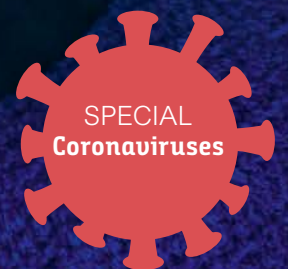


BfR 2 GO

The Science Magazine
of the German Federal Institute for Risk Assessment
Issue 1/2020

E-cigarettes

Mysterious vapour



Milk from the farm

**Raw
is risky**

Organic pesticides

**Not necessarily
harmless**

Biorhythm

**How cells function
properly**

Dear Readers!

The novel coronavirus has made an impact on public life this year in an almost unprecedented way. The pathogen is also an issue at the BfR. The media and concerned citizens have asked whether and how long the virus sticks to food or other goods and is infectious. Considering the pandemic, these are justified fears. One article, therefore, focuses on the question of the risks posed by viruses that are transmitted via food – and the role that coronaviruses play in this.

This issue's main topic is no less up-to-date: e-cigarettes and similar “tobacco surrogates”. Their consumption has increased significantly in recent years and is becoming more and more important as an alternative to the conventional cigarette. It is, therefore, all the more important that BfR scientists clarify how risky “vaping” is.

CRISPR/Cas9 type DNA scissors have a promising future in medicine and nutrition. They allow genetic material to be altered with unprecedented accuracy. But what do consumers think about this revolutionary development in biotechnology? The BfR organised a consumer conference on “genome editing” (the technical term), at which there was lively debate, finished with a joint vote. Read the report in this issue.

I will leave it at that with these three examples. They stand pars pro toto for the diversity and significance of the work of the BfR – and, of course, for the other interesting topics and exciting stories in the magazine.

Someone who helped raise the Institute's profile in a leading position and for many years was Dr. Roland Solecki. Initially as Head of the Pesticides Safety Department and then as Acting Vice President. In his interview, Roland Solecki talks about how the health risk assessment of pesticides has developed and what tasks lie ahead for us. Professor Dr. Tanja Schwerdtle, the new BfR Vice President, is excellently equipped to meet these and other challenges. And not only professionally, as a renowned food chemist, but as a practised runner – 40 kilometres a week! – she also has the proverbial stamina. More in the portrait in the new BfR2GO.

I hope you find this issue a stimulating and exciting read.

Professor Dr. Dr. Andreas Hensel
BfR President





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Dangerous waters

Vibrios are present in coastal waters and river estuaries around the world. Some of these aquatic bacteria can cause diseases such as diarrhoea or wound infections and are also regularly found in German waters. The aim of VibrioNet is to study the biology of vibrios and to investigate possible risks. The BfR coordinated this group of international experts within the framework of a research project funded by the Federal Ministry of Education and Research (BMBF). In the last few years, other international researchers have joined, resulting in the emergence of a scientific “vibrio community”. Research on vibrios is all the more relevant due to the consequences of climate change, as global warming has an impact on seawater temperature and there is a significant increase in vibrio concentrations in water during summer months. Experts predict that the number of infections with pathogenic vibrios will increase through contact with seawater or the consumption of contaminated seafood.

More information (in German):
www.bfr.bund.de > Das Institut
> Referenzlaboratorien > Konsiliarlabor
für Vibrionen

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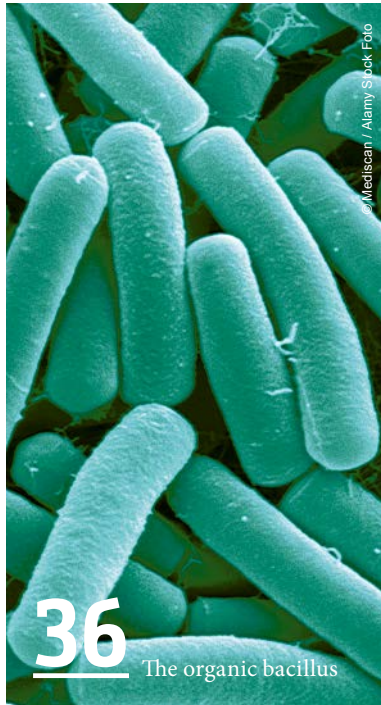
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Research.
Communication.



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Imprint

BfR2GO – Issue 01/2020

Publisher:

German Federal Institute for Risk Assessment (BfR)
Institution under public law

Represented by the President of the BfR,
Professor Dr. Dr. Andreas Hensel
Responsible according to the German Press Law:
Dr. Suzan Fiack

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10589 Berlin, Germany
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Edited by:

BfR Press and Public Relations Unit

Layout, graphics & image editing:

Studio GOOD, Berlin

Printed by:

ARNOLD group, Großbeeren
printed on PEFC-certified paper

Copies printed:

4,000 (German) 1,500 (English)

Print-ISSN 2567-8949

Online-ISSN 2567-8957

DOI 10.17590/20200609-122125

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contact the editors at: publikationen@bfr.bund.de

The opinions of external interviewees expressed in the
BfR2GO interviews reflect their own views.

The BfR science magazine BfR2GO
is published twice a year.

Free subscription:

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SARS-CoV-2 & others

Hunting the invisible

Professor Dr. Reimar Johne evaluates and carries out research on how viruses that cause disease spread via food. The ways in which coronaviruses can be transmitted are also being investigated.



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Reimar Johne takes one of the flasks from the incubator in the laboratory and carefully sways it back and forth. The reddish liquid inside sloshes gently up and down. It is a nutrient solution. “A thin film of human cells infected with hepatitis E viruses is growing at the bottom of the flask,” explains the veterinarian. “But the individual cells are invisible to the naked eye and, of course, the viruses even more so.” The flask does, in fact, appear to be completely clear.

Johne’s task is to make the invisible visible. He specialises in detecting viruses in food. And from those, he looks for unimaginably small pathogens that do not have their own metabolism and always require a host cell in order to replicate. “Detection is difficult because often only a few viruses are found on contaminated food,” says Johne, who carries out his research at the Berlin-Marienfelde site of the BfR.

To begin with, a sample is taken from the material that will be tested; frozen strawberries, for example. This is then processed. The berries are shaken in a special buffer solution (this regulates the acidity level, among other things). In the next steps, the viruses are enriched from the liquid and their genetic material is amplified using the PCR method – a kind of quick copier for genetic information. This method makes it possible to detect even a small number of pathogens.

Coronaviruses in fruit and vegetables?

Of course, the novel coronavirus SARS-CoV-2 has had Johne and his team on tenterhooks since the beginning of the year. Many consumers were concerned that the virus could be transmitted via contaminated food, for example, through fruit from particularly affected regions. “However, this is unlikely,” says Johne. “There is no scientific evidence to support this.”

However, this does not mean that transmission via food is not possible. For example, an infected person could sneeze on an apple, then another person would come into contact with the viruses shortly afterwards by touching it or by eating the apple and then become infected via the mucous membrane of the mouth, nose or eyes. Theoretically possible. But not likely for several reasons.

Like other viruses related to it, SARS-CoV-2 is primarily transmitted via the respiratory tract. It is transmitted via droplets that contain the virus, which mainly pass from those infected to healthy people when they cough or sneeze. It also appears that a smear infection is possible if viruses capable of replication reach the nasal mucous membrane via hands and fingers, for instance by touching door handles, triggering an infection thereafter.

Good hygiene prevents infections

On the other hand, coronaviruses are relatively sensitive (to soap, for example) and do not survive long outside of the host. “Under laboratory conditions, it has been shown that the novel coronavirus remained ‘infectious’ for two to three days at most after heavy contamination of various surfaces. We assume that the virus inactivation is significantly faster under normal conditions”, says Johne. “If you follow basic kitchen hygiene rules and wash fruit and vegetables thoroughly before putting them on the table, then, based on what we currently know, you have nothing to fear”.

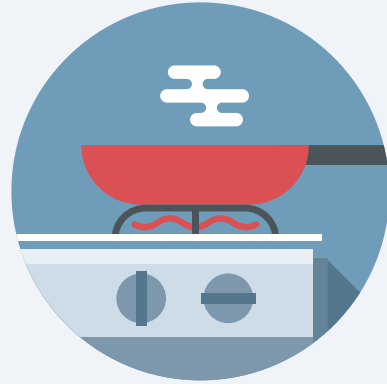
A research project should contribute to closing gaps in knowledge that still exist. In Johne’s laboratory, food chemist Dr. Katja Schilling-Loeffler is investigating whether coronaviruses and other pathogens can be transmitted via drinking glasses after they have been washed by a procedure commonly used in restaurants.



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If we wanted to draw up a “profile” for a typical pathogenic virus in food, in some cases it would be almost the opposite of the novel coronavirus. “A pathogen like this must be very tenacious to survive the attack from stomach acid, for example,” explains Johne. “And it must be stable in the environment – at least until it has found a host in which it can replicate.” Finally – the third characteristic – a few virus units should be sufficient to trigger an infection. This is because pathogens are often found only in small quantities in food.

Diarrhoea: a common consequence

If these characteristics are used as a benchmark, then few viruses remain that can be considered as typical causes of foodborne infections. “We are mainly dealing with noroviruses, rotaviruses and the pathogens that cause hepatitis A and E,” says Johne. Noroviruses and rotaviruses cause gastrointestinal illnesses along with diarrhoea and vomiting, while hepatitis viruses cause inflammation of the liver (“jaundice”).

Foodborne infections caused by the tick-borne encephalitis (TBE) virus are significantly less common. It can lead to severe encephalitis and meningitis. The TBE virus is mostly transmitted by tick bites. However, if goats are infected with the pathogen via ticks, it can pass into the milk and, after consuming raw milk products, trigger the disease in humans. “The example shows that vi-

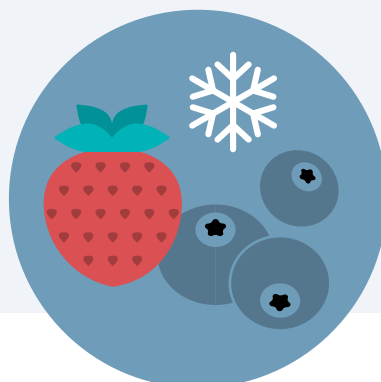
ruses that have actually developed other transmission pathways can, in some cases, also use food to spread,” explains Johne.

Frozen berries are frequently the cause of disease outbreaks. A typical foodborne viral infection can start as early as the harvest. Berries are usually picked by hand and an infected person can contaminate the fruit with noroviruses or hepatitis A viruses. The pathogens then spread throughout the entire harvest when the berries are washed. Or the viruses get onto the berries as soon as the plants are irrigated if contaminated water is used.

Illness caused by few pathogens

Since few viruses are sufficient to trigger a disease, mass infections can be caused in this way. An example of this is the 2012 norovirus epidemic in Germany that resulted in almost 11,000 children and young people becoming ill. The cause were frozen strawberries from China, which had been processed by a caterer. “Almost every package in the shipment contained the virus,” recalls Johne.

The most important measure against these kinds of incidents is good hygiene practice so that the fruit, vegetables or other food do not become contaminated in the first place. Consumers can also be proactive by observing kitchen hygiene rules and, for example, washing fruit



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© BfR

and vegetables thoroughly. “We also recommend heating frozen berries before consumption,” says Johné. “This is because cold doesn’t affect viruses – but heat destroys them.”

The situation is somewhat different with the hepatitis E virus. It does not contaminate food on the outside; it infects pigs and wild boars. The animals do not become ill, but they carry the virus inside them. If food is produced from these infected animals and not heated sufficiently before consumption, this can trigger disease in humans. The same applies to pork: heat it through properly!

A reference laboratory for good quality

Johné and his team’s tasks have again evolved considerably since the end of 2019. The newly created “National Reference Laboratory for Foodborne Viruses” (NRL), headed by Johné, has been established at the BfR (see page 49). The NRL is the link between the equivalent EU reference laboratory in Uppsala (Sweden) and the German federal states (Laender)’s testing laboratories. It aims to make food safe from viruses and reduce infections as far as possible. Its areas of activity include quality assurance of food monitoring authorities with inter-laboratory comparisons (“ring trials”), detecting viruses in food and developing better detection methods.

This also explains the research on hepatitis E viruses in the human cell culture mentioned earlier on. Because until now, it has been very difficult or impossible to replicate this pathogen in cells. However, “virus cultivation” like this would help us to better understand the virus and maybe even make it easier to detect in food. Reimar Johné’s sceptical look at the flask from the incubator reveals that he has not yet quite reached his goal. ■

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There is no scientific evidence to support the transmission of the novel coronavirus via fruit and vegetables.

More information:

Johne, R., E. Trojnar. 2020. The establishment of a new National Reference Laboratory for Foodborne Viruses. *Rundschau für Fleischhygiene und Lebensmittelüberwachung* 4: 130–132. [Article in German]

www.bfr.bund.de/en > A-Z index: COVID-19/corona



E-CIGARETTES



Mysterious vapour

E-cigarettes are considered by many users to be modern, cool, and less harmful to health in comparison to tobacco cigarettes. Their basic principle: vaporising the ingredients instead of burning them. The BfR has investigated this alternative to smoking. The result: e-cigarettes are not without harm.



“

We simulate human vaping behaviour using a smoking machine.

The machine hums and bubbles as it sucks in air. Nadja Mallock stands in front of the box with four holders. The scientist has put an e-cigarette, shaped like a very long USB stick, in one of them. The smoking machine draws vapour from the device using a pump. 55 millilitres in three seconds, over and over. Mallock is interested in its constituents. The vapour is formed when the filling in the e-cigarette, the liquid, is heated to around 200 degrees Celsius. The substance vaporises, then passes through a glass fibre filter in the holder, followed by a liquid. “We simulate human vaping behaviour,” says Mallock. “This allows us to study the amount of vapour, problematic substances and nicotine release.”

The pharmacist has been researching tobacco products for her doctoral thesis at the BfR for three years, which is why she is also taking a close look at e-cigarettes. There are many varieties available on the market (see illustration on page 13). Most models consist of a heating element and cartridge. E-cigarettes in the “sub ohm” category are conspicuously large. They have a larger battery and the resistance of the heating coil is low. This increases the power flow. The devices are more powerful and, therefore, emit more vapour, which is inhaled directly from the device into the lungs. The temperature is adjustable between 150 and 350 degrees Celsius. Most recently, Nadja Mallock investigated pod devices in the laboratory – a plug-and-play system. In this system, the heating coil and liquid are in a closed capsule, which is placed on the battery and thrown away after use. She has also researched another alternative to tobacco cigarettes, called “Heat not Burn”. These devices do not burn the tobacco directly; they heat it.

Long-term effects are unknown

Dr. Harald Tschiche, who also works on electronic cigarettes at the BfR, says: “The health risk posed by an e-cigarette is less than that posed by a conventional cigarette when used as intended.” The reasons for this: there are fewer carcinogenic substances produced than with a cigarette, which burns at up to 900 degrees Celsius. However: “Assessing the health risk of e-cigarettes in general is difficult when faced with the variety of models and liquids,” says Tschiche. “For example, the consumer inhales far more vapour with a ‘sub ohm’ model than with other devices.” In addition, the substances may decompose more at higher temperatures. This may result in more substances that are harmful to health being produced, and these get directly into the lungs.

Science is focusing on the liquid in order to further understand the health risks to which people are exposed when vaping. The liquid consists of propylene glycol and glycerine; both are vaporising agents that, when heated, produce the vapour that is also used in fog machines. Fragrances, flavouring substances and nicotine are added. For Tschiche, the components are anything but harmless. “Many of the substances used in e-cigarettes have not been sufficiently investigated.” The chemist mentions the vaporising agents, which are harmless when used for a short time, as examples. Nobody knows how they might affect health when inhaled over a long period of time. Vaporisation produces substances such as acrolein, acetaldehyde or the carcinogenic formaldehyde. Besides this, nicotine in e-cigarettes is also harmful to health and is addictive.

Vitamins and caffeine are prohibited

In Germany, e-cigarettes containing nicotine are subject to the Tobacco Products Regulation, which is based on the EU Tobacco Products Directive. It allows manufacturers to add a maximum of 20 milligrams per millilitre of nicotine to the liquids. Carcinogenic substances as well as additives that pretend to have a health benefit or a stimulating effect are prohibited. Examples of these include vitamins and caffeine. In addition, the packaging must contain information on the ingredients. “The tobacco law is designed to protect consumers,” sums up Tschiche. He therefore criticises nicotine-free liquids, which are only subject to the Product Safety Regulation and the Chemicals Regulation. In comparison, these regulations are far less strict. Here too, manufacturers are obliged to use flavouring and aromatic substances that are not harmful to health. But: often it has not been investigated which influence these substances have on health when they are inhaled once vaporised. Furthermore, the ingredients contained in these liquids, which are also called e-shishas because of their flavours, do not have to be specified.

A problem arises when liquids contain undeclared substances or impurities, such as heavy metals. “Liquids that are not subject to European legislation can be bought worldwide via the internet,” warns Tschiche. In contrast, fillings and components for liquids sold in Germany are checked randomly by the state laboratories.



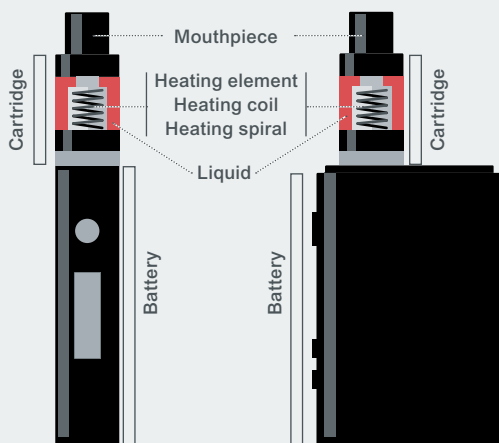
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Cases of poisoning

The BfR and the Society for Clinical Toxicology have evaluated enquiries about e-cigarettes at German poison control centres. Of the 851 poisonings and suspected cases recorded in their “PiMont” study (Pilot Project to establish a national Monitoring of Poisonings), 82 percent related to the accidental ingestion of liquids. These often contained nicotine, which, if swallowed, led to health problems and, in larger quantities, is life-threatening. Small children were often affected. Eight percent of all recorded cases of poisoning or cases of suspected poisoning were due to inhaled vapour from e-cigarettes.

The composition of standard e-cigarettes

There are two models of e-cigarettes, which are comparable in their composition. The model on the right, due to a more powerful battery, emits more vapour, which is inhaled directly into the lungs.



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Shaped like a long USB stick: how much vapour forms from different e-cigarettes? The devices are weighed in the lab in order to find out.



Shaken and checked: the vapour's components are extracted from the smoking machine's filter pad and then analysed.

Fatalities in the USA

It is possible to use self-mixed liquids in e-cigarettes with a fillable tank. Tschiche sees a danger with these open systems: "In principle, any fluid can be mixed into the liquid." This invites misuse, in other words, adding unauthorised or illegal substances.

The BfR advises against self-mixing e-liquids. This applies especially if consumers do not possess sufficient knowledge and experience. DIY mixing, for example, involves the risk of mineral and vegetable oils being used. Liquids should never contain fatty oils, which may lead to serious respiratory disorders if inhaled. Numerous cases of poisoning in the USA may be ascribed to this. By mid-February this year, at least 68 people who had used e-cigarettes were killed and more than 2,700 people were hospitalised. According to the US health agency, the CDC, the poisonings are related to liquids that often contained cannabis oil. They were probably laced with the diluting agent vitamin E-acetate, an oil produced from vitamin E. According to the CDC, initial indications suggest that this substance could be responsible for the lung diseases. There are no known fatalities in Germany. This may be attributed to EU legislation that bans vitamins in liquids.

Vapour is separated into its individual components

In the laboratory, Nadja Mallock opens the smoking machine and takes the filter out of the holder that held the e-cigarette before. Nicotine has stained the once white filter pad slightly yellow as the vapour was drawn through the apparatus. On its journey, remaining substances were collected in impingers, special containers holding a liquid. The scientist injects the samples into different chromatographs in order to be able to examine the traces. The devices separate the components, ultimately revealing the contents of the vapour.

The BfR has been looking at e-cigarettes since 2008, and the work will continue. The technology is changing quickly, as is user behaviour. New models are continually coming onto the market and little is known about their health risks. Therefore, there is great interest in the work of the BfR. Nadja Mallock is certain: "This field of research is becoming more and more interesting." ■

More information:
www.bfr.bund.de/en > A-Z index: electronic cigarette



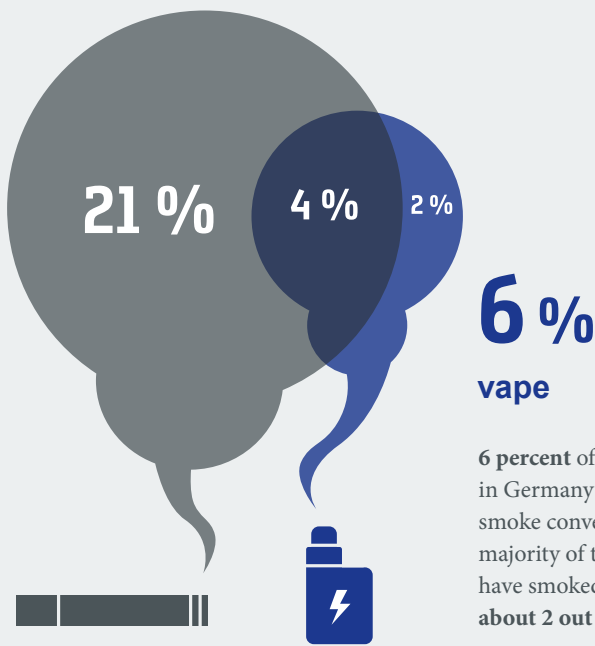
E-cigarettes & Sars-CoV-2 virus?

Infected people can transmit coronaviruses to the mouthpiece while vaping, where these can survive for a certain period. An indirect contact infection of another person is possible if the virus reaches the mucous membranes of the oral cavity. To minimise this risk, e-cigarettes should not be shared with others.

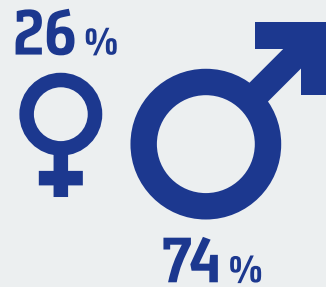
More information:
www.bfr.bund.de/en > A-Z index: COVID-19/corona

Vapour is in the air

A BfR survey shows how widespread e-cigarettes are in the population living in Germany and what they think about the associated health risks.

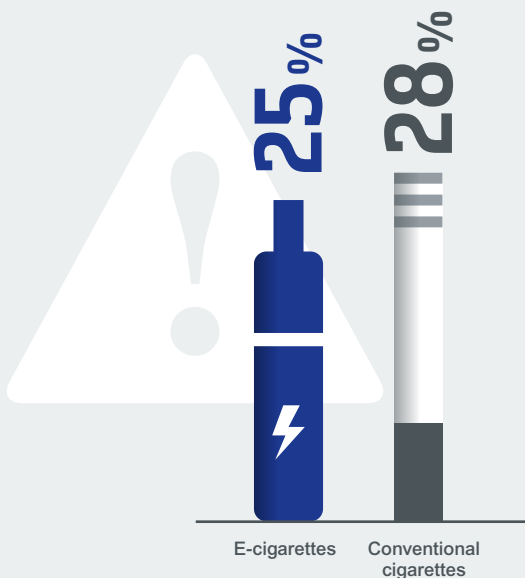


6 percent of the population living in Germany vape; a **quarter (25%)** smoke conventional cigarettes. The majority of those who vape (**90%**) have smoked cigarettes before; **about 2 out of 3** use both.

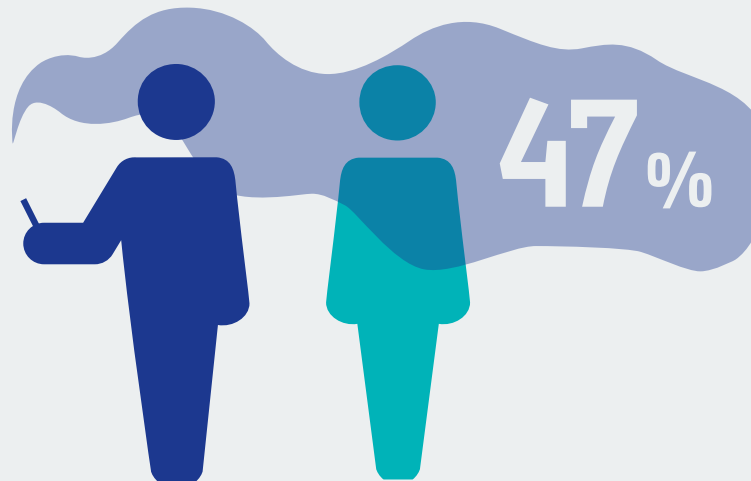


Noteworthy: more men than women vape (74% m, 26% f). The gender ratio among smokers is almost balanced (54 % m, 46 % f).

Higher health risks?



The majority of respondents agree that using e-cigarettes poses potential health risks, particularly effects on the lungs and cancer. Opinions differ, however, when it comes to which of the two products poses greater health risks: 25 percent classify the e-cigarette and 28 percent the conventional cigarette as more risky.



Risks through second-hand vaping

Almost half of the respondents (47%) see potential health risks caused by passive vaping. As many as 30 percent do not expect any risks for bystanders.

Underlying study:
 Representative telephone survey of 1,006 people (German-speaking population in Germany aged 14 and above) in December 2019

More information:
www.bfr.bund.de/en > Publications > Brochures > BfR Consumer Monitor > BfR 2019 Consumer Monitor, Special E-cigarettes



“Young people are experimenting with e-cigarettes”

Dr. Elke Pieper assesses the health risk of e-cigarette ingredients at the BfR and supervises related research work. In an interview, the chemist talks about passive smoking, the fascination of technology and the cases of poisoning in the USA.

Ms. Pieper, according to what we currently know, there are fewer harmful substances in e-cigarette vapour than in cigarette smoke. Is passive smoking harmless?

The liquid, meaning the fluid that is vaporised by e-cigarettes, contains nebulising agents, flavouring substances and often nicotine. The latter is notoriously harmful to health. If the substances are vaporised, aldehydes, including the carcinogenic formaldehyde, arise. The health risks of these substances can also affect passive smokers. We recommend using e-cigarettes in an open environment only and not in public buildings or non-smoking areas. Even if the exposure is reduced in comparison to tobacco cigarettes and an e-cigarette cannot glow, the vapour emitted contains significantly more problematic substances than the normal ambient air.

Do e-cigarettes have any benefits for people who want to quit smoking?

Switching to e-cigarettes is not quitting, of course. However, e-cigarettes may be an alternative for people who find it hard to quit smoking – even if they are not approved for smoking cessation. E-cigarettes do not force people to change their usual smoking behaviour. At the same time, these consumers inhale fewer problematic substances than before, although still significantly more than non-smokers.

E-cigarettes are advertised as a lifestyle product. This has led to criticism that young people are tempted to vape and that they later switch to tobacco cigarettes because they are addicted to nicotine. Is this a realistic assumption?

There are no studies supporting this scenario for Germany. Most vapers used to smoke cigarettes. The number of non-smokers who start using electronic cigarettes is very small. There is also no evidence that they eventually switch to tobacco cigarettes. One thing is certain: young people experiment with e-cigarettes; they test them as a technical device. They try out what it is like to vape. And most of the time they leave it at that. The number of young vapers has increased in the last few years. The increase in Germany is much lower than in the USA.

A team in the Product Research and Nanotechnology Unit at the BfR is researching the health risks of smoking alternatives such as e-cigarettes, heat-not-burn tobacco products and e-shishas. Elke Pieper is one of them.

In the United States, there is already talk of a “vaping epidemic” in schools and of a new generation of nicotine addicts. What is going on there?

An e-cigarette manufacturer in the USA ran an advertising campaign that was very much aimed at young people. Competitions ran on social media, for example. As a result, around a quarter of high school students regularly vape – half of them use the brand that was specifically advertised. This product is easy to use and contains comparatively high levels of nicotine.

“

The number of young vapers has increased in the last few years. The increase in Germany is much lower than in the USA.

Which aspects of e-cigarettes are currently being researched at the BfR?

One core research area deals with e-cigarette models that are popular with young people, especially the “pod” devices. We are investigating how much nicotine the liquids contain and how much of it is found in the vapour. The latter is crucial. We also looked at “sub ohm” devices, where power and temperature can be regulated. These investigations will determine the concentration of potentially harmful substances at specific settings.

What will the BfR be investigating in the near future?

An analysis of how the individual components of liquids affect lung cells is planned. Liquids often contain food flavourings that were never intended to be used in e-cigarettes. Little is known about how flavouring substances can influence our health when they are inhaled. We also want to investigate the impact of vitamin E acetate on lung cells. This substance is supposed to be responsible for numerous cases of poisoning in the USA. ■



Revolution in the gene laboratory: what do citizens demand?

Targeted gene alteration is becoming easier with new methods in biotechnology. What does the population think? The BfR has made it possible for consumers to vote on this.

Heat-resistant wheat, gene therapy against hereditary diseases, the body's own cancer defence genes. All of this could come true with the help of novel DNA scissors. Genome editing is the technical term for precisely cutting out and replacing individual gene sequences/hereditary molecules (DNA). Customised editing of genetic material has been practised for several years. "But only 14 percent of the population are familiar with the new technology," explains private lecturer Dr. Gaby-Fleur Böl, Head of the Risk Communication Department at the BfR. This was shown by the biannual BfR surveys on consumer topics. "In a democracy, revolutionary technological methods that raise ethical and socio-political questions should be publicly discussed and public participation should be facilitated." In order to achieve this dialogue, the BfR utilises and explores the approach of consumer conferences.

BfR consumer conference on genome editing

The BfR wanted to know: what do consumers think about the use of DNA scissors to alter the genome of plants, animals and humans? This was debated by 20 randomly selected men and women, sometimes heatedly but mostly objectively, at the BfR consumer conference on the application of genome editing in nutrition and human health. The conference was held over the course of three weekends in Berlin in 2019; two were used for preparation, and on the third, everyone came together for the final meeting with an expert hearing,

the drafting of the consumer vote and the vote's public presentation. "Consumer conferences are an instrument for making the opinions of the population visible and for taking them into account in political decisions," explains Dr. Leonie Dendler, who is providing scientific support for the project at the BfR and is conducting research into how scientific institutions can make the best use of regular participation procedures. Consumer conferences focus on the discourse on benefits and risks and not the representativeness of opinions.

Genome editing: from breeding to design

People have always influenced the genetic blueprint through breeding, initially through selection. Starting in the 1970s, genetic engineering made it possible to transfer entire hereditary factors (genes). Modern procedures can alter the individual genetic material (genome). To do this, the hereditary molecule DNA is cut through to remove or add genes. This edits the genetic material – hence the term "genome editing". The most well-known method is CRISPR/Cas9, which was developed by microbiologist Emmanuelle Charpentier from the Max Planck Unit for the Science of Pathogens.

What is a consumer conference?

This is a moderated method of direct citizen participation in contentious public issues. It captures a differentiated – but not representative – opinion of citizens. This aims to make the diversity of opinion in a society more visible and incorporate it into the socio-political decision-making process. The result is a vote that is presented to decision-makers. This method is particularly useful for topics with low levels of public awareness. In 2006, the BfR held a consumer conference on nanotechnology. The concept is based on the model of so-called “consensus conferences” originating from Denmark.

Recruiting citizens

The BfR used posters, social media and radio to find citizens all over Germany for the consumer conference. 147 people applied. Socio-demographically similar profiles were identified to allow for the selection of a heterogeneous group: by age group, gender and professional status. “From these groups, 10 women and 10 men were selected at random to include many different opinions, thought-provoking impulses, socio-political demands as well as hopes and fears,” says Head of BfR Communications Böl. Each participant received a reimbursement of 500 euros.

Information-based discussions

To ensure that the consumer group take an information-based approach to the topic, an external communications agency led the consumer conference. The BfR did not take part in the moderation, discussion and drafting of the vote and in fact only organised the process: researching specialist texts on genome editing, requesting expert participation and inviting politicians, representatives from the industry and the public to present the vote at the Federal Press Conference building as well as transmission via the internet. A scientific advisory board with experts in the fields of technology assessment, social science and risk management ensured that information was balanced.

The consumer vote

The consumer vote is a mirror of society. From the outset, it is highlighted that “as the consumer group was made up of a diverse range of people, the views

expressed are accordingly heterogeneous”. The vote describes the opportunities and risks of genome editing in general and for humans, animals and plants in four chapters. Each chapter contains specific demands and policy guidelines. “The result is really fascinating,” says Dr. Emilia Böhm, who as Scientific Officer at the BfR was responsible for executing the project, “as it contains very specific legislative proposals and demands as well as laying out guiding principles for a value-based societal handling of the technology. For example, the vote states: “It is important that no new technology obfuscates or thwarts the necessity for society to become more sustainable.” In the vote the consumer group suggests that if there are diverging opinions, not the technology but the final product should be assessed.

What happens with the vote?

The vote was presented to representatives from politics, science, industry and consumer associations. In its accompanying scientific research, the BfR is evaluating the societal response to the vote and investigating how the participatory dialogue with the population can be improved and how success can be measured. In a before-and-after survey on participants’ attitudes to genome editing, it is also being investigated whether an intensive exchange on a topic can change attitudes. These are important findings for improving the risk communication of the BfR, which contributes to political decision-making. A follow-up meeting with the consumer group is scheduled for 2021. ■

More information:
www.bfr.bund.de/en > A-Z index: genome editing



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20 people, 3 weekends and a 15-page vote – the conference procedure

20 people, strangers until then, meet for the first time at a venue in Brandenburg over a meal – the start of the **first conference weekend**. They get to know each other in a moderated process and exchange views on the scientific, technical and social issues around genome editing and their expectations of the vote. Specialist articles, websites, podcasts, books – a variety of sources are presented so that participants can quickly familiarise themselves with the topic. “The intensive familiarisation phase was good. A trusting atmosphere was created in which we had very heated discussions with each other; but they were always well-meaning, respectful and never rude,” describes one participant.

They get together again three weeks later: is genome editing safe compared to conventional plant breeding? Is it ethically permissible to enhance athletic performance or to alter the genome of human embryos to reduce their risk of contracting HIV? These are questions that the consumer group wants to clarify, also with the help of experts. The group invites 14 of 32 possible experts to a hearing. They formulate questions; the vote’s focus is being refined. “I invested a lot of time, read specialist articles sent to me by others in the group in the evening.” – “Everyone was always concerned about striking a balance in the matter;” describe the participants. “I was impressed by how committed everyone was,” comments one participant.

On the third weekend, the 20 people meet for the last time for the **three-day concluding conference**. The schedule is tight: expert hearing, drafting the vote and the vote’s public presentation. “The expert hearing was rewarding, the discussions very worthwhile. Better than any article,” the “votees” remarked several times. “We struggled to find the right wording in our vote.” It resulted in a 15-page booklet, solidly filled with thoughts and demands for politics, the economy and society, which is presented to the public on Monday morning at the Federal Press Conference building by two members of the consumer group and broadcast worldwide via livestream. They begin: “Those who are crazy enough to think they can change the world are the ones who do it. We are 20 of those people.” – “The vote is a plea to politicians, and we demand that the results be taken into account in any further decisions. We were all highly motivated.” – “Read it! Reflect on it. Act on it.”

Is it safe enough?

“Risk” is a central concept when we think about health and safety. More knowledge, however, seems to contribute to a sense of insecurity. A guest article by Professor Dr. Daniëlle Timmermans from the Vrije Universiteit Amsterdam.

In January 2011, a factory in Moerdijk, a small town in the Netherlands, burned down. Large black clouds of smoke and blazing flames, combined with the fact that it was a chemical company, immediately evoked the image of a disaster. Experts said that there was no danger to public health. However, a week after the fire, the public was still concerned and uncertain about possible health effects. Another example of different perceptions of a health risk is mobile telephony: despite the fact that more than 30 years of research have not shown any negative health effects, people are worried. More research showing a lack of effect cannot convince these people to change their mind. Risk is not equal to danger. A risk is a measured or quantified uncertainty. This quantification generates knowledge about a possible negative event and provides tools for making decisions for the future.

Nowadays, “risk” is one of the central concepts we use in thinking about health and safety. More knowledge and a better management of risks, however, seem to contribute to a sense of insecurity rather than to a sense of security. People often are concerned about risks, which experts say are negligible. What can explain this difference in perception?



Professor Dr. Daniëlle Timmermans was a Maria Sibylla Merian Fellow at the BfR from October to December 2019. The Dutch psychologist received the BfR accolade for her scientific achievements. During her stay, Ms. Timmermans worked on the development of a joint research project on risk communication.

Risk perception: more than a number

Apparently, larger risks like serious overweight due to an unhealthy lifestyle or health problems from heavy smoking are less threatening to people than the much smaller health risks caused, for example, by the above named fire. The difference is that environmental and technological risks are less known to most people, both in size and in terms of consequences. Moreover, they are not voluntarily chosen and not controllable.

A risk is thus perceived as more than a number. It is not only about the probability, but also about the nature of the risk, the severity of the consequences and the degree of control.

Risk perception: it happens or it does not happen

It is an old idea in psychology that we process information – including risk information – in two parallel systems, which roughly correspond to the everyday concepts of intuition and reason. While analytical thinking is logical and sequential and follows rules, intuitive thinking is associative, expressive and often emotionally charged. The intuitive, affective evaluation of risks often serves as a guideline for judgments or decisions. A positive evaluation of a technology or activity results in a lower perception of the associated risk. When a technology has no direct benefit for us, is associated with a negative feeling, the health risk is seen as larger.

In that sense, it does not matter whether there is a probability of one in thirty or one in three thousand. We have an image, a mental model of the potential negative consequences of the hazard. This also applies to risk perception of toxic substances. For experts, the harmfulness of toxic substances depends on the dose and the degree of exposure. In the perception of many people, substances are dangerous or not. Moreover, they value the mere presence of a chemical in food as unacceptable.

Negative feelings or fears we have with regard to certain health risks are real in the sense that the feared consequences are possible. It makes us cautious, especially in uncertain situations. Often that is wise, but these negative feelings sometimes have a disproportionate influence on our judgments and decisions. Our fears then do not match the facts. Risk perception, therefore, is about facts and probabilities, but also about fears. This should be sufficiently acknowledged to make risk communication successful. ■



“I am a risk assessor”

Professor Dr. Tanja Schwerdtle has been the new Vice President of the BfR since March 2020. A visit shortly before taking up her new post.

Tanja Schwerdtle does not show signs of any stress. Recently returned from a three-day marathon of meetings at the European Food Safety Authority EFSA in Parma, northern Italy, the scientist is still fresh, friendly and focused on our conversation. We meet on a wintry cool Friday afternoon in Rehbrücke, a small town near Potsdam. This is – for the moment – still the food chemist and toxicologist’s workplace: in a building complex at the University of Potsdam and the German Institute of Human Nutrition Research.

Schwerdtle comes out of a meeting with her working group and rejects the coffee provided on the conference

table. “I’ve had enough,” she declares. She is still a professor at the University of Potsdam’s Institute of Nutritional Science. But in a few weeks, she will take up her post as Vice President of the German Federal Institute for Risk Assessment, when she will be 45. An occasion to look back – and, more importantly, to look forward.

It all began with metal species. They have shaped Schwerdtle’s scientific career. But what exactly are metal species; what is it all about? This launches us into the middle of the scientific discussion. Schwerdtle looked at how different metal compounds – different “species” – have an effect on the body.

A team player: chemist Tanja Schwerdtle appreciates flat hierarchies. In her free time, she likes to go jogging and be alone with her own thoughts.

Arsenic has two faces

A good example of this is arsenic, which Schwerdtle and her working group studied for many years. Arsenic is a metal-like element. In a sense, it has two faces, an “organic” one and an “inorganic” one. Organic arsenic is part of a carbon compound, like a sugar molecule. More than 200 organic arsenic compounds can be detected in food. Many are comparatively harmless, as long as they are soluble in water.

Inorganic arsenic is different. It contains no carbon and has a simple structure – here the arsenic is more exposed and has a more direct effect. This makes it a risk. Inorganic arsenic compounds, such as arsenite, are therefore highly toxic and can cause cancer. “Whether a food contains arsenic is not so important for the health risk,” explains Schwerdtle. “Because it is not the metal alone that accounts for the effect, but rather the chemical compounds in which it is contained – they determine the toxicity.” The risk is a question of the (metal) species. One arsenic compound can be 10,000 times more toxic than another.

Criticism of animal-based foods

Taking a close look, assessing the risk in a differentiated way and also keeping an eye on the benefits – these principles are important to Tanja Schwerdtle. This means, for example, taking the health benefits of fish consumption into account, which can outweigh contamination by problematic substances. Or taking a closer look at the current trend towards new types of food: “Animal-based foods are currently being criticised – but how do I know that meat alternatives, full of additives, are healthy? How do I know that lupine sausage is safe?”

Even if the advantages of a healthy diet and a sufficient supply of trace elements have to be taken into account, Schwerdtle clearly sees “the other side” as a priority. “I’m a risk assessor,” she says. After studying chemistry and food chemistry in Karlsruhe, the Pforzheim native turned to toxicology, the science of toxic substances. Her doctorate in Karlsruhe was followed by positions at the Technical University of Berlin, the Universities of Münster and – since 2013 – Potsdam. Tanja Schwerdtle’s other main area of interest has to do with her work as a chemist: the development of replacement models for animal experiments in toxicology.

Further improvement of consumer protection

Schwerdtle appreciates flat hierarchies. She is looking forward to her new role at the BfR, where she has identified an “incredibly strong midfield”. She has known this for many years as a member and head of the scientific advisory board. “I love research,” she says, “but at my new institute, I also have the opportunity to strategically shape and improve food safety and consumer protection. An important basis for this is the interdisciplinary cooperation between many disciplines, which the BfR offers. “You can learn a lot here and make a big difference,” summarises Schwerdtle.

Work and family (husband, daughter and dog) doesn’t leave Schwerdtle much time for hobbies, but she does take the time to keep fit. “I run 40 kilometres a week – I can be alone with my own thoughts and even though I am physically exhausted afterwards, I am mentally more relaxed and more communicative,” she says.

Evening has arrived and the university has emptied. Schwerdtle sees her guest to the door. We get the impression that the scientist’s working week between Parma and Potsdam has not yet come to an end. ■



Toxic fish

Tropical fish can contain substances which, when consumed, can cause serious health effects. The BfR wants to facilitate the detection of these substances and to raise awareness of this problem in the public.



© PicturePartners/Stockphoto

Northern Germany, November 2012: within a few days, patients with similar unusual symptoms visit hospitals and emergency departments. They complain of diarrhoea and vomiting as well as pain in their arms and legs and abnormal temperature sensations. Some feel cold as heat and vice versa, and experience the feeling of an electric shock when they come into contact with cold water. In some cases symptoms last for several months; in the majority of cases at least a few weeks. Further cases are registered in Hesse, Rhineland-Palatinate and Bavaria.

Poison Centres provide the first clues of the cause when responding to calls from the public. Several consumers enquire about poisoning from “red snapper fish fillets”. The local food control authorities then collect samples throughout Germany. A total of 23 reports of poisoning from fish fillets reached the National Reference Laboratory (NRL) for the Monitoring of Marine Biotoxins and the Poisoning and Product Documentation Centre at the BfR.

Triggered by ciguatoxins

“Due to the unusual, rarely occurring symptoms here, it quickly became clear to us that we were most likely dealing with ciguatera, the ciguatoxin fish poisoning,” recalls Dr. Herbert Desel, who was Head of the Poison Centre GIZ-Nord at the time and is now Head of the

Poisoning and Product Documentation Centre at the BfR. This unit assesses poisoning reports from doctors and the eight German Poison Centres as an important contribution to the risk assessments of the BfR.

Ciguatoxin, a tongue twister! The word is pronounced “ci-gua-toxin” and refers to a harmful substance that can be taken up into the body when tropical fish is consumed. “Cigua” comes from the Cuban Spanish. The people there call the sea snail *Cittarium pica* “cigua”. They have been familiar with the aforementioned symptoms for centuries and gave the disease the name “ciguatera” because it is said to occur after eating that particular sea snail.

Today, we know that there is not just one ciguatoxin, but several ciguatoxins (CTX) having similar chemical structures. CTX are marine biotoxins (algae toxins). They are mainly produced by microalgae (phytoplankton) that marine animals feed from. More than 20,000 phytoplankton species are known worldwide, but only a few produce marine biotoxins. Humans can ingest them through fish, mussels and other seafood. Algae that produce CTX prefer warm water temperatures, which is why these algae – and, therefore, the contaminated fish – are found in tropical and subtropical regions. Accordingly, fish such as various species of snapper, barracuda or tropical types of mackerel in particular may contain the toxins.



The English sailor James Cook was one of the first Europeans to describe the symptoms of ciguatoxin poisoning. He recorded an incident in his diary on 24 July 1774:

“The night before we came out of Port Sandwich, two red fish the size of a large bream were caught using a hook and line. [...] The following night, everyone who had eaten the fish was seized by violent pains in head and bones, together with scorching heat all over the skin and a feeling of numbness in their joints. There was no doubt that this was caused by the fact that the fish was of a poisonous nature [...] and it took a week or ten days for all the men to recover.”

Contaminated fish not detectable

It is still unclear how ciguatoxins are digested in the human body. “What is certain, however, is that these toxins are very potent. Very low doses are enough to trigger symptoms,” Desel says. However, the probability of dying from the poison is very low. Ciguatoxins cannot be destroyed by frying or cooking, nor by stomach acid. They are preserved for a long time in frozen fish. A particular problem arises for both retail and consumers: fish containing ciguatoxins cannot be distinguished from fish that are not contaminated. The poisons do not alter the appearance, smell or taste.

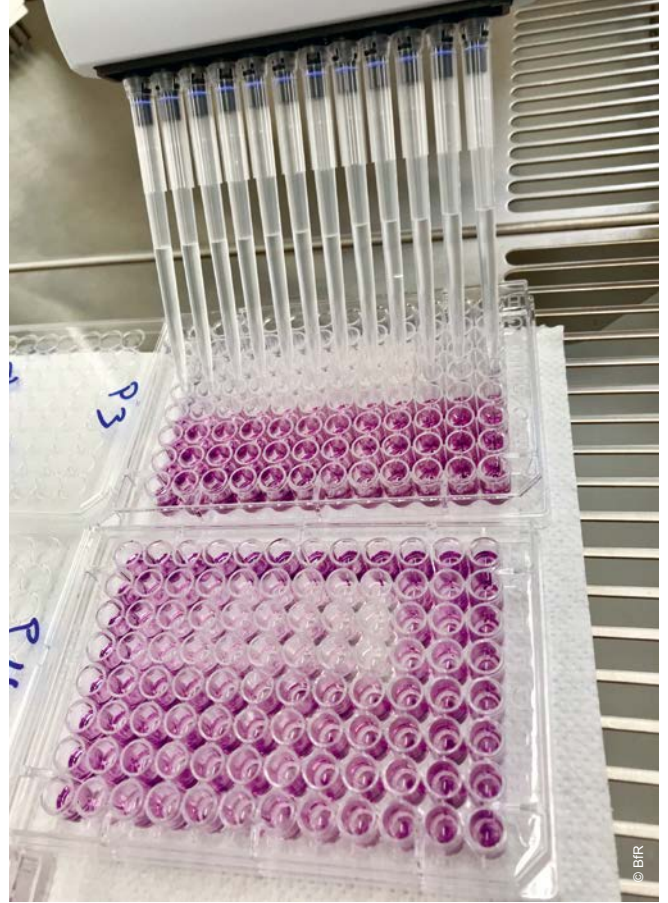
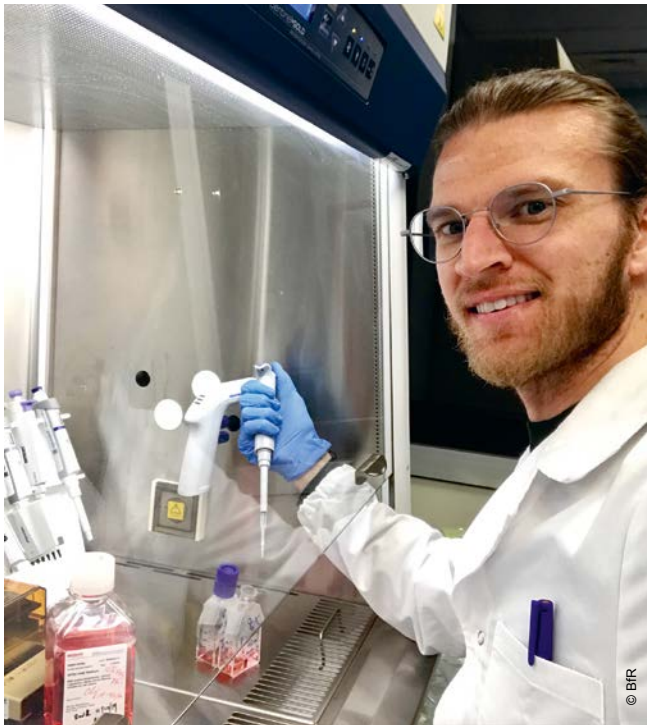
July 2016. Several ciguatera cases in Germany, again. Red snapper fillets, again. All of those affected have eaten fish imported from India. “Ciguatoxins are very similar in structure. Depending on the region, there are minimal differences in the structure of the poison with different effects,” Desel says. CTX are divided into three groups according to their geographical occurrence: P-CTX (Pacific), I-CTX (Indian Ocean) and C-CTX (Caribbean Sea). Ciguatera is the most common fish poisoning in the world. There are an estimated 50,000 to 500,000 cases every year around the world, most of them in the tropics. However, fish imports also lead to ciguatera outbreaks outside of these regions – as a result

of global trade and maybe climate change. Consumers in Germany are, therefore, also affected. This is why the BfR will continue to address this topic in the future.

Detection without animal tests

It is difficult to detect ciguatoxins in fish. “Ciguatera symptoms may develop after a typical fish meal containing a CTX level of only 0.01 nanograms per gram of fish. This corresponds to the weight ratio of an ant to a full-grown blue whale,” Dr. Astrid Spielmeier says, who is, among other things, responsible for CTX analysis at the NRL.

Initially, animal tests were used to detect CTX. It is now possible to detect them using mouse cell lines – without animal experiments. The BfR treats cells with extracts from fish samples to determine the amount of ciguatoxin contained in them. If these samples contain no CTX, a dye added to the cells changes colour. If CTX are present no colour change is observed (see box). The so-called “mouse neuroblastoma cell assay” (N2a) allows numerous samples to be examined within a short time. However, the assay does not allow any assertion about CTX structures. These must be confirmed by mass spectrometry after liquid chromatographic separation.



Mouse cells plus fish extracts: scientists at the National Reference Laboratory for the Monitoring of Marine Biotoxins at the BfR are investigating whether fish samples contain ciguatoxins.

One of the challenges of ciguatoxins analysis is that many of the toxins are not available as reference substances but necessary to unequivocally identify ciguatoxins. Currently, about 40 different ciguatoxin subtypes are known. Those from the Pacific are most extensively investigated. According to Spielmeyer, no official methods for routine testing of fish for ciguatoxins are available. Furthermore, fish contains a lot of protein and some species also contain a lot of fat. Both components are an obstacle for the CTX analysis.

Ciguatoxins cause certain ion channels (“locks”) of cell membranes to remain permanently open. This impairs the cells’ functions and can lead to cell death. “This effect is used in the N2a assay,” Dr. Dorina Bodi, head of the responsible NRL, says. If sufficient amounts of ciguatoxins are added, e.g. from a fish sample, the cells are not or only partly able to chemically convert a specific dye which is also added during the analytical process. Living cells convert the dye from a colourless to a purple compound. “We can determine how much ciguatoxin is present in a sample based on the colour intensity of the newly formed compound.”

“They interfere considerably with detection and this can become a problem in samples with low concentrations of ciguatoxins,” chemist Spielmeyer says. In addition, CTX attach to proteins and are fat-soluble. “Here, we are dealing with the figurative squaring of the circle. But we hope to be able to establish an analytical method at the BfR soon.”

The BfR is actively involved in the EuroCigua Project: a group of European scientists that have joined forces. Under the umbrella of the European Food Safety Authority (EFSA), it involves 15 European organisations from six EU member states. Two of the aims are to characterise the risks of ciguatoxin poisoning in Europe and to develop and establish new reliable detection methods. Improved analytical methods are necessary because researchers at the BfR expect that the frequency of ciguatera poisonings will rise in Germany. People are increasingly eating exotic dishes, which include fish from the tropics. If symptoms occur, consumers should seek medical advice and store the fish leftovers, if possible, to make them available for laboratory analysis. ■

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



Old masters rediscovered

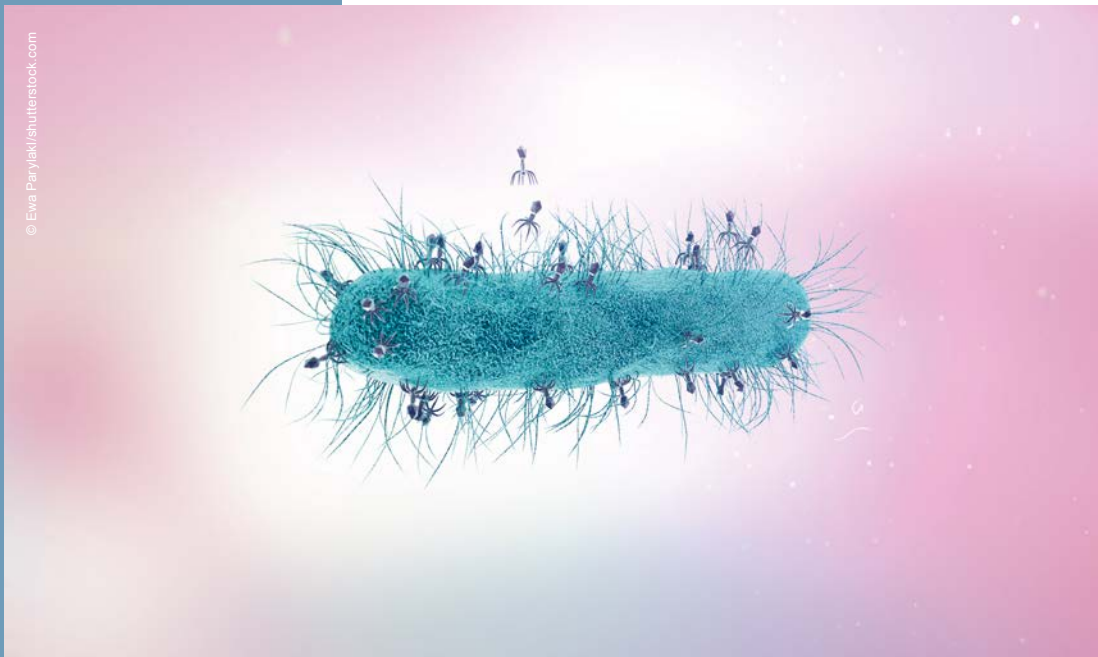
A natural remedy can put pathogenic bacteria such as listeria or salmonella in their place – even those for which antibiotics are no longer effective: bacteriophages.

A test tube with yellowy-cloudy contents sits on the laboratory bench. It contains a solution with bacteria. Dr. Stefan Hertwig, a microbiologist at the BfR, adds a shot of another liquid. The liquid will become clear and transparent within a few hours. This is the visual indication that the bacteria are dead.

They have been defeated by bacteriophages. These are viruses that can infect and kill bacteria. The little bacteria-eaters use what nature has given them: with the help of the genetic material in their heads, they enter certain types of bacteria and multiply millionfold.

This leads to a burst of the infected bacteria, therefore immobilising them. All of this takes place invisible to the human eye: the bacteria that have been attacked are 50 times smaller than the diameter of a thin human hair. Bacteriophages, like other viruses, measure in at just one tenth to one hundredth the size of bacteria.

Bacteriophages can be found in large numbers wherever bacteria are found themselves: in the ground, in water or in food. They are harmless to humans. Bacteriophages contribute to maintaining a healthy balance in our intestine, where millions of useful bacteria live.



Bacteriophages stick to the surface of bacteria with their spikes and insert their genetic material into the bacteria for virus replication.

The benefits of bacteriophages were already recognised at the beginning of the 20th century – for treating bacterial infections. After the discovery of antibiotic substances and their wide use as medicines, bacteriophages were forgotten in most countries. However, they are once again coming to the fore due to the spread of antimicrobial resistance. A clinic in Georgia is a pioneer in this field with the largest phage collection in the world. For patients with persistent wound infections, including those from Western Europe and the USA, appropriate therapies are developed on site within a few days – and with great success. But phages also have potential in the fight against bacteria in food.

Researchers like Stefan Hertwig, who work with bacteriophages, have been completely won over by the bacteria-eating viruses: “They are very efficient. Very few phages can destroy a large number of bacteria,” says Hertwig. Phages would only destroy the unwanted bacteria in a targeted way. All other ‘good’ bacteria, such as those that are important for human digestion, remain intact and continue to function. Furthermore, no genetic engineering is involved because phages occur naturally in vast numbers. “We collect them from nature and select the most effective ones in the laboratory.” And finally, they can be easily produced in large quantities.

Bacteriophage compounds can already be used in the Netherlands and Austria against listeria, for example, but this is not yet allowed in Germany. Listeria are involved in disease outbreaks caused by food time and again. Since they can survive almost anywhere and, therefore, cannot be completely destroyed, a phage compound might make food safer. The only challenge: since phages are inanimate, they would have to be sprayed on their targets in large quantities, preferably as a liquid film, on production lines in factories or on food. Types of phage must also be thoroughly researched as “disinfectants”, says bacteriophage researcher Hertwig. “And they must not insert their genetic material into the attacked bacterial cell.”

The use of phages in the European Union is still in its infancy – both in food production and medicine, but studies and successful applications open up prospects for their wider application in the future. ■

More information:

www.bfr.bund.de/en > FAQ: Bacteriophages
www.bfr-akademie.de > Archiv: Vorträge des
 20. BfR-Verbraucherschutzforums “Bakteriophagen”
 (lectures in German)

Medicine through the back door

Stronger, more focussed, more productive – many people take food supplements to “optimise” their own health. In most cases, this is unnecessary, sometimes even risky, because sometimes they work like drugs.



Red yeast rice, for example. Used in Asia for centuries, it is said to have various positive properties. It supposedly helps to treat heart and vascular diseases, among other things, and lower cholesterol levels. This is helpful for marketing, but not for those who take it as a food supplement. For the substance it contains, monacolin K, has the same effect as the drug lovastatin. The crucial difference is that drugs containing lovastatin are available only on prescription and are only prescribed after a medical examination to determine whether their use is acceptable in terms of health. Food supplements containing red yeast rice, on the other hand, are usually bought and consumed on a person's own initiative. Most people are often unaware of possible adverse effects, which can range from nausea to damage to the skeletal muscles. According to the European Food Safety Authority (EFSA), the current data available are not sufficient to specify a maximum dose that is still considered safe.

Plant power to fight menopausal symptoms?

Some food supplements contain isolated or enriched isoflavones. These are substances occurring in plants such as soya or red clover, which may have a weak effect in the body similar to that of the hormone estrogen. It is purported that they can be used by women to relieve menopausal symptoms. Health claims of this sort regarding isoflavones have so far been rejected by EFSA.

Scientific evidence on the safety of isolated isoflavones, especially with respect to long-term use, is currently still inadequate. It is therefore not recommended that women who have previously suffered or are currently suffering from estrogen-dependent disease (cancer) of the mammary gland or uterus take food supplements containing isoflavones.

Food or medicine?

Food supplements do not require official approval for the German market. They are subject to food law. Manufacturers are responsible for their safety and must inform the Federal Office of Consumer Protection and Food Safety (BVL) before they place their products on the market. Medicines are subject to stricter provisions; quality, efficacy and safety must be proven for their approval.

Not only does this difference sometimes appear complicated for the population, but questions about the general necessity of food supplements often arise. The BfR recommends not to use them uncritically. The best way to clarify whether a food supplement might be useful in certain cases is to seek medical advice. ■

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



Global trade influences substances in food

Due to the globalisation of the flow of goods, foods from all corners of the globe may end up on the German market. Depending on their geographical origin, they might contain different concentrations of undesirable substances. How does this influence the intake of substances in the population living in Germany, and is this sufficiently taken into account in standard exposure estimates? An example: the BfR has compared data on kiwi fruits from southern Europe, New Zealand and Chile, which are sold in German shops all year round. One result: kiwis from the EU contain less aluminium than kiwis from non-EU countries. In this example, the variation in concentrations is already taken into account in the standard exposure estimates. But this does not apply to all foods. Exposure assessments have to be refined, where applicable. A prerequisite for this is to better identify and document the food's origin.

More information:

Fechner, C. et al. 2020. Refinement of dietary exposure assessment using origin-related scenarios. *J Expo Sci Environ Epidemiol* 30: 492–503. DOI 10.1038/s41370-019-0117-6 (open access)

On the trail of animal ingredients in feed

The addition of animal ingredients in animal feed has been strictly regulated since the largest occurrence of mad cow disease (BSE) with more than 35,000 cases worldwide, particularly in Great Britain at the beginning of the 1990s. In the ANIMAL-ID research project, scientists from the National Reference Laboratory for Animal Proteins in Feed at the BfR, together with project partners, have developed analytical methods to detect certain animal ingredients in feed. The results are three new analytical methods: simultaneous detection of blood plasma from eight animal species, simultaneous detection of cattle's blood plasma, muscle and bone as well as detection of haemoglobin, the colorant of red blood cells, from ruminants. In the follow-up project ANIMAL-ID2, these methods will be tested according to international criteria and their application will be extended to the food sector (e.g. regarding the concentration of various animal ingredients in raw meat products and cooked sausages).

More information:

Niedzwiecka, A. et al. 2019. A novel antibody-based enrichment and mass spectrometry approach for the detection of species-specific blood peptides in feed matrices. *Food Control* 98: 141–149. DOI 10.1016/j.food-cont.2018.11.036

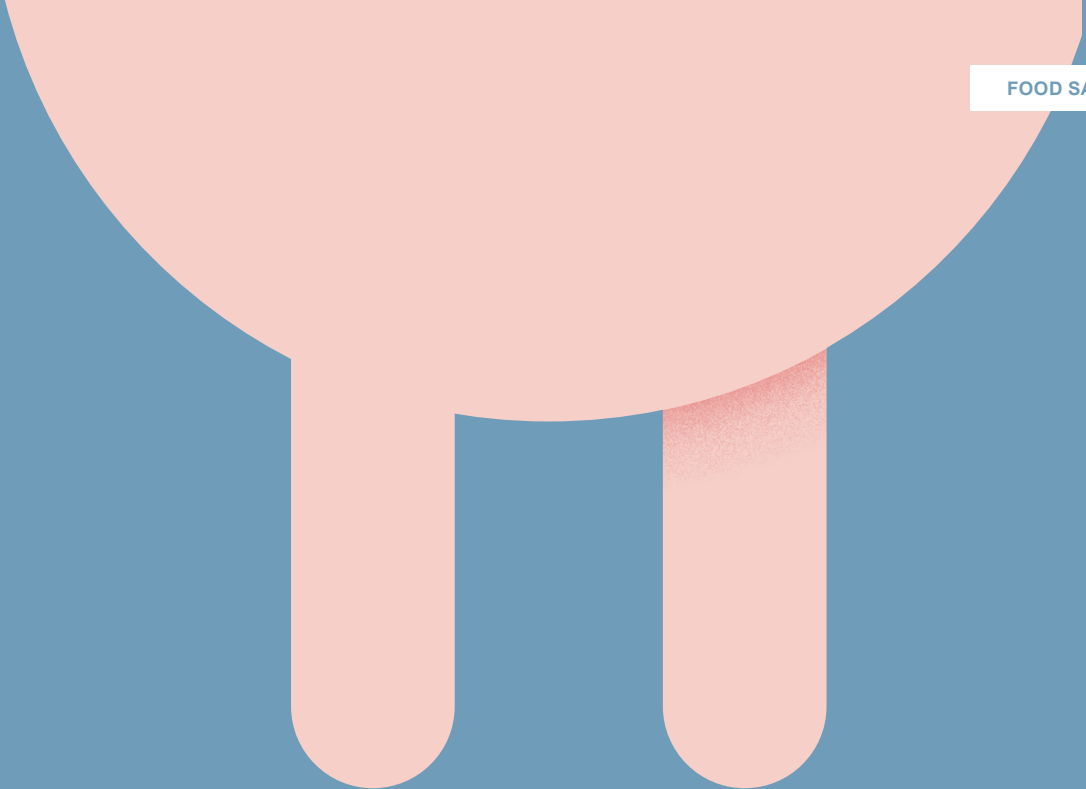


Tracing aquatic animals and molluscs in food

Fish, shellfish and snails are eaten around the world. However, they can trigger allergies. Determining traces of these animal groups in food is a highly complex challenge, since they are among the richest in species. This is the exact aim of AQUALLERG-ID: to completely break down the allergenic proteins and genetic traces of molluscs, crustaceans, fish and, for the first time, insects in food. The three-year project is funded by the German Federal Ministry of Food and Agriculture (BMEL) and has been coordinated by the National Reference Laboratory for Animal Proteins in Feed at the BfR since November 2019. In addition to immunological rapid tests and affiliated partners' state-of-the-art gene decoding technology, DNA-based overview procedures are used at the BfR.

More information:

www.bfr.bund.de/en > Research > Third party projects of the BfR > Authenticity testing of food and feed



Raw is risky

No packaging, direct from the producer, short transport routes – “natural” foods are currently the trend. Even raw milk is popular. However, it can contain pathogens, such as *Campylobacter*.



For some time, the number of reported cases of illness after consuming raw milk has been increasing. The number one cause of illness: *Campylobacter* bacteria, which are actually found in the intestinal tract of many game animals, pets and livestock such as cattle. Even though *Campylobacter* cannot multiply outside this warm biotope, they are still capable of surviving and causing infection.

The two most important pathogenic *Campylobacter* species, *Campylobacter (C.) jejuni* and *C. coli*, end up in milk mainly via faecal contamination during the milking process. It is not clear how long they can survive there. The few existing studies indicate a limited ability to survive, but also show that the different strains of *Campylobacter* can adapt to their environment with varying degrees of success.

***Campylobacter* bacteria cause diarrhoea**

Animals carrying *Campylobacter* often show no clinical symptoms, whereas humans may develop *Campylobacter* enteritis or *Campylobacter* enteritis if they consume contaminated food. Just a few bacteria are enough to cause an infection. This leads to watery, occasionally bloody diarrhoea, stomach ache or cramps, fever and tiredness. The illness lasts up to a week, sometimes even longer. Complications rarely occur. Many infections also run their course without symptoms.



How can I protect myself?

Even if farms lure you in with cups, cocoa powder and a comfy seat for drinking fresh raw milk, it should not be consumed without first being heated. The BfR points out that raw milk from “milk filling stations” must be boiled before consumption to kill any pathogenic bacteria. Infants, toddlers, elderly people and people with certain underlying illnesses in particular should only consume raw milk if it has first been boiled, since bacterial diseases can be more severe for these consumers and they generally have a higher risk of illness.

The Robert Koch-Institute (RKI) records about 60,000 to 70,000 cases of these reportable enteritides in Germany every year. *Campylobacteriosis* is the most frequently reported bacterial disease and is mainly caused by bacteria in food. In most cases, the infection occurs via animal-based food, such as insufficiently cooked poultry or other raw foods that have come into contact with the pathogen. Infection can also occur via contaminated drinking water or pets.

Raw milk is often the cause

Over the past five years, one type of food has attracted particular attention: unheated or insufficiently heated raw milk. The largest *Campylobacter* outbreaks can be traced back to the consumption of raw milk. In autumn 2015, around 100 people in Lower Saxony fell ill after drinking milk from a dispenser on a farm. The two largest outbreaks in 2018 – in Thuringia and Bavaria – were also linked to the consumption of insufficient or unheated raw milk.

Boiling kills bacteria

The reason for the trend: farmers are increasingly offering raw milk from “milk filling stations” on their own farms. The milk is stored in a cool place, giving the bacteria little chance to multiply. However, this does not reduce the number of existing bacteria. Because of the health risk posed by raw milk, dispensation is specially regulated by law. For example, milk dispensers must clearly and legibly display the information “Raw milk – boil before consumption”. This is intended to prevent people from drinking raw milk directly and, therefore, possibly becoming infected.

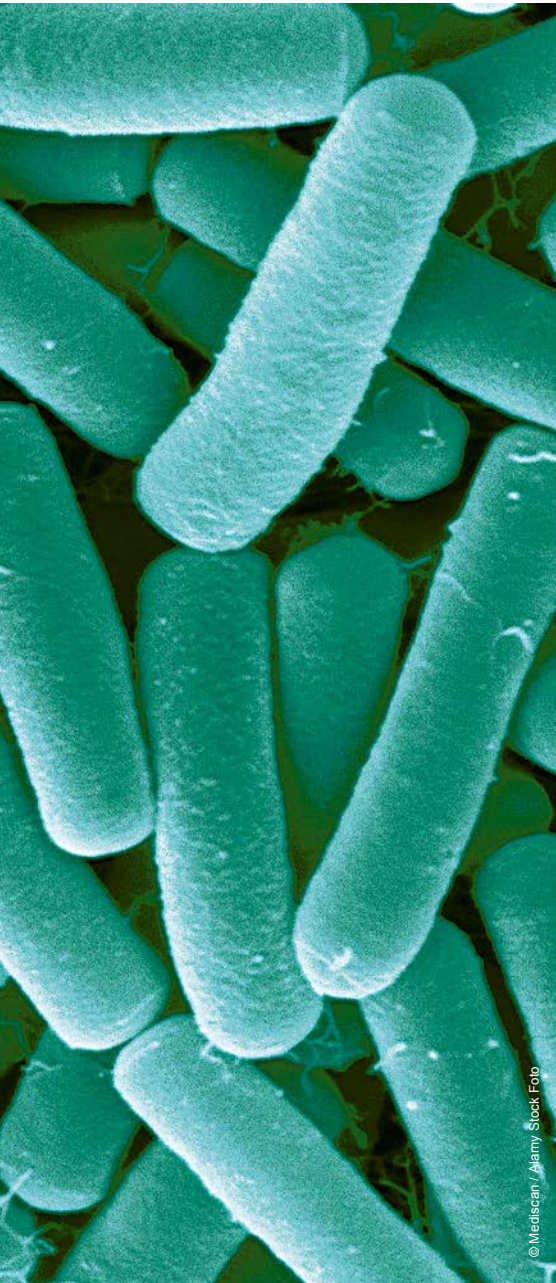
In addition to farm dispensers, raw milk is also available in shops as certified raw milk, called “Vorzugsmilch” in German. Strict regulations apply to its production and treatment, and milk producers are monitored individually. There is a use-by date on the packaging, which must not be longer than 96 hours after milking. Nevertheless it cannot be ruled out that certified raw milk may also be contaminated with pathogens. The probability of foodborne infection here is lower than that from raw milk from milk filling stations due to the stricter regulations. However, because there is still some risk, certified raw milk must not be distributed in group catering contexts, such as in nurseries, schools or hospitals. Incidentally, there are no such risks with commercially available pasteurised milk, as pasteurisation sufficiently kills any bacteria. ■

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



The organic bacillus

***Bacillus thuringiensis* is a bacterium that likes to feed on insects.
This makes it a widely used organic plant protection product.
But are there any side effects?**



Look closely. The rod-shaped bacterium *Bacillus thuringiensis* (right, a scanning electron microscope image) can often be found on tomatoes.

Using a little imagination, *Bacillus thuringiensis* looks like a protracted fried egg under the electron microscope. The oval “egg yolk” inside the bacterium is the spore, durable like a permanent preserved food for times of hunger. In the spore, the microorganism’s genetic material holds out for better times. But the “egg white” should not be underestimated as it contains a large diamond-shaped crystal. It turns out to be toxic cargo. If the bacteria enter the intestine of certain insects, the crystal consisting of protein breaks up. The protein breaks down the animals’ intestinal wall, which then become paralysed and die within a day or two. *Bacillus thuringiensis* (Bt) now finds plenty of food in the insect carcass and can awaken from its “sleep”.

Roughly translated, *Bacillus thuringiensis* means “Thuringian bacillus”. The soil and plant dweller owes its name to the German microbiologist Ernst Berliner. He worked at the Institute for Cereal Processing in Berlin and found the bacteria in infested Mediterranean flour moth caterpillars. These had been sent to the institute from a mill in Thuringia in 1909.

The insecticidal toxin poses no danger to humans

Little did Berliner know that many decades later, Bt would make a career out of being a plant protection product. Today, the spores and the toxin are used against pests all over the world such as the European corn borer or cabbage butterfly. Based on what we currently know, the Bt protein used as an insecticide is harmless to humans, acts specifically on certain insect species depending on the variant, spares many beneficial insects, is easy to use and is even environmentally friendly. Bt compounds have, therefore, become practically indispensable, particularly in organic farming.

Organic pesticides are regularly reviewed by the European assessment authorities, as are conventional “chemical” plant protection products. The BfR is also involved in the health risk assessment of active substances and products. Several Bt active substances are currently undergoing the process of re-evaluation and renewal of the approval. Only after an extensive and EU-wide scientific review by the European Food Safety Authority (EFSA) and the competent authorities of the member states can the approval of the active substance be renewed by the EU Commission. The EU-wide approval is in turn the prerequisite for the authorisation of plant protection products in the respective member states.

Bacillus species can cause diarrhoea

However, this review is not simple. The main reason for this is the fact that *Bacillus thuringiensis* is part of a group of closely related *Bacillus* species. This *Bacillus cereus* group includes 18 species, including its namesake *Bacillus cereus*. In practice, the group members are usually not treated separately. However, some of them can cause gastrointestinal illnesses if they are ingested via food. The key question for EFSA assessors: might bacteria from organic pesticides also trigger these diseases? Does this make them a source of danger? Let’s look for an answer.

The cause of human diseases due to members of the *Bacillus cereus* group are other bacterial toxic substances that have nothing to do with the “useful” Bt protein against insects. One of these toxins, cereulide, causes vomiting. However, it has not yet been discovered in Bt strains. Enterotoxins are much more common than cereulide. These are toxic substances that can cause diarrhoea. The genetic make-up (genes) for this can also be detected in Bt.

The diseases are usually mild, rarely last longer than 24 hours and are not contagious. Nevertheless, if Bt spores are used as an organic pesticide, there is a possibility that they could be ingested in larger quantities with fruit or vegetables, for example, and “germinate” in the human intestine. The more Bt spores enter the body in this way, the greater the risk might be of getting diarrhoea.

Bacteria from organic pesticides are found on peppers and tomatoes

Dr. Hendrik Frentzel, biologist at the BfR, and his team have checked how often and in what quantity Bt from organic pesticides are found on vegetables. In doing so, they closed a significant knowledge gap for EFSA assessors. They found *Bacillus cereus* species on peppers in 41 per cent of cases; on tomatoes it was 28 per cent. 93 per cent (peppers) and 99 per cent (tomatoes) turned out to be Bt.

Frentzel and his colleagues took a closer look at some of these bacterial findings, known as isolates. They wanted to know how many of them came from spores of sprayed Bt. The result: more than half of the isolates from pepper and tomato samples examined came from organic pesticides.

Does this mean there is a health risk now? Furthermore, the “dose” of the microbes found, in other words the number of them, can provide information on this. It was within the tolerable range with very few exceptions. This is reassuring. Nevertheless, Frentzel thinks that it is necessary to further investigate possible health risks from Bt. “*Bacillus thuringiensis* is a useful alternative to chemical pesticides,” he says. “But ‘organic’ does not automatically equate to harmless.”

What happens with the spores in the environment?

“We need more information about what happens to the spores after they are spread on the field,” says Dr. Sabrina Feustel. She is in charge of the health risk assessment of Bt at the BfR. In the field, the spores are largely inactivated by ultraviolet radiation from the sun. It is a different matter in the greenhouse, where the spores can survive longer. On the other hand, the use of Bt against insects in the forest, such as the oak processionary, is less problematic. Its caterpillars have long “stinging hairs” that cause severe skin reactions. These are particularly dangerous to those working in forests.

It must also be taken into consideration that Bt and its relatives are widely distributed in nature and are frequently found in the soil, for example. Fewer than 100,000 of these “bacilli” per gram of food are considered acceptable. This is used by the BfR as a reference value for the assessment. This value should not be exceeded if plant protection products are used properly. However, the risk assessment is complicated by the fact that the formation of toxins varies according to the strain of bacteria.

Therefore, there are quite a few questions that still require more precise answers. Nevertheless, Sabrina Feustel agrees with the assessment of her colleague Hendrik Frentzel. She sees organic pesticides as alternatives that complement chemical active ingredients, however, there are many areas in which they cannot be completely replaced. As with chemical pesticides, an extensive health risk assessment is essential for organic pesticides. “This year, I will use Bt for the first time on cabbage and boxwood,” says Feustel. “I am curious to see how they stand up to the caterpillars.”

Bt plants: banned in Germany

No article on Bt would be complete without referring to plant genetic engineering. The genetic blueprint for Bt insecticide has been integrated into the genome of crops, such as corn and cotton by seed producers, so that they now produce their own insecticide and fight off predators. Such plants are grown in countries like the USA, India and China. The use of chemical insecticides in corn fields, for example, has declined significantly since then.

In the EU, only a single type of Bt corn is approved as a genetically modified plant. However, in light of the opposition to plant genetic engineering, Germany has chosen to prohibit growing this type in this country as well. Not all Bt is created equal, it seems. ■





3D printing: practical, modern – a health risk?

Private individuals can now produce spare parts, household goods or gifts themselves with the help of a 3D printer. The most common devices melt down thermoplastic and apply it layer by layer until the three-dimensional object is finished. These plastics may also contain additives such as metal and wood, although the exact composition is often unknown. The BfR is currently investigating possible health risks for users. Scientific studies show that the heating process of 3D printers releases particulate and volatile substances. In the hobby sector most 3D printers do not have an exhaust system. Thus, emissions are released directly into the indoor air. To assess the risks of emissions from a health perspective and to make recommendations for consumer health protection, the BfR systematically examines various 3D printers and materials from different manufacturers.

More information:
BfR Communication No. 048/2019 of 04 December 2019

When sprays hit the lungs

In the NANOaers research project, an international team has investigated how the lungs react to tiny particles (nanoparticles) from aerosols. Headed by the BfR, scientists have recreated different liquid mixtures and sprayed them in special measuring chambers. The question: how do the solvents and additives, which also enhance the dirt-repellent properties of proofing sprays, affect the respiratory tract? The result: the use of solvents reduces the droplet size of the aerosols. Smaller particles can penetrate deeper into the lungs and, therefore, potentially pose greater health risks. Spraying the mixtures led to lower lung cell activity in the laboratory test, even when using individual components of the mixtures. The addition of nanoparticles partially increased the effects. Fewer spray bumps resulted in a lower absorption of nanomaterials by the cells.



Protective clothing in the field

Plant protection products are safe – in principle. However, a prerequisite is that they are used properly and for their intended purpose. This means, for example, that when used in the field, protective clothing such as overalls, breathing masks and gloves must be worn if this is in the instructions for use. New regulations for the protection of health during use and for people living in the vicinity have been in force since 2019. Anyone who does not follow the instructions for use can expect to be fined. The instructions are there for risk mitigation and are based on assessments made by the BfR. They are made mandatory when a plant protection product is approved. Authorities, crop associations and German federal states (“Laender”) are currently discussing regulations that are easy to implement in practice, easy to understand and that take into account the diversity of agriculture.

More information:
BfR Communication No. 006/2020 of 23 January 2020

“Our food has definitely become safer”

Dr. Roland Solecki worked at the BfR and its predecessor institutes for 30 years, testing and carrying out health risk assessments on active ingredients in plant protection products. In this interview, he takes stock – and looks ahead.

Mr. Solecki, after all these years – is it hard for you to hear the G-word?

You are alluding to glyphosate, the active ingredient in plant protection products, which was, and still is, the subject of much controversy, in which we were also involved. However, I can assure you that the G-word has played only a minor role in my entire 30-year career at the Institute. It cannot permanently spoil the fun that I have experienced in my work. I have tried to contribute to making pesticides safe to use and food safer.

Has the debate on glyphosate changed the risk assessment of pesticides?

It had the positive effect to the extent that risk assessment was critically reviewed and further improved. Within this course, the assessment processes have been made even more transparent for the public.

Is there actually a biological alternative to glyphosate?

Definitely, it is one I became familiar with at the age of twelve: picking up a hoe, walking along the rows of turnips and pulling out the weeds. I don't know whether this has a future considering the enormous demand for food. And when I drive a tractor across the field and mechanically remove the weeds or wild herbs, I have a similar effect on biodiversity as using glyphosate, as studies have shown.

What future prospects do you see?

I am confident that we will be able to reduce the use of chemicals in the future using modern technology. My grandson sat on a tractor at Green Week, which shows the driver where there are lots of weeds in the field and where there are fewer. In this way, satellite technology and GPS can be used to spray more or less in a targeted manner and in doing so, plant protection products

can be used more sparingly. I think integrated plant protection is a good compromise – it protects nature, and the use of “chemicals” can be reduced. But they are used when it is justifiable and necessary.

Organic farming also uses pesticides, but these are not supposed to be “chemical or synthetic”. What is the health risk assessment on this?

Organic farming must also ward off pests. For this purpose, a significantly smaller number of active ingredients are approved in integrated plant protection. These are also associated with residues, but normally in significantly smaller quantities. However, it is a misconception that active ingredients from nature are, generally, non-toxic. Furthermore, substances from nature can often only be acquired with the help of chemicals or they are “chemically and synthetically” recreated. It is also possible that natural substances, such as copper, which is used against fungal infestations, are already abundant in our food due to their prevalence in other food and, therefore, there are high levels of natural exposure. Thus, these substances must also be examined for health risks with the same methodology and care.

During your time at the BfR and its predecessor institutes, how has the work of the health assessment authorities for authorising plant protection products changed?

In the beginning, there was an individual assessment by national authorities worldwide, who were unfamiliar with one another. Today, we have come to a common international understanding of risk assessment. The level of assessment is better and the scope has increased. We now also take into account the exposure of local residents, and we have better methods – from detecting pesticide residues to testing toxicity and determining how much is actually ingested.



© BfR

Positive perspective: Roland Solecki points out that plant protection products have become safer. Nevertheless, there is still a lot to be done.

What does this mean for consumer protection; has it made the use of pesticides safer?

Our food has definitely become safer with regard to pesticide residues. When I started in 1990, we had more than 1,000 different active ingredients on the European market. These were reduced to about 300 by the introduction of the European approval procedure and a few new, better and less dangerous alternatives also came along. We have also taken a huge step forward in biocides outside of agriculture. I am thinking, for example, of wood protection products, about which we knew very little at the beginning of the 1990s. Biocides are now subject to a standardised assessment throughout Europe and are, therefore, also safer for the consumer.

certainty are required. And we need more specific measurements as far as humans are concerned: how many pesticides do they ingest? How do these behave in the body? We also need a better basis of data. In addition to methods that do not involve laboratory animals, computer programs that are capable of learning can be particularly helpful here, which can evaluate our studies and help us to determine a substance's hazard potential. I see the innovative development of these alternative testing strategies as one of the most important missions of the BfR in the future. And last but not least: the international division of labour and cooperation between authorities should be further intensified because we now get our food from all over the world. ■

What do you think are the most important “construction sites” in the health risk assessment of plant protection products? What needs to be addressed now?

We should do even more to ensure that animal experiments are reduced more consistently. Alternative testing methods that can detect health risks with the same

Rhythmic detoxification

For cells to function properly: the German Centre for the Protection of Laboratory Animals at the BfR is investigating how the internal clock can be used to replace animal experiments.

In the morning, daisies open up, humans awaken with new vigour and mice withdraw to their hide-outs to go to sleep. In the evening when dusk falls and night approaches, flowers close, humans become tired and mice come to life. The same spectacle repeats itself day after day, night after night: from single-celled organisms to animals and plants, organisms have adapted to our planet's rotation, therefore increasing their chances of survival in one way or another.

Right down to each individual cell, the human metabolism has also adjusted to the rhythmic alternation of day and night. This even applies to detoxification – if you want to test health risks posed by chemicals on cells, there is no getting around setting the clock of the cells correctly. This is indicated by the research results obtained by biologist Dr. Michael Oelgeschläger and his team from the German Centre for the Protection of Laboratory Animals at the BfR.

Curious: a circadian rhythm in cells?

“In the beginning, everyone thought it was absurd – a circadian rhythm in cells!” recalls Oelgeschläger referring to the start of the research. However, it is now known that there is a whole molecular mechanism of hereditary factors (genes) that fulfil the tasks of an internal clock in human cells. As clocks, they control behaviour, hormone release, sleep, body temperature and metabolism. “It is estimated that up to 43 per cent of all genes are subject to the circadian rhythm,” explains the scientist. In 2017, three pioneers researching the body clock received the Nobel Prize for Medicine. No more talk of absurdity.

Oelgeschläger wants to replace animal experiments with experiments on cells wherever possible. For example, those that investigated the effect of poisonous (toxic) substances. Therefore experiments “in the Petri dish” must come as close as possible to the conditions in humans. Of course, this also applies to the biorhythm. But while in the human organism all cells function

properly thanks to a control centre in the brain, time chaos reigns in the Petri dish because every cell follows its own biorhythm.

As a consequence, laboratory results are distorted when compared to the real conditions in the body. Oelgeschläger and his team avoided these pitfalls. By bathing the human cells in dexamethasone – a substance related to the body's own hormone cortisol – they set their clocks to a single common time. Dexamethasone acted like a stopwatch that makes everything start over – with dramatic consequences, as it turned out.

Functioning together, reacting better to toxic substances

Oelgeschläger now confronted the cells with a toxic dioxin compound called TCDD. It turned out that the synchronously functioning cells showed an enhanced reaction to the substance compared to non-synchronised cells. Simply put: as in animals, the reaction to environmental toxins in cells is dependent on the time of day. However, to verify this, all cells must “go to sleep” or “wake up” at the same time.

Oelgeschläger and his team have broken new ground with their findings. “It was a feasibility study,” says the scientist. “We showed that biorhythms are also significant in cell culture.” Now it is up to researchers to bring the cell tests even closer to the reality in humans. In the end, it could become apparent that even conventional experiments on animals need improving. Because a mouse that slips out of its hideout at night functions differently than a human being who crawls under their duvet at the same time. ■

More information:

Ndikung, J. et al. 2020. Restoring circadian synchrony in vitro facilitates physiological responses to environmental chemicals. *Environment international* 134: 105265. DOI 10.1016/j.envint.2019.105265

Focusing on fish. Biologist Nils Ohnesorge is investigating the nervous system of zebrafish at the German Centre for the Protection of Laboratory Animals.



When in doubt, for the fish

**Research for animal welfare:
biologist Dr. Nils Ohnesorge is investigating how
zebrafish embryos react to unpleasant stimuli.**

“What It Is Like To Be A Bat” – this is the famous essay by the American philosopher Thomas Nagel. In it, he explains why we humans will maybe never be able to put ourselves in the consciousness of a bat and experience the same sensations. The gulf between bat and human being is simply too wide. It is even greater with Dr. Nils Ohnesorge and his laboratory animals.

The biologist is investigating whether the zebrafish feels pain and if so, how exactly this happens. Ohnesorge wants to improve the conditions in which *Danio rerio* (the Latin name for the zebrafish) are kept. “I research the animal for the animal,” says Ohnesorge. This is done at the German Centre for the Protection of Laboratory Animals in Berlin-Marienfelde, which is part of the BfR.

The zebrafish is slender and fast. The sociable animals, whose “zebra stripes” sparkle bright blue when exposed to oblique incident light, are the length of a match stick, reproduce rapidly (a female can lay 300 eggs per week) and are easy to breed. They are popular in science because they can be used to study hereditary factors, body processes, diseases or the effects of toxic substances. Around 70 percent of zebrafish genes are found in a similar form in humans.

Today, there is a real boom in research on zebrafish. After mice and rats, “zebras” are the most widely used laboratory animals. This also has to do with the fact that new procedures, such as the CRISPR/Cas9 DNA scissors, make it possible to breed fish with desired characteristics in no time.

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It was assumed that fish were unable to feel pain.

The fish: a strange creature

“Just a few years ago, the fish was a strange creature,” explains Ohnesorge. “A creature that could not express itself, whose behaviour was difficult to interpret.” That perception has changed and “fish welfare” has become more important. The German Animal Welfare Act also stipulates that suffering in experiments must be kept as low as possible. “It was thought that fish were unable to feel pain,” says the researcher. “But a debate has now been sparked.”

The prerequisites for pain perception are also present in fish. There are “pain sensors” (receptors) and corresponding nerve cells; the animals perceive unpleasant stimuli and evade them. “All the signals that report harm work,” says Ohnesorge. But does that mean pain? “Pain is an individual, negative experience,” explains the biologist. “And, therefore, a feeling that is incredibly difficult to detect – unlike physical stress, which can be measured.”

The feeling of pain is probably different for fish than for humans, but if this feeling exists, it must be taken into account. For example, in animal experiments with fish, where painkillers should also be used.

Zebrafish bustle about in 60 aquariums

Ohnesorge suspects that fish perceive pain. But a conviction is not proof. It has to be tested in a laboratory. And on that note: welcome to zebrafish husbandry at the German Centre for the Protection of Laboratory Animals at the BfR, which the scientist has built over the four years that he has been at the Institute. Around 60 aquariums are connected to a pump system that automatically circulates the water, cleans it, heats it to 28 degrees Celsius and controls the pH value (acidity).

As schooling fish, zebrafish live together without problems in a comparatively small space. A pair is only transferred to the breeding aquarium to spawn. Zebrafish mature as though in a time lapse. Where a human embryo

needs one month for one stage of development, the fish embryo needs just one day. The embryos still rolled up in the embryonic membrane and the freshly hatched larvae are hardly visible to the naked eye. This is not only because they are so tiny; they are also completely transparent. The transparency allows Ohnesorge to look inside the animal without hurting it. The microscope allows a view of its rapidly growing brain, in which every single cell is still visible.

A pain imprint in the brain

How do unpleasant stimuli, such as a certain chemical substance, affect the nervous system of fish larva? Do they perhaps leave their own pattern behind in the animals’ brains, a kind of pain imprint? This would be a strong argument for Ohnesorge’s assumption that zebrafish actually have this feeling. He is conducting research on genetically modified animals whose nerve cells (more precisely: the nuclei of these cells) light up under laser light if they are active. The special microscope is, therefore, able to register every single nerve cell at work in the brain and even record its progress. By doing so, a film can be recorded that shows the consequences of an unpleasant stimulus on the brain.

All of this is still a long way off for Ohnesorge. The technical possibilities are as immense as they are challenging; we are talking about tens of thousands of nerve cells and their behaviour. To begin with, the biologist wants to determine which regions of the brain are likely to be important to pain perception. He will then use them to determine the effects of pain stimuli and how they can be prevented in animal experiments, for example, with drugs.

A great deal of work lies ahead of Ohnesorge and his team. But the researcher is driven by the fact that his work directly benefits experimental animals. Just as with bats, perhaps we will never truly understand zebrafish. But there are remedies also for fish in animal experiments that can alleviate potential suffering. ■



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Making science more accessible

In February, as part of a series of seminars on the 3R principle held at the German Centre for the Protection of Laboratory Animals at the BfR, Dr. David Mellor from the non-profit Center for Open Science (USA) reported on various strategies for more transparency and higher quality in science. The 3R principle describes the goal of reducing the number of animals in experiments (“reduce”), lowering the level of suffering in experiments (“refine”) or completely replacing animal experiments (“replace”). According to Mellor, the provision of raw data and details of the methods used as well as the pre-registration of preclinical and clinical trials are important for this. The non-publication of original data as well as incorrectly evaluated test results have led to the fact that many research experiments are irreproducible. Greater transparency and improved quality in science could therefore only be achieved through the joint efforts of all parties involved.

More information:
<https://osf.io/>

All animals count

Around 10 million animals are used in animal experiments throughout Europe every year. However, the number of laboratory animals is actually significantly higher. 14 million additional animals were systematically recorded for the first time for 2017. A large part of them is the result of breeding, which often results in more animals being bred than ultimately needed. Furthermore, the number also includes animals bred for tissue and organ sampling. Researchers can help to reduce these numbers. For this purpose, the German Centre for the Protection of Laboratory Animals has developed the “Animal Study Registry” database, in which animal experiments can be registered with all necessary details and by doing so, avoid unnecessary repetition of experiments. Moreover, the Centre is committed to placing the welfare of all laboratory animals more in the focus of science and society. In this way, it contributes to ensuring that really all animals count.

More information:
 Lewejohann, L. et al. 2020. Cut back on surplus laboratory animals. *Nature* 578: 515. DOI 10.1038/d41586-020-00517-3 (open access)



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Better reproduction of animal experiment data

The question of how the quality of animal studies and, therefore, their validity can be improved has long been discussed in international research. In order to support the reproducibility of laboratory animal studies, the German Centre for the Protection of Laboratory Animals at the BfR organised a special meeting on pre-registration of preclinical studies as part of the Reward/Equator Conference 2020 in February in Berlin. At the meeting, the requirements that animal registries must meet were discussed and how pre-registration can be encouraged and its success be measured. The “Animal Study Registry” database set up at the BfR at the beginning of 2019 can make a contribution to reducing the number of animal experiments by reducing the number of redundant studies and preventing follow-up studies based on qualitatively insufficient data.

More information:
 Heini, C. et al. 2019. Rethinking the incentive system in science: animal study registries. *EMBO Reports* 21(1): e49709. DOI 10.15252/embr.201949709 (open access)

INTERNATIONAL NEWS



Consumer protection mission to Albania

Closer to EU standards: as part of the EU’s TAIEX expert mission, the BfR and the Federal Office of Consumer Protection and Food Safety (BVL) imparted knowledge on consumer health protection in Tirana in October 2019. With lectures and seminars, the BfR and the BVL contributed to boosting risk assessment, risk communication and risk management in Albania, aligning them with EU standards. Also included were BfR findings in crisis prevention and education as well as crisis communication and stakeholder management.

High-tech food safety in Montenegro

Digitalising food risk assessment – for this, Montenegro’s government is funding the establishment of a centre of excellence at the University of Donja Gorica. The BfR is supporting the establishment of a modern next-generation sequencing laboratory and the development of methods in the field of authenticity and providing advice on selecting suitable IT tools for risk assessment. The BfR also offers laboratory training courses in Montenegro and Berlin.

More food safety professionals

As a member of the European Food Safety Authority’s (EFSA) scientific advisory board, the BfR chairs the discussion group on capacity development in food risk assessment. The long-term goal of the group is to develop a European master’s degree programme in “Food Safety Risk Assessment”. International experts are currently developing the content and structure of the course.

PERSONNEL



Award-winning BfR research on tattoo inks

Dr. Ines Schreiber, head of the junior research group “Tattoos” at the BfR, has received the “Young Scientist Toxicology Award” for her work in the field of tattoo ink research. The prize along with 2,500 euros is awarded annually by the Society for Toxicology. It acknowledges the outstanding, independent contribution to scientific progress and Ms. Schreiber’s resulting scientifically high-level publications.

INTERNAL



New National Reference Laboratory at the BfR

Food can be contaminated with pathogenic viruses. Pathogens that cause diarrhoea and hepatitis viruses play a role here. Since mid-December 2019, the BfR has been home to the National Reference Laboratory for Foodborne Viruses. It performs this role in accordance with Article 100 of Regulation (EU) 2017/625. The BfR develops detection methods and ensures monitoring quality, among other things.

Detection in food is often very laborious because of the often low concentration of the virus and the complex composition of food. Noroviruses and rotaviruses can cause gastrointestinal diseases and infections with hepatitis A and E viruses can lead to liver inflammation.

System assessment quality management mastered

The revised standard DIN EN ISO/IEC 17025:2018 places extended demands on the competence of testing laboratories, which have been integrated into the quality management system of the BfR laboratories. In February, this system was successfully assessed by the German Accreditation Body (DAkKS). The BfR will receive an accreditation certificate that has been amended accordingly probably in the middle of the year, the appendix of which shows the flexibly accredited test areas and an excerpt of the accredited test procedures at the BfR. The BfR proves its special competence in these laboratory areas.

Award for best short lectures

Anne-Margarethe Enge and Marja Kornhuber have been recognised with the award of the German Society of Toxicology for the best short presentation. Both BfR scientists are sharing the award, which they received on 5 March 2020 at the "German Pharm-Tox Summit" in Leipzig. Enge researches pyrrolizidine alkaloids (PAs) at the BfR. These are substances which are formed by some flowering plants, and which can be toxic. In her presentation, she presented a study which analysed the association between the intake and transportation of PAs, and the toxicity thereof. Kornhuber's research focuses on environmental chemicals and their influence on the endocrine system. Laboratory animals are still frequently needed in order to identify and characterise them. Kornhuber presented a new test method in her lecture. The Society of Toxicology is a member of the German Society of Experimental and Clinical Pharmacology and Toxicology (DGPT). It meets once a year at the "German Pharm-Tox Summit".



SUBSCRIPTION:
Consumer health protection to go



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