WHY NOT CHANGE THE WORLD?

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To whom it may concern:

Three years ago, I became acquainted with and keenly interested in the technologies developed by ***Better Air***.

Together with many colleagues and a substantial part of the international health care research & providers community, I feel concerned about the increase of antibiotic resistant bacteria and fungi in our environment. The rapid development and spread of antibiotic resistant microorganisms is especially alarming in nursing homes and hospitals.

We are observing how "super bugs" infect and kill hundreds of thousands every year. With the immune-compromised constituting particularly a high-risk group, we frequently stand helpless when even applying next generation antibiotics without success.

It seems apparent that we are dealing with an ecological problem resulting from an artificial (man-made) disturbance of the "natural" balance in microbiological populations. The build-up of resistant bacteria results from selective pressure of "stress" factors such as antibiotics; the strains surviving these conditions will eventually dominate the microbial population of the area (ecosystem). Without a selective factor such as an antibiotic, non-resistant strains will usually outcompete resistant strains, especially those with a transferable resistance trait (Holzapfel et al., 2018). Hygienic principles are based on the proper disinfection of working spaces and devices and by using antiseptics for cleaning of wounds and living tissues. In spite of these essential measures, we realize that the rate of illness caused by pathogenic outbreaks is not reversed but continues to increase. Moreover, we are also alerted by the radical increases in levels and extent of allergies, especially of young children growing up in the "artificial" environment of a modern city. According to the hygiene hypothesis the reduced exposure to microbial stimuli in early life programs the immune system toward a Th2-type allergic response (Toh et al., 2012). On the other hand, particle exposure (e.g., as related to present-day air pollution) may be a major reason for the historical loss of native American lives to infections (Ghio, 2017). "Biotherapeutic" approaches have been suggested to overcome or correct some of the growing deficiencies in the human population. It is also scientifically well established that children from caesarean birth suffer from various atopic and other skin conditions and a lower abundance and diversity in the beneficial gut microbiota (Browne et al., 2017). Data suggest that pleiotropic stimuli from a complex microbial population such as (multiple strain) probiotics may direct improved immune modulation and the restoration of unbalanced (disturbed or dysbiotic) conditions in the human ecosystem, including the skin and gut microbiome (Chen et al., 2018).

When ***Better Air*** introduced their technologies to me about 3 years ago, I have found their concepts and problem-solving approach highly interesting. In the laboratory, the formation of a natural inhibition zone by some *Bacillus* strains against a pathogen indicates some form of antimicrobial activity

that may be applied for controlling of detrimental microbes in the environment and/or within a specific ecosystem. By controlled application of such a carefully elected antimicrobial agent (bacterial strain) the need for use of chemicals and antibiotics may be reduced.

Initially, Better Air requested my team at Handong Global University in South Korea to evaluate safety features of selected strains that they envisaged to apply. They then contracted my company (HEM) to conduct a safety tests on these strains.

Thanks to extensive experience and direct involvement in research and safety assessment of microorganisms over the last 30 years, also as director of the Federal Institute for Hygiene and Toxicology in Karlsruhe, Germany, from 1987 to 2007. Amongst others, my team has conducted joint research as partner in several EU-funded projects. Moreover, I have been an Advisory Board member of the German Food and Nutrition Industry (from 1989 to 2015) and have advised several pharmaceutical companies on safety assessment of bacterial strains intended for commercial application. I have been advisor to more than 100 graduates (PhD and Master's students).

Literature and professional data show the safety of specific strains of *Bacillus* species such as *Bacillus subtilis* and *Bacillus amyloliquefaciens* for humans (see e.g., AlGburi *et al*., 2016; Lefevre *et al*., 2017). The *Bacillus* strains (being food originated) that will be used by Better Air have no known history of toxicity to humans, and have been shown in well controlled studies neither to be harmful to animals nor detrimental to the environment.

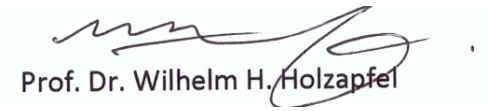
I have found that both the FDA and EPA had approved other applications with similar species as will be used by Better Air. Species such as *Bacillus subtilis* and *Bacillus amyloliquefaciens* are known to be natural occurring, and to be associated with some fermented foods. These particular (Better Air) strains have not been genetically modified. In 2017/2018 HEM has genotypically identified *Bacillus subtilis* strain 3, *Bacillus subtilis* strain 281 and *Bacillus amyloliquefaciens* strain 298, and conducted safety tests which confirmed the absence of beta-hemolysis, lecithinase, and showing sensitivity to the eight selected antimicrobial agents according to the breakpoints suggested by European Food Safety Association (EFSA). In the *in vivo* inhalation and respiratory infection test, these strains (at levels much higher than those to be used in practice by Better Air) were confirmed as safe for the respiratory tract infection, as was also confirmed by the 100 % survival rates of the mice; also, none of these strains was detected in the lungs after sacrifice

In addition, I have reviewed tests conducted in the United States by the GLP laboratory, such as toxicity substance analysis, pulmonary injection, acute dermal, skin & eye Irritation, to complement our safety research. The findings were in line with the conclusions by HEM's scientists, and confirmed no adverse impact on public health. These tests were in line with present approaches for toxicological safety assessment (Baird et al., 2017).

I have also found that other colleagues, such as the Israeli health committee, have approved the product as safe for clinical studies on Asthma patients under the Helsinki protocol.

I believe Better Air has made every effort that might be required by principles of good practice for the

safety assessment in order to ensure the safety of the product for use in an indoor environment. There the effect of removing pathogens and allergens will not be compromised by any health risk with regard to a normal healthy population.



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Please See PROF. DR. WILHELM HOLZAPFEL-Short Biography Below:

PROF. DR. WILHELM HOLZAPFEL-SHORT BIOGRAPHY

Professor, Handong Global University, Pohang, South Korea.
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Short Biography:
Wilhelm Holzapfel obtained his doctorate (Dr. rer. nat.) at the Technical University of München, Germany, at the age of 27. He joined the University of Pretoria, RSA, first as Senior Lecturer in Microbiology in 1972, and was promoted to Associate Professor (1982-1984) and Full Professor (1985-1987). He was head and director of the Institute for Hygiene and Toxicology in Karlsruhe, Germany, from November 1987 to January 2007, and was also Hon. Professor for Industrial Microbiology from 1996 to 2007 at the Technical University of Karlsruhe (now KIT), and was also extraordinary Professor for Microbiology at Stellenbosch University, RSA, until 2007. Presently he is Chair Professor at the Graduate School of Advanced Green Energy and Environment (AGEE), and is also associated with the School of Life Sciences at Handong Global University, South Korea. He is president of the ICFMH of the IUMS (International Committee on Food Microbiology and Hygiene of the International Union of Microbiological Societies) since 1996. He has published over 300 scientific papers, 63 book chapters and edited five scientific books. He is member of various microbiological societies and honorary member of the Hungarian Society of Microbiology. He has also presented various keynote and plenary lectures at international meetings. His major interest is in the lactic acid bacteria, their physiology, functionality, taxonomy, biodiversity and role in different ecosystems. Present research focus is on probiotics and their impact on gut microbiota.
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