR Study Centre “Land Use-Related Assessment Methods and One Health Concepts (LaBeOH)”. Topics include research on forest, game and bees. Research is primarily being carried out in federal forest areas. The BfR frequently uses samples of game meat taken during the respective hunting seasons; it also investigates other contaminants and plant protection products in addition to studies on the occurrence of parasites.

It is six in the morning at a hunting ground in Brandenburg; it is dark and cold. Wrapped up warm, BfR scientist Kaya Stollberg listens to the hunt leader's instructions. She is surrounded by 15 hunters who are about to go to work. They hunt to maintain the grounds. Stollberg, in a safety vest so she can be spotted easily, walks through the bushes with the others, noisily, in order to startle wild boar, roe and red deer. It is clearly defined when the first and last shot can be fired. The trained vet has brought along transport boxes and test tubes, which she will later fill with samples of the hunted game. In the afternoon, when the mort sounds from the hunters' horns, signal for the end of the hunt, she and her colleagues drive to the BfR laboratory and prepare the collected samples for testing. The lab team is looking for parasites.

The BfR is investigating parasites' prevalence

Roe deer, wild boar and red deer can carry parasites, such as *Toxoplasma*, *Alaria alata*, *Trichinella* or *Sarcocystis*. The problem is that although game meat is not frequently consumed, it is still a popular delicacy, especially over the Christmas period. If however the meat contains parasites that have not been killed during cooking, they can be transmitted to humans and make them ill.

The BfR is working on a research project to increase our understanding about the occurrence of parasites in game meat and their respective health risks to humans. "Up to now, the search for parasites in game has not been very systematic. We are now looking in more detail," says Dr. Martin Richter. The pharmacist heads the "Diagnostics, Pathogen Characterisation, Parasites in Food" unit at the BfR. The planned game studies allow for a long term assessment of parasite prevalence. "Since we always sample the same areas, we can determine whether the animals have been infected with potentially disease-causing pathogens to a greater or lesser extent over the years." A comparison with climate data also makes it possible to assess the extent to which a rainy year or a dry summer influences animals contracting a parasite. The more data collected and evaluated over the years, the easier it is to assess the potential health risks associated with consuming game meat or food made from it.

Toxoplasma and *Alaria alata* in game

Preliminary results from Martin Richter's laboratory show that around 25 percent of wild boar, 16 percent of roe deer and 4 percent of red deer carry antibodies against *Toxoplasma gondii*, the pathogen that causes toxoplasmosis. Another parasite found in wild boar tested in the BfR laboratory is *Alaria alata* – or more precisely a certain development stage of this trematode which occasionally occurs as an incidental finding when investigating meat for *Trichinella* infestation, which is mandatory also in wild boar. Whether this parasite can make people sick has not yet been clarified. However, the related species *Alaria americana*, has been reported to have caused severe disease in isolated cases but this particular species has not yet been detected in Europe. As a precaution, Switzerland has classified *Alaria alata* already as a zoonotic pathogen. Richter's laboratory team is developing new methods to extend the spectrum of methods on how these pathogens can be detected reliably. Further, the aim is to contribute to identifying more effectively which health risks these parasites pose to humans in particular.

It is now Kaya Stollberg's second hunting season collecting samples in the team. In addition to monitoring parasites, the BfR uses these samples for numerous other research projects (see box). Since parasite occurrence often varies from region to region, more areas in Germany will be included in these studies in the future. ◘


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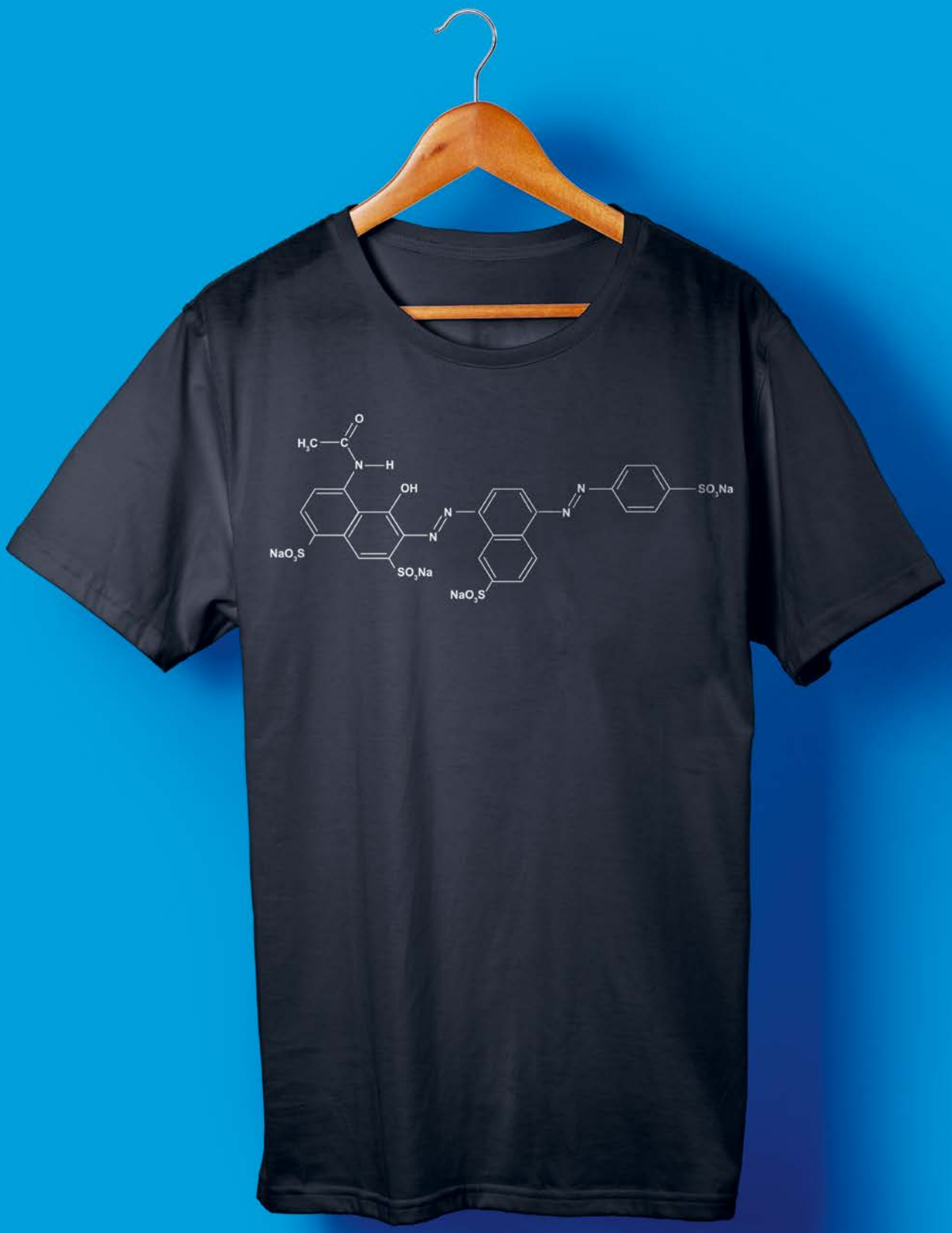
How can I protect myself?

The following applies to all game meat connoisseurs who want to apply precautionary measures to protect themselves from parasitic diseases. These measures are particularly relevant for consumers with a weakened immune system: game meat, raw sausages and products made from game, such as smoked ham, should only be consumed if thoroughly cooked – minimum requirement: cooked for at least two minutes at 72° Celsius core temperature.

More information:
BfR Opinion No. 045/2018 of 21 December 2018



Up close 24/7: Textiles

Textiles are our second skin: we sleep and dress in them. We are in contact with them 24 hours a day, seven days a week. They therefore ought to be safe. A new regulation now lays down limit values for certain chemicals in textiles.

Clothes should protect us from the cold and heat and shelter us from view. We like them to be soft, comfortable and want them to keep their shape. We also want them to look chic, with different colours, materials and functions. Just how this is achieved is something to which we give less thought. Whether made of cotton, wool or polyester; when we buy something, it is not clear which chemical substances are contained in the fabric. Manufacturers have to name the textile fibres. Labelling all substances used in a bed sheet, towel or jumper is not required by law.

Textiles contain chemicals

Shirts in bright, trendy colours, crease-resistant trousers, waterproof outdoor jackets, sportswear that does not smell of sweat; for the fashion world to be able to offer all this, it needs colouring, finishing and auxiliary agents for textile production (see overview). "Manufacturing clothing textiles without chemicals is not possible," says Dr. Ralph Pirow. The biologist works on textile safety at the BfR. "This makes it all the more important to restrict the use of substances of concern and try to replace them." This particularly applies to substances that are carcinogenic, mutagenic or toxic for reproduction, meaning causing cancer, altering the genetic material, impairing fertility or endangering pregnancy. They are referred to as CMR substances.

New limit values for certain CMR substances

There are no uniform and comprehensive legal regulations for clothing textiles. In Germany, they are subject to the Food, Feed and Consumer Goods Code (LFGB) as consumer goods. This prohibits the manufacture or treatment of consumer goods in a way that may be harmful to health. In addition, there are individual legal provisions that regulate the use of certain chemicals for textile and leather consumer goods. These are laid down, for example, in the European Regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), which has been in force since 2007.

The regulation made it possible to set limit values for 33 CMR substances at the same time. The BfR, together with other EU member states, contributed

Limited CMR substances in textiles starting in 2020

- chlorinated aromatic hydrocarbons (solvents for disperse dyes)
- certain phthalates (softening agents for plastics such as PVC)
- formaldehyde (basic material for synthetic resins for crease-resistant and non-iron finishing)
- polycyclic aromatic hydrocarbons (impurities in e.g. spinning, twisting and knitting oils used in production)
- heavy metal compounds with cadmium, chromium (VI), arsenic, lead (i.a. in colourants, as stabilizers in plastics)
- polar aprotic solvents (for spinning synthetic fibres)
- the dyes Disperse Blue 1, Basic Red 9 and Basic Violet 3
- certain aromatic amines and quinoline (including residues from dye production)

Chemicals in textiles

Dyes	They are the most common chemicals in textiles.
Auxiliary agents	They are required for production and are removed during the production process. However, residues may remain on the textile.
Finishing agents	They are intended to remain on the textile to impart a certain property during use (e.g. water repellency, UV protection, crease resistance).
Biocide finishing	This is intended to protect the textile against infestation with insects, ticks, mites (defensive compound, repellent). Other biocides like silver have an antimicrobial effect and therefore counteract odours through the microbial decomposition of sweat.

to this. "We reviewed and commented on a list of 286 CMR substances from the EU Commission: Are the substances used in textiles? Are there any methods to analyse them?" says Pirow. "Afterwards the proposals of all member states and the expert opinions of professional associations and testing institutes were discussed with the EU Commission and in 2018 the Regulation (EU) 2018/1513 was issued." This means that the use of these CMR substances in clothing, sportswear, bags and shoes will be restricted from November 2020. "For most of these substances, the limit values are so low that they amount to a de facto ban on use," says Pirow. The limit values also apply to imported textiles from third countries that do not belong to the EU.

Black box colourants

In terms of health risks, colourants are the most significant substances in textiles. "Of around 4,000 existing dyes, half are azo dyes," says Suna Nicolai, who works with Ralph Pirow at the BfR on this group of substances. Some of these compounds can be cleaved into carcinogenic aromatic amines by enzymes from the body's own bacteria on the skin or in the intestine.

The dilemma: "There are hundreds of azo dyes and we don't know which effect they have if they enter the body," explains Nicolai, a biotechnologist. 22 aromatic amines are already listed in REACH. The regulation states that azo dyes that can be cleaved into these aromatic amines may not be used. But what other cleavable azo dyes can be found in textiles?

BfR research project on registered azo dyes

Since 2018, there has been a complete overview of the chemicals used in the EU for the first time in Europe. Only through REACH did manufacturers have to register all chemicals intended for use in the EU with the European Chemicals Agency (ECHA). The final deadline for registering chemicals ended in 2018.

As part of an ongoing research project, the BfR and other project partners are now assessing the relevant azo dyes registered for use in textiles. The aim is to test both the dyes and their cleavage products for their possible mutagenic effects. "We have already identified around 400 dyes and over 500 cleavage products," says Nicolai. However, data is often lacking for a health risk assessment. The next step will be technical discussions held with professional associations and official project partners to collate the available data. "Depending on the data density, a decision will then be made on how to proceed," explains Nicolai. ◘

How can I protect myself?

Wash clothing before first use: this removes residues of releasable chemicals. Instructions such as "wash separately" or "wash with similar colours" indicate that dyes are released during washing and therefore also when worn. Use tested products with a textile seal of quality: these must meet certain requirements, some of which go beyond the statutory regulations.

More information:
www.bfr.bund.de > A-Z-Index: Textiles

New test strategy for mixtures

26 European institutions, including the BfR, have developed a strategy to investigate and assess the health risks of mixtures of multiple chemicals in an EU-funded research project. In addition to pesticides, the focus was on contaminants and potentially harmful ingredients in food. At the successful conclusion of EuroMix in May 2019, the BfR showed that animal experiments for assessing the combined exposure to multiple chemicals can be reduced – by using a new strategy that combines various in-vitro tests. The BfR also analysed the legal basis and assessment approaches, and proposed recommendations for implementing the new testing strategy. Alternative test methods and harmonised procedures should further improve the risk assessment of combined exposure to multiple chemicals.

More information:
www.euromixproject.eu

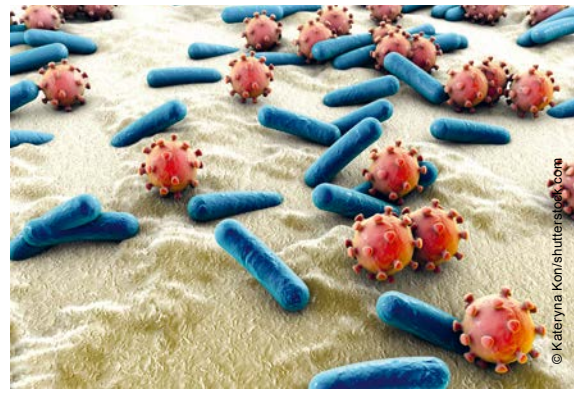
Rotter, S. et al. 2019. Overview on legislation and scientific approaches for risk assessment of combined exposure to multiple chemicals: the potential EuroMix contribution. Crit. Rev. Toxicol. 48: 796–814

Luckert, C. et al. 2018. Adverse outcome pathway-driven analysis of liver steatosis in vitro: a case study with cyproconazole. Chemical Research in Toxicology 31(8): 784–798

When microbes on the skin become toxic

Microbes on the skin influence the toxicity of substances with which people come into contact. This is confirmed by studies with a new co-culture system from the BfR. For the first time, the influence of the skin microbiome on toxic effects of substances on the skin can be analysed directly. Microbes live on all surfaces inside and outside the body and are not normally harmful. Their metabolic diversity is significantly greater than in humans and can lead to the toxification of foreign substances both in the intestines and on the skin, even from consumer-related products. Studies at the BfR have already shown this. Possible health risks from this have so far been inadequately assessed due to a lack of models. Even animal models are only suitable to a limited extent. Initial investigations with the 3D co-culture model developed at the BfR now show a clear influence of the microbiome on the condition, immunology and biology of the skin.

More information:
Tralau, T. et al. 2015. Insights on the human microbiome and its xenobiotic metabolism: what is known about its effects on human physiology? Expert Opin. Drug Metab. Toxicol. 11(3): 411– 425



Under the skin: metal from tattoo needles

Metallic micro- and nanoparticles from tattoo needles can accumulate under the skin and in the lymph nodes. This is the conclusion reached by the BfR and international partners. Tattoo needles are made of steel and therefore also contain nickel and chrome. The research team has determined that metal particles abrade from the needle during the tattooing process – if the tattoo ink contains the white pigment titanium dioxide. Nickel and chromium are released mechanically from the needle and enter the skin. The particles can then migrate into the lymph nodes. Up until now, it has been assumed that mainly colour pigments contaminated with nickel and chromium cause allergies. The study shows that tattoo needles may also pose a health risk. Future studies will investigate whether the additional absorption of nickel and chromium increases the probability of allergies.

More information:
Press release No. 33/2019 by the BfR dated 27 August 2019

There's something in the air ...

We spend a lot of time indoors. We are constantly breathing in substances emitted from carpets, paints, cleaning products, and even decorative items and toys. How much? This was now determined by the BfR for the first time.

Scientist Morgane Even measures volatile organic substances in test chambers of different sizes at the BfR.

Today, people in industrialised western countries spend an average of 80 to 90 percent of their time indoors. Efficient insulation keeps the air inside. The consequence: volatile organic compounds, so-called VOCs, which are emitted from materials, accumulate in the indoor air. These substances are most frequently released by building materials, cleaning agents or by cooking. However, toys and decorative items are also possible sources. The problem is that besides from bad smell, these chemicals can also impair our health. "So far, we don't have sufficient data to estimate the amount of VOCs emitted from consumer products," says Morgane Even from the "Chemicals and Product Safety" department, which is carrying out the relevant tests at the BfR. This complicates the assessment of health risks imposed by VOCs.

Finding a practical method

The aim of Even's research project was therefore to develop analytical methods to measure the release of volatile chemicals from everyday consumer goods. "The new processes are based on methods that are usually applied to measure emissions from building materials but which had to be adapted to test consumer products," says Even.

Emissions are typically determined in closed chambers made of stainless steel or glass – materials that themselves emit or absorb no or only small amounts of volatile compounds. The temperature, humidity and air exchange within the chamber can be varied to simulate the conditions in a real indoor space. Emission chambers come in different sizes: for building materials, they are usually very large-scale; however, smaller ones are needed for measuring rubber ducks, mobile phone covers or designer lamps. The advantage of small chambers is that several samples can be analysed in parallel and that they are lower in cost – important criteria for official control laboratories that intend to use these new analytical methods in the future.

Small test chambers deliver accurate results

But do "micro-chambers" also produce realistic results? Morgane Even has tested different sizes in her research. For this purpose, she placed plastic plates with the same VOC quantities in the chambers for 28 days. The result: emission chambers with a volume of 44 millilitres, 24 or 203 litres give similar results if the ratio of air exchange to loading is kept constant. Her conclusion: "The smaller micro-chambers are an alternative to determine emissions from consumer products."

VOCs escape more easily from soft plastics

In further experiments – this time with real toy samples – Even showed that toys made of soft plastics such as polyvinyl chloride (PVC) or polyethylene (PE) release more volatile substances into the environment than toys made of harder plastics such as polypropylene (PP). Emissions decreased significantly in the first few hours after unpacking, as time-dependent measurements revealed. It would therefore be advisable to ventilate toys outdoors for a while before using them for the first time. Converted to indoor air concentrations, the measured emission values were in all cases well below the existing national and European guideline values for indoor air. However, for multiple toys or in significantly smaller air volumes these values may indeed be exceeded.
"That would be the case in small children's rooms with lots of toys," says Even. But also when children play with toys at close distance, as it is usually the case. ◘

More information:

Even, M. et al. 2019. Emissions of VOCs from polymer-based consumer products: from emission data of real samples to the assessment of inhalation exposure. Front Public Health 7: 202. doi: 10.3389/fpubh.2019.00202

Even, M. et al. 2019. Emissions of volatile organic compounds from polymer-based consumer products: comparison of three emission chamber sizes. Indoor Air. 00: 1-9. https://doi.org/10.1111/ina.12605

The blue miracle from Bordeaux

Copper compounds combat fungal infestation in agriculture – however, they are not harmless to health.

Botanist Pierre Millardet was a perceptive man. Riding through the vineyards of St. Julien in Bordeaux in October 1882, he was confronted with the sad sight of paltry vines covered in powdery mildew. With one exception: on a plot of land along the road, magnificent leaves and grapes were found. However, the plants were covered with blue powder. The winegrower told Millardet that he had dyed the wine on the street to keep thieves away thanks to the colour and the unpleasant taste. He had accidentally discovered a substance that also kept fungi away. Millardet seized upon the idea and developed the "Bordeaux mixture". The mixture of slaked lime and copper sulphate was the first successful fungicide.

Back to the present. Millardet's Bordeaux mixture and other copper compounds are still in great demand as plant protection products against fungal and bacterial infestation in viticulture, arable farming (e.g. potatoes), vegetable farming (such as tomatoes) and floriculture. Copper is also used in biocidal products against algae, snails and crabs. It is toxic to microorganisms even in small quantities. Copper blocks essential protein molecules, inhibits photosynthesis (energy production from light) in algae and plants, causing cell damage and making cell envelopes permeable.

In Germany, copper compounds are mainly used in fungicides for hops, wine, fruit and potatoes. Copper is indispensable, especially in organic farming. While farmers in integrated and conventional farming can rely on all approved plant protection products, this is not possible in organic farming due to the regulations. Some people may be surprised to learn that there is also "chemical-free" agriculture – using the heavy metal copper, of all things. The reason given for this is that copper is a "natural substance"; it is not an artificial product developed by mankind.

The two faces of a heavy metal

Natural, yes. But harmless? Copper has two faces. As a trace element, it is essential. On the other hand, too much copper can be dangerous. High doses can lead to liver damage. "The kidneys and the blood formation process are also impaired," reports Dr. Jens Schubert, a copper expert at the BfR who is responsible for the health risk assessment of copper as a plant protection product. It is also being discussed whether the heavy metal used as a pesticide causes antimicrobial resistance. Furthermore, copper compounds accumulate in the soil and can damage soil organisms. Since pure copper is an element, it cannot be broken down.

According to the EU chemicals regulation REACH, a substance is deemed to be concerning if it fulfils the PBT criteria. PBT stands for persistent (non-degradable), bioaccumulative (accumulates in the organism) and toxic (poisonous). Copper compounds such as the "Bordeaux mixture" are persistent and toxic. It is therefore a stated long-term goal to replace them with more harmless substances. Copper is a "substitution candidate" for plant protection in the EU. The Federal Government also presented a strategy for phasing out copper as early as 1998.

"Phasing out" postponed for now

Organic farmers were therefore eagerly looking to Brussels in 2018. The question was whether the approval of the "substitution candidate" should be extended. The decision was made at the end of the year: copper compounds were approved by the EU Commission for use in plant protection products for a further period of seven years. During this period, farms may apply a maximum of 28 kilograms of pure copper per hectare.

Humans ingest copper via food and drinking water. Nuts, cocoa and animal liver are rich in copper. An adult needs one milligram (mg) daily and about 2 mg are supplied. Up to 10 mg a day is safe; prolonged exposure to 30 mg or more is harmful to our health.

"At the moment we do not see any unacceptable health risk to the general population," says Jens Schubert. "However, we don't have much headroom; it is possible to exceed the beneficial maximum values." This applies, for example, to farmers who use copper. The BfR is now working on an overall assessment of copper from the point of view of consumer health protection. Not an easy task, not least because the metal enters the human body via very different paths – not only via the blue grapes of Bordeaux.

Insights into the worm

The roundworm *C. elegans* is transparent and tiny. In the wild, it lives in compost. In the laboratory, it might help to replace elaborate animal experiments.

If you hold the Petri dish against the light, you can see it. Just. Tiny, whitish commas. Wispy fluff, a little longer than a millimetre. But this dust is alive. On closer inspection, we can see what is wriggling around: roundworms. Nematodes. They belong to the species *Caenorhabditis elegans*, *C. elegans* for short. In the laboratories at the German Centre for the Protection of Laboratory Animals in Berlin-Marienfelde they are being researched to find further alternative tests to conventional animal experiments. The centre is part of the BfR.

"The cool thing about the worms is that they are completely transparent," says project leader Dr. Silvia Vogl. A doctoral student puts a few worms under the microscope. Looking at the creatures twitching under the lens, you can immediately see what Silvia Vogl means. The elegant worm is fascinating. Its entire anatomy is visible, as if under an X-ray screen. The animal essentially consists of an intestinal tube that moves through its small world, such as compost heaps or decaying leaves, slurping bacteria. Its elongated body is filled with eggs at various stages of maturation. They are lined up like a string of pearls. The worm has 300 offspring in its three-week life span.

The principle of self-fertilisation

C. elegans conveniently self-fertilises its eggs. The worm is a hermaphrodite, a male-female hybrid. There are also pure males, but they are rare and make up only 0.2 percent of the population. It is actually "more an accident when they occur," says Dr. Vogl with a smile. They are still important because sexual reproduction "refreshes" the worm's genetic material and protects it from demise. Lungs, kidneys, liver, heart, eyes? Nothing. *C. elegans* doesn't need any of that. It has exactly 959 cells (the male 1031) and each one of these cells followed a predetermined development plan. Transparent, frugal, harmless, rapidly reproducing, inexpensive to keep, good to study – there are many reasons why the roundworm became the most widely researched multicellular organism. And also the first whose complete genome was deciphered in 1998.

And there's more. The worm casts a spell over scientists and never lets them go. "*C. elegans* researchers make up an international community," says Dr. Vogl. They meet every two years for the international conference. Almost all information needed for breeding is available online free of charge in the "WormBook". Innovative solutions to some worm problems are often published in the "Worm Breeder's Gazette". There is a bit of a wink, the research, however, is to be taken very seriously: to date, six scientists have received Nobel Prizes for their work with *C. elegans*.

The road to becoming the "model organism"

One of the Nobel laureates was British biologist Sidney Brenner. At the beginning of the 1960s, Brenner was looking for the simplest possible multicellular organism to study its development down to the smallest detail. He found what he was looking for in *C. elegans*. He began to study the animal in December 1963. Since then,

> **The roundworm can help to investigate the effects of chemicals**

developmental biology, genetics, neuroscience and cell research have learned from and with *C. elegans*. The worm became a "model organism".

The well-connected and diverse scene of *C. elegans* research makes it easy for Silvia Vogl and her colleague Dr. Paul Wittkowski to work with the exact variant of the animal that they need for their questions. The approach of using roundworms to investigate the effect of potentially toxic substances is still new. Toxicology, the "science of poisons" – has so far found it somewhat difficult to accept *C. elegans* as a test animal.

Understanding exactly how a toxic substance works

Toxicologists traditionally work with laboratory animals like rats and mice, which, like humans, are mammals. This procedure is often required by law. But this area is changing. Experiments with cell cultures ("in vitro") or computer calculations ("in silico") complement conventional animal experiments ("in vivo"). Today we want to understand in detail how certain substances affect the organism, the cell or even individual genes. In addition, testing mixtures of substances, such as plant protection products, hormonally active substances or small amounts of toxic substances, poses a particular challenge. And finally, there is the 3Rs principle, which must be adhered to in science.

It describes the goal of reducing the number of animals in experiments ("reduce"), reducing suffering in experiments ("refine") or completely replacing animal experiments ("replace").

Enter *C. elegans*. It does not have all the organs that distinguish mammals. But the worm has far more in common with humans than those outside of the discipline might expect. The nematode has nerve cells, an (albeit simple) digestive tract, muscles and a reproductive system, as well as hormones and behaviour controlled by simple sensory stimuli. "The animal can even learn," says Silvia Vogl. "For example, to favour or avoid certain paths in a labyrinthine environment."

In addition, the genetic make-up of *C. elegans* has many similarities with that of mammals (such as humans). This concerns, for example, genes that are responsible for metabolism, communication between cells and detoxification. A short span between generations and rapid reproduction also help to make experiments faster and simpler than in conventional animal experiments. As a very small organism, *C. elegans* fills a gap between testing cells and experiments with vertebrates.

Fast test, lots of information

The BfR has been working with the roundworm for several years already. Paul Wittkowski developed an automated four-day test for *C. elegans*. This makes it possible to test many chemicals and mixtures of chemicals quickly and comprehensively. Using five different azole fungicides (substances that kill off fungi) as an example, Wittkowski studied how potentially toxic substances influenced growth and fertility of the worm. At the same time, he was able to determine whether residues of the azole fungicides had accumulated in the animal and which genes the substances had activated. Some reactions corresponded to those of mammals. In addition, the working group is testing chemical substances that have hormone-like effects in the body as an undesirable side effect.

In the future, the scientific community hopes that *C. elegans* will help to determine the mechanisms of action of chemicals. This approach may also reduce suffering because certain tests may no longer be necessary in conventional animal experiments. However, Silvia Vogl rules out that "exactly one worm experiment will replace one other animal experiment that is subject to approval". It is a bit more complicated than that. It is, however, conceivable that combining *C. elegans* tests with in vitro and in silico methods will work out. In any case, the worm has a future. ◘

Alternatives to animal experiments: evolution or revolution?

How can alternative methods to conventional animal experiments be further developed to test potentially toxic substances? One possibility is to break new ground in small steps ("evolutionary") and on the basis of previous animal experiments. "Revolutionary", on the other hand, is a second approach that uses the basic processes in the human body as the standard. International experts discussed both approaches in a joint BfR and Dutch National Institute for Public Health and Environment workshop. One result: although new methods still need to be further developed, they could not only help to reduce animal experiments, they will also help to gain deeper insights into the effects of chemical substances on the human body.

More information:
Burgdorf, T. et al. 2019. Workshop on the validation and regulatory acceptance of innovative 3R approaches in regulatory toxicology – Evolution versus revolution. Toxicol In Vitro 59: 1–11

Symposium on research funding

In biomedical research, alternative methods to animal experiments are becoming increasingly important. Various funding programmes aimed at replacing, reducing and refining experiments ("3R principle") are pushing the development and acceptance of alternative methods. To spotlight scientific animal welfare for even more scientists, the German Centre for the Protection of Laboratory Animals at the BfR held a symposium in Berlin in autumn, providing information about nationwide funding options. Best practice projects were presented as well as current strategic challenges in the transfer of knowledge among publishers. The event with 150 participants was supported by: the Federal Ministry of Education and Research, represented by the Project management Jülich, the German Research Foundation, the set Foundation, the Federal State of Baden-Württemberg and the Federal State of Rhineland-Palatinate.

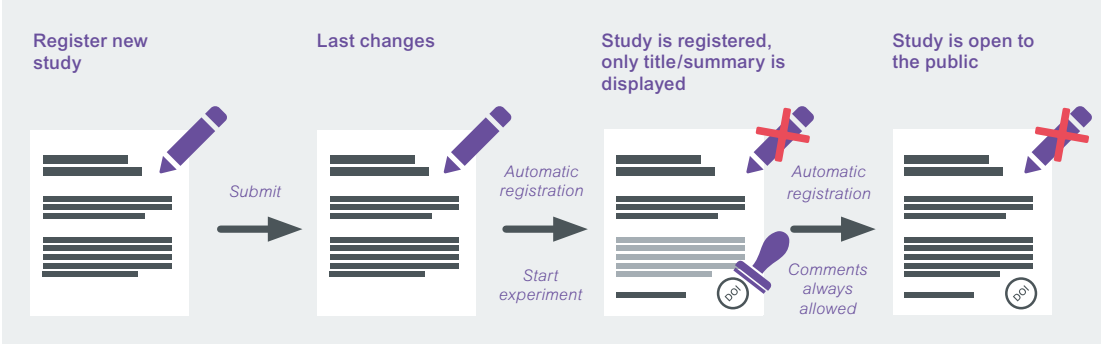
@Bf3R_centre

For more hashtags on the issue of animal welfare: since spring, the German Centre for the Protection of Laboratory Animals at the BfR has been providing information about its activities and innovations in the development of alternative methods to animal experiments via the Twitter account @Bf3R_centre.

More information:
Twitter: @Bf3R_centre

Better for man and mouse

The Animal Study Registry is intended to make science more transparent and to increase the protection of laboratory animals



Studies are the fruits that ripen on the tree of science. But not all of them are palatable. Some are, in their own way, spoiled and covered with mould. Unlike real fruit, however, we cannot tell if a scientific study is good quality at first glance. But the discussion about research quality is in full swing.

The list of shortcomings includes the fact that scientific results often cannot be confirmed. Unwanted results are brushed under the carpet or embellished. One way to improve the situation are study registries – a new one for animal experiments went online at the German Centre for the Protection of Laboratory Animals at the BfR in January 2019.

Entry in the registry helps to organise our thoughts

In the online and worldwide available "Animal Study Registry" (ASR), a researcher can register a planned animal experiment quickly, free of charge and protected by copyright. A form with detailed questions helps sort ideas, develop the study design and choose the right methods and statistical procedures. In order to protect intellectual property, studies can be made inaccessible for up to five years before they are published. "We are happy to support scientists in planning their studies," says Dr. Bettina Bert, the veterinarian responsible for the study registry. "It's not about control; it's about achieving reliable results."

Scientists who register are more credible

The study registry is not only helpful when it comes to the technical details of an experiment; scientists who register their experiment also increase their credibility. "The study is therefore trustworthy and increases in value," says Dr. Céline Heinl, who is in charge of the ASR together with Bettina Bert. Bert and Heinl hope that the ASR will improve the quality of scientific work and, in addition, encourage the publication of supposedly unwelcome results. It is precisely those experiments that do not produce the desired result that may contain important information for others, if they are published. Better and more transparent – i.e. comprehensible – research is one of ASR's goals. The other is the protection of laboratory animals. The two cannot be separated. According to a report about animal experiment registries in "Nature" magazine, it is estimated that between a third and a half of all animal experiments are never published. This "great silence" not only distorts scientific perception, it also means that animals are wasted in experiments.

Animal welfare and good science hand in hand

In contrast, an experiment recorded in the ASR cannot be concealed. Anyone who registers an animal experiment in the ASR commits to animal welfare – also because the subject of animal husbandry plays an important role in the ASR. It is based on guidelines for animal experiments established by the National Centre for the 3Rs (NC3Rs), the British scientific organisation committed to replacing and reducing animal experiments and reducing the stress of the animals upon which experiments are carried out.

Registries for biomedical studies have long been setting a precedent. The largest is the U.S. "Clinicaltrials.gov". It was launched in 2000 and now has more than 300,000 entries for clinical trials. Therefore, studies in which human subjects participate.

No obligation to make an entry

As of yet, the situation has been quite different with animal experiments. Entry in the ASR is voluntary. There is no means of pressure to force registration. Nevertheless: "As a federal institute dealing with animal welfare, we are the right institution to set up this kind of study registry reliably and in the long term," says Bettina Bert.

The task now is to make the scientific community aware of the directory and to convince it of its usefulness. A long road ahead – but not without the prospect of success. The voluntary study register "Open Science Framework" has already recorded more than 30,000 entries since its foundation in 2012. "It is highly regarded by psychologists and social scientists," says Bert. Who says that ASR cannot become just as popular in research that works with animals? ◘

More information:
www.animalstudyregistry.org

Bert B., Heinl C., Chmielewska J., Schwarz F., Grune B., Hensel A., Greiner M., Schönfelder G. (2019) Refining animal research: The Animal Study Registry. PLoS Biol 17(10): e3000463. https://doi.org/10.1371/journal.pbio.3000463

INTERNATIONAL NEWS

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Risk assessment in Latin America
Together with the Uruguayan Ministry of Agriculture, the BfR hosted the first Latin American Risk Assessment Symposium (LARAS) in August. In Montevideo, Uruguay, scientists and political decision-makers both from the region and Europe discussed the assessment and communication of microbiological and chemical risks. The conference provided approaches for developing risk assessment and risk communication in Latin America.

© CAMPY-TRACE consortium

Tracking down *Campylobacter*
Campylobacter is the most common cause of foodborne bacterial diseases. However, existing detection methods are costly and prone to error. For this reason, the German Federal Ministry of Education and Research funded the CAMPY-TRACE project for four years. Together with national and international partners, the BfR developed a detection method for the chicken food chain that distinguishes between dead and living pathogens without cultivation. The method is currently being validated in an international ring trial.

Dialogue with Japanese partners
The scientific exchange with Japanese partner authorities was the focus of the delegation's trip to Japan in July. At the Ministry of Agriculture, the focus was on the safe application of plant protection products. The BfR delegates exchanged views on marine biotoxins at the Japan Food Research Laboratories. The assessment of the toxicity of mixtures of substances was discussed with the Japanese Commission for Food Safety.

Small fish with a big impact
Processed small fish in Ghana, Uganda and Kenya are the focus of the network project "SmallFishFood – Small Fish and Food Security". The project is funded by the German Federal Ministry of Food and Agriculture. The aim is to improve production processes for higher quality and safety as well as longer preservability of the products obtained. As a project partner, the BfR is mainly investigating dried and smoked fish. In the first of three years of the project, samples from Ghana were analysed.

More information:
www.bfr.bund.de/en > Research > Third party projects of the BfR


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Animal health and food safety in Uganda
One Health, human health, animals and the environment in Uganda and Kenya is the focus of the project "BuildUganda", which is directed by the International Livestock Research Institute. The inaugural meeting took place in Uganda in June. Issues in which the BfR is involved include: antimicrobial resistance, food hygiene during the slaughtering process, diseases in goats and sheep. The German Federal Ministry of Economic Cooperation and Development is funding this international project.

INTERNAL AFFAIRS

BfR scientist receives Deutscher Studienpreis
How do the tattoo colour pigments behave in the body? This is the question, important to millions of tattooed people around the world, that BfR scientist Dr. Ines Schreiver asked herself in her dissertation, which earned her a doctoral degree at the Freie Universtität Berlin. Her answer was so good that she received second prize in the Deutscher Studienpreis (German Student Award) for young scientists in the category of natural and technological sciences. The Deutscher Studienpreis is one of the most well-paying prizes for young scientists in the Federal Republic of Germany. It is awarded annually by the Körber Foundation for outstanding dissertations that are of particular societal importance.

More information:
BfR Communication No. 033/2019 of 28 August 2019
www.bfr.bund.de/en/bfr_opinions_2019.html


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BfR Vice President post
Dr. Roland Solecki has been the Vice President of the BfR since 1 October 2019. He took over from Professor Reiner Wittkowski, who retired at the end of September. Solecki will hold this position until 29 February 2020. The official selection procedure for the vice-president post is still ongoing.

EVENT

© BfR (stand at IGW 2019)

International Green Week Berlin 2020
Eating and consuming sustainably is a concern for our society. The BfR is addressing this topic at its stand at International Green Week. From 17 to 26 January 2020, the BfR will provide information on health risks associated with a sustainable approach to food in everyday life: does mouldy food have to be thrown away? How safe are packaging alternatives like bamboo cups? How do ingredients change when food is preserved and fermented? The BfR stand will be located in Hall 3.2, on the grounds of the Erlebnisbauernhof (Event Farm). Open 10 am-6 pm.

More about this and other BfR events:
www.bfr-akademie.de

SUBSCRIPTION:

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Title: Anton Hallmann