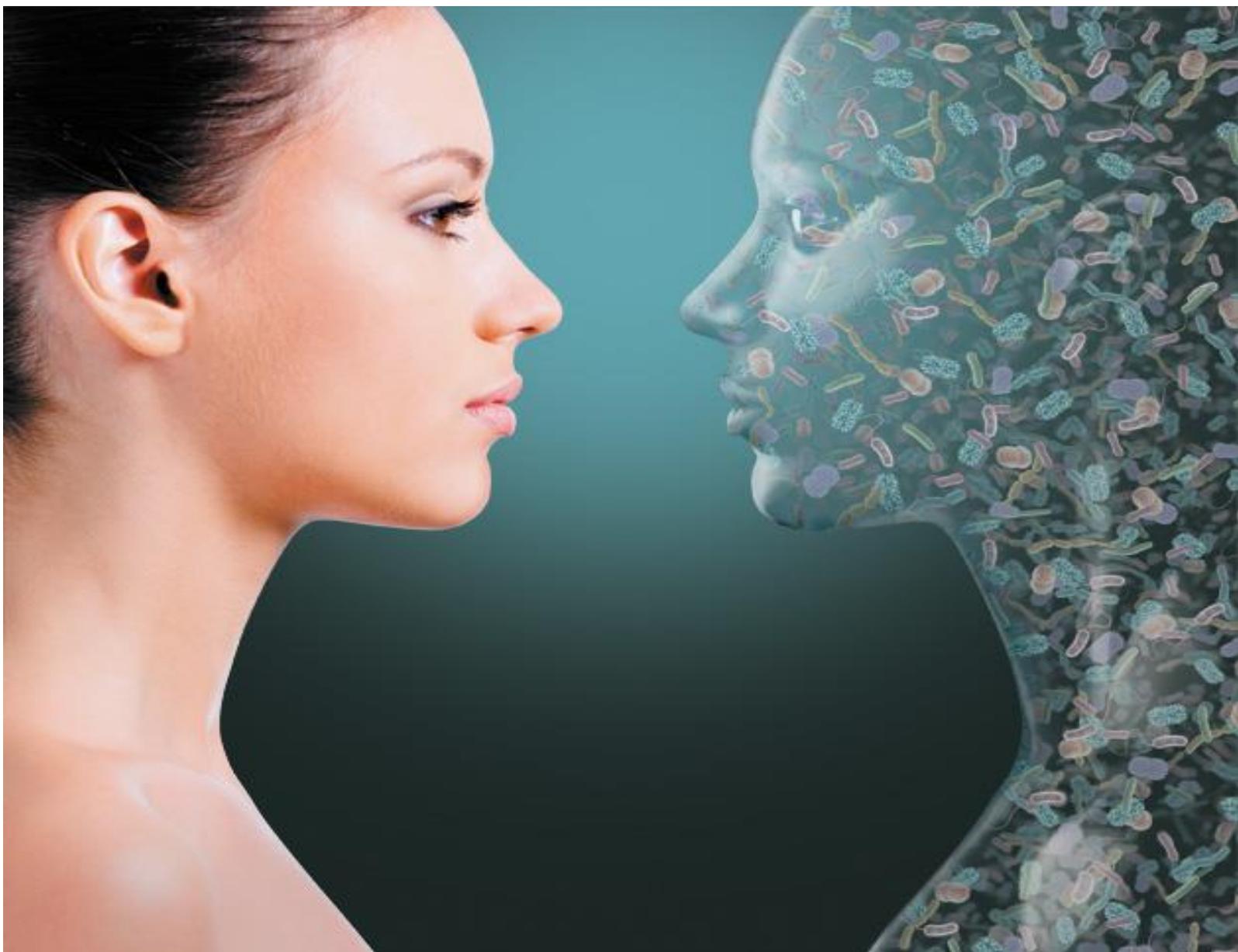


# Synbio®

Synbiotic skin cleansing  
and care

Respecting your natural microbiome!



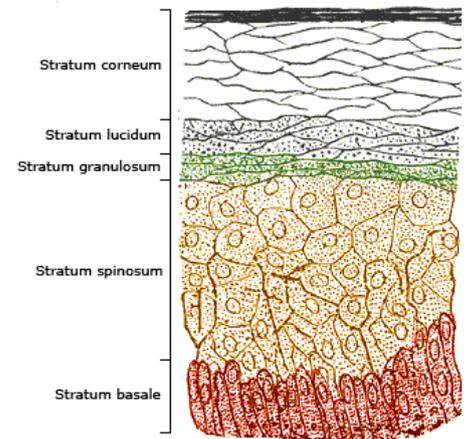
## Synbiotic skin care

In humans, the skin is considered to be the largest organ and, like the internal organs, contains several layers of specialized cells (tissues) that function together. The condition of the skin sometimes provides important information about whether or not the body as a whole functions properly. Our skin is the first and most important barrier to the outside world and protects us against harmful influences and infections.

Moreover, it has become clear in recent years that the skin carries a large number of micro-organisms (= skin microbiome or skin flora) that fulfill an important function. When the skin flora or the skin are disturbed, this can lead to a large number of (serious) problems. To prevent or solve such problems, Chrisal has developed the synbiotic skin care. This patented technology is the most natural and safe guarantee for healthy and well-functioning skin! With this document, we would like to provide you with more background information on how this technology works.

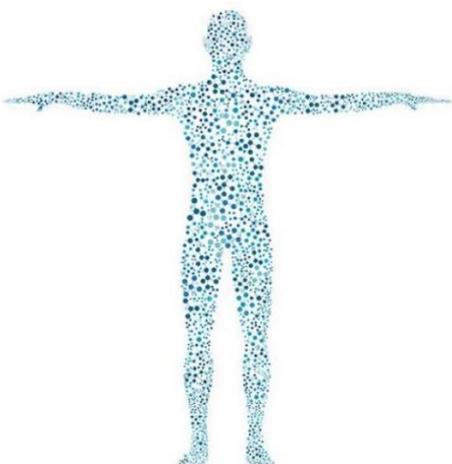
### The skin and its microbiome

Human skin has an area of 2 square meters and consists of 3 main layers: the epidermis, dermis and hypodermis; each of which still consists of several sublayers with a specific function. Each square cm of the skin contains about 100 sweat glands, 10,000 cells and 200 nerve endings in addition to blood vessels!



The skin has several important functions:

- **Protection** against harmful germs and the outside world
- **Measure** via the nerve endings of e.g. outside temperature
- **Temperature control** via intensive blood flow
- **Moisture regulation** via the sweat glands
- **Storage** of fats, vitamin D and other vital substances
- **Absorption** of oxygen or, for example, medicines via ointments or patches
- **Social function** in which the color and health of the skin play a role in human interaction



In addition to the skin (structure) itself, recent research also shows that the microflora present on the skin (= **skin microbiome**) plays a very important role. A microbiome is the total number of micro-organisms (mainly bacteria) that are located somewhere; whether they work together as a community or not. The best known microbiome is that of humans and includes, for example, the micro-organisms present in our mouth, digestive system and on our skin. Even though these microorganisms do not all work together, they do determine the "state (or health)" of the place where they are located. A stable, healthy microbiome is therefore of great importance for our health and that of the entire environment. Human skin naturally contains millions of micro-organisms!

## Skin disorders

The skin structure and its microbiome are both important to protect us from many harmful influences and infections. When one or both are damaged, there is a good chance that we will have skin or health problems. Very often these problems are directly or indirectly linked to microbiology. When the skin is physically damaged, certain microorganisms can suddenly cause infection, while not doing so on intact skin.



Some of the most common skin disorders:

- **Acne:** inflammation of the sebaceous glands with possible secondary infections of the wounds
- **Allergy:** reaction of the skin to all kinds of external or internal substances
- **Atopic eczema:** chronic inflammation of the skin causing damage
- **Dermatitis:** acute skin infections with different causes
- **Dry skin:** damage to the skin due to an incorrect water balance
- **Shingles:** inflammation of the skin due to the Varicella virus
- **Psoriasis:** disordered skin renewal process with unpleasant symptoms
- **Fungal infections:** inflammation of the skin due to infection with Candida or other fungi
- **Staphylococcus infections:** serious infections and inflammations with the Staphylococcus bacteria
- **Warts:** skin damage from viral infections

It is also possible that an underlying condition (e.g. cancer) has a negative effect on the skin, causing it to be damaged and thus causing additional problems.

**In the prevention and cure of most skin conditions, it is crucial to keep the skin structure and the skin microbiome in good condition!**

## Classic soaps and disinfectants

Until a few years ago, people were not yet aware of the great importance of the skin microbiome. The soaps, shower gels, shampoos that had been developed until then mainly aimed at cleaning the skin as powerful as possible, often with very strong degreasing effect. On the one hand, such degreasing damages the skin itself, but especially also the natural microflora that is on the skin. This greatly disrupts the skin and its microbiome, causing them to lose their protective function.

Disinfectants are absolutely harmful to the skin and its microbiome. These products date from the era of asepsis in which they wanted to kill all micro-organisms in order to obtain good hygiene. In the meantime, science has shown that a large number of micro-organisms exist that are useful or even necessary for our good health. Disinfectants also kill these good microorganisms and also create resistance among the bad germs.

**Classic chemical soaps and certainly disinfectants damage the skin and the microbiome, increasing the risk of skin problems!**

## Synbio® skin cleansing and care

After many years of research, Chrisal has developed a technology for skin cleansing and care that maximally respects the skin and its microbiome and keeps it in good condition! This patented (EP3210612A1) technology is based on synbiotics:

**Synbiotics:** the combination of probiotics and prebiotics.

**Probiotics:** good bacteria that improve human and animal health

**Prebiotics:** nutrients that stimulate the development of good bacteria



The Synbio® skin care products contain a high concentration of probiotics and prebiotics. The probiotics reduce the risk of infections and install a good protective microbiome on the skin. The prebiotics support and stimulate the growth and activity of naturally good skin bacteria. In addition, the probiotics are active dirt removers that clean the skin on a microscopic level. This leads to a permanent skin cleansing and therefore a smooth and healthy skin.

The main goal is to prevent an unhealthy skin microbiome. Because the Synbio® products actively add high numbers of good bacteria (the probiotics) and stimulate the growth of existing good skin bacteria through the prebiotics, a very stable and healthy microflora is formed and maintained.

### **BAD MICROFLORA WITH CLASSIC SOAPS AND DISINFECTANTS**



### **GOOD MICROFLORA WITH SYNBIO® SKIN CLEANSING AND CARE PRODUCTS**



This stable healthy skin microbiome provides many benefits, both preventive and curative. Chrisal and other academic research institutes have conducted extensive research into the effects of this technology, which makes the claims made clinically proven!

## Effects of synbiotic skin care

The use of Synbio® products for skin cleansing and care offers, in addition to a good cleansing effect, the following scientifically proven benefits:

### Reduced risk on bad germs and infections

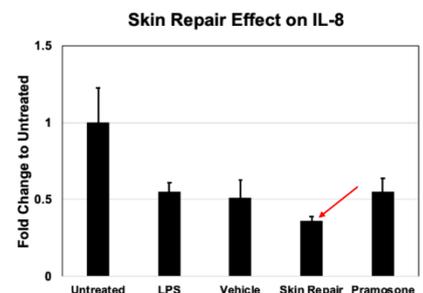
Studies at the universities of Ghent (Belgium) and Ferrara (Italy) have shown that the use of synbiotic products reduces the risk of the presence of germs and therefore also a lower number of infections. As indicated earlier, the high numbers of probiotics and prebiotics ensure a healthy microbiome, which obviously does not cause infections.

#### Literature:

Vandini et al. 2014 PLOS ONE. (Reduced risk on bad germs, pathogens)  
Caselli et al. 2018 PLOS ONE. (Reduced number of infections)

### Anti-inflammatory

Many skin problems such as acne, eczema and psoriasis have to do with an inflammatory reaction (inflammation) of the skin as a result of an allergy, infection or underlying condition. Research in the USA (North Carolina) has shown that Synbio® products on the skin reduce the inflammatory response. In particular, the production of IL-1 $\beta$ , IL-8 and TNF- $\alpha$  was reduced. These are chemicals (cytokines / chemokines) that the body produces to cause inflammation.



The Synbio® products include the probiotic *Bacillus subtilis*, which very actively produces certain biosurfactants, called surfactins. These surfactins have a proven anti-inflammatory effect. This anti-inflammatory effect ensures less itching and redness in many skin conditions.

#### Literature:

Zhang et al 2015. INFLAMMATION. (Surfactine reduces inflammation)  
Sung Dae et al 2006. J MICR BIOTECH (Anti inflammatory effect of Bacillus subtilis)

### Skin barrier repair

A clinical study conducted in the USA by Dr. Jean-Philippe Therrien on Chrisal's Synbio® formulation showed that after skin irritation, the skin barrier was repaired more quickly. After three days there was already a noticeably better recovery of the skin compared to the control. A quick repair of the skin barrier is important for the prevention of infections of damaged skin. In addition, intact skin also has visual advantages because the skin looks healthier and more beautiful.

#### Literature:

Savitskaya et al 2019. Helyon. (Skin repair by Bacillus subtilis)

The clinical studies conducted by Enviotic Ltd. and Chrisal are being expanded and the results will be published in the future.

## Safety

Because synbiotic skin care is a new technology, Chrisal has paid a lot of attention to demonstrating the safety of the products from the beginning of its development. Naturally, all products comply with the cosmetic guidelines and are registered in the mandatory European CPNP (Cosmetic Product Notification Portal) database.

### All Synbio® products meet the following criteria:

1. All probiotics used belong to ATCC safety class 1 (= highest safety)
2. The pro/prebiotics are 100% natural, not genetically modified (non-GMO)
3. The pro/prebiotics are approved for food according to the European Food Safety Agency (EFSA) and the US FDA (GRAS status)
4. Passed the following official OECD safety tests:
  - a. OECD 403 Inhalation toxicity
  - b. OECD 404 Acute skin irritation / corrosion
  - c. OECD 405 Acute eye irritation / corrosion
  - d. OECD 406 Skin sensation
5. The prebiotics and probiotics meet the criteria for use in cosmetics, where the mandatory dermatological tests have been successfully performed.
6. The probiotics and prebiotics used also meet the safety criteria for the EU Ecolabel
7. 10 years of safe use in hospitals and clinical trials



#### Letters to the Editor

#### Safety of probiotics used for hospital environmental sanitation

Sir,

There is consensus about the need for efficient control of microbial contamination on hospital surfaces, as these surfaces represent significant pathogen reservoirs that may contribute to transmission of healthcare-associated infections (HCAs). The emergence of multidrug-resistant pathogens in hospitals is a global concern.<sup>1</sup>

Control of surface bioburden is routinely addressed by use of conventional chemical-based detergents/disinfectants; however, these are ineffective in preventing recontamination, and may select resistant strains. Recently, cleaning agents containing probiotics of the genus *Bacillus* have been proposed for hospital sanitation [Probiotic Cleaning Hygiene System (PCHS); Copma srl, Ferrara, Italy]; these have been shown to stably decrease surface pathogens up to 90% more than conventional disinfectants, and to be genetically stable even after years of continuous contact with surface pathogens.<sup>2-4</sup> The rationale for the use of probiotics as sanitizing agents lies in the idea that a healthy microbiota might protect against colonization by, and expansion of, pathogens in the environment as well as in the human body; this has been called 'bidirectional' hygiene.<sup>5</sup>

The three species contained in the probiotic cleansers (*Bacillus subtilis*, *Bacillus pumilus*, and *Bacillus megaterium*) are considered non-pathogenic for humans.<sup>6</sup> Nevertheless, a theoretical risk of infection exists, and a few anecdotal cases of infection by *B. subtilis* have been reported in surgical patients.<sup>7</sup> However, systematic assessment of adverse events in probiotic intervention studies is lacking, whereas it has recently been proposed that the most appropriate way to investigate whether probiotics are safe is to use the 'totality of evidence' rather than single case reports.<sup>8,9</sup> Active surveillance for cases of probiotic-associated infection in all probiotic-based trials has been advocated.<sup>8</sup> Thus, we have analysed whether the *Bacillus* spp. included in cleaning products may themselves be a source of HCAs. We investigated whether any infections with *Bacillus* spp. occurred in seven healthcare institutions in the province of Ferrara (Italy) that used the PCHS throughout.

In addition to routine culture of all 32,139 clinical samples from around 90,000 patients and 800,000 hospitalizations

days, a quota of samples was also analysed by a *Bacillus*-specific real-time quantitative polymerase chain reaction, as previously described.<sup>7</sup> The numbers of analysed samples from each institution, as well as the period of environmental sanitation by PCHS, are shown in Table 1. Both culture-based and molecular testing showed complete absence of PCHS-derived bacilli in any clinical sample, for the entire period of the survey. This suggests that probiotic *Bacillus* spp. do not cause infections, even in the subjects at high risk of opportunistic infections.

We think that this surveillance model represents an essential part of the infection control policy associated with the use of probiotics, as it provides ongoing assurance of safety. Accordingly, we are now undertaking a multi-centre study to evaluate a larger number of healthcare institutions for a prolonged period.

**Table 1**  
Analyses performed in the years 2011–2015 in the healthcare structures (HS) continuously using the *Bacillus*-based Probiotic Cleaning Hygiene System (PCHS)

Healthcare structures	Analyses per year with PCHS sanitation system)					Total analyses (per HS)
	2011	2012	2013	2014	2015	
HS-1	429	—	—	—	—	429
HS-2	103	704	701	613	765	2886
HS-3	—	—	6346	7290	7593	21,229
HS-4	—	76	1025	969	1154	3224
HS-5	—	72	631	713	750	2166
HS-6	—	240	403	498	554	1695
HS-7	—	—	—	—	510	510*
Total <sup>a</sup>	532	1092	9106	10,083	11,326	32,139

HS-1, Old S. Anna Hospital (Ferrara), PCHS application March 16<sup>th</sup> to August 28<sup>th</sup>, 2011; HS-2, S. Giorgio Hospital (Ferrara), PCHS application since November 1<sup>st</sup>, 2011; HS-3, New S. Anna Hospital (Cona, Ferrara), PCHS application since January 1<sup>st</sup>, 2013; HS-4, Delta Hospital (Lago-santo, Ferrara), PCHS application since June 1<sup>st</sup>, 2012; HS-5, Cento Hospital (Cento, Ferrara), PCHS application since July 1<sup>st</sup>, 2012; HS-6, Argenta Hospital (Argenta, Ferrara), PCHS application since July 1<sup>st</sup>, 2012; HS-7, Quisisana Hospital (Ferrara), PCHS application since January 1<sup>st</sup>, 2015.

\* A quota of these samples was simultaneously analysed also by molecular assays (qPCR).

<sup>a</sup> A unique central Microbiology Laboratory (S. Anna University Hospital, Ferrara) performed the analyses by conventional microbiological assays.



## Synbio® products

Chrisal has developed a number of products for synbiotic cleansing and care of the skin, with specific attention to hand hygiene because the hands are often the most stressed. The products are all cosmetics, divided into cleaning and care.

### Skin cleansing and care with rinsing (Rinse-off cosmetics)

Everyone washes, especially hands, with soap and water every day. The soaps in the Synbio® products are mild to the skin and provide good cleaning and degreasing without damaging the skin. The probiotics that remain numerous on the skin even after rinsing ensure a permanent extra removal of organic pollution that is located in the skin pores. This ensures a thorough biological cleansing of the skin. The prebiotics stimulate our own probiotics in their activity and also the already present good microorganisms. **Pure skin with a healthy microbiome!**

**Products: Synbio® Hand soap and Synbio® Shower gel**



### Skin cleansing and care without rinsing (Leave on cosmetics)

It is not always possible to clean the skin with water. That is why Chrisal developed a number of products to clean or care for the skin without water.

#### Synbio® Skin cream

A revolutionary skin cream with a high-quality composition that cleanses, softens, moisturizes and actively repairs the skin! Can be used daily for women, men and children to keep the skin and her microbiome in optimal condition with a reduced risk of infections or inflammatory reactions. It is recommended to use this synbiotic cream daily as a preventive measure, or several times a day in case of certain skin problems such as acne, eczema, psoriasis or dermatitis.



#### Synbio® Handgel

This synbiotic hand gel cleanses the skin through the biological effect of the probiotics that the gel leaves on the hands. The limited amount of alcohol in the product ensures rapid evaporation of the product so that the hands dry quickly again and the probiotics and prebiotics can do their work. Despite the presence of alcohol, this gel is not a disinfectant! The cleansing and protection is provided by the synbiotics that stay active for hours.



## Wat makes the Chrisal products unique?

To enjoy the maximum effect and advantages of the synbiotic technology, the products themselves must of course meet several important quality criteria. Working with live probiotics and natural prebiotics is not easy and requires expertise!

### Product composition

The selection of the types of probiotics and prebiotics are crucial for the proper functioning of the product. A wide variety of species is available and it is very important to know what effect a particular species has under certain conditions. Chrisal has been conducting research for many years to select the most performing probiotic bacteria and prebiotic sugars for the desired application. For example, a probiotic Lactobacillus, known from the probiotic food supplements, will be practically worthless for skin applications. The Bacillus strains that Chrisal uses are ultra performant and naturally occur on the skin!



### Product stability

The number of pre- and probiotics in the product is also very important. Often the organic or microbial pollution on the skin is very strong. A synbiotic product with only a few probiotics will not work. Chrisal products contain an absolute minimum of 50 million probiotics per ml. Certain products go up to half a billion per ml! The prebiotics and prebiotics also have to survive the entire life of the product. Chrisal is by far the market leader in stability and gives all its products a shelf life of at least 3 years!



### Product quality

To guarantee the proper functioning and safety of each product, a solid quality system is of great importance. Chrisal has had the ISO9001 quality certificate since 1999. This guarantees the proper functioning of the entire company.

In addition, Chrisal has 2 laboratories that are equipped with all required, modern technology to be able to perform a thorough quality control. Producing products with probiotics is not easy and guaranteeing purity requires modern equipment and specialized lab technicians.



## Conclusion

With the Synbio® technology, Chrisal has developed a series of revolutionary products for safe, efficient and above all healthy cleansing and care of hands and skin in general. The importance of the skin microbiome is now very clear and must be treated with the utmost respect to avoid health problems. The Synbio® products are perfect for daily, even intensive, hand hygiene, avoiding the harmful effects of disinfectants.

The same Synbio® technology is also used for surface cleaning with a similar philosophy, striving for a healthy microflora in order to minimize the risk of problems with germs and infections.

Further research and product development will show in the coming years that Synbio® is the most appropriate technology to guarantee the health of us and our environment. But of course we count on you to use and spread this technology as much as possible; only then can we make a real improvement for a healthy future!

**Be part of the difference  
that makes a better world!**

