

IMPLICATIONS OF EU REGULATION 511/2014 ON RESEARCH ON THE HUMAN MICROBIOME

SUBMISSION

Prepared by the ICC Task Force on Access and Benefit Sharing

Summary and highlights

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Executive Summary

It is ICC's view that the human microbiome should not be subject to due diligence obligations under the EU Regulation 511/2014 (Regulation) because States have no sovereign rights over the human microbiome of their citizens. This view is based on the following arguments:

- The Convention on Biological Diversity (Convention) and the Nagoya Protocol (Protocol) are based upon the principle of sovereign rights of Contracting Parties over their natural resources. The CBD and the Protocol are not applicable to human material.
- The term "human" is not defined in the CBD, the Protocol or the Regulation but must include all normal functions of the human organism, including cells that live in and on our bodies which are necessary for the proper functioning of the human body. The human microbiome is therefore an integral and indispensable part of a human being and should therefore be considered as human material.
- This is clearly different for pathogens which are not essential for the proper functioning of human physiology but in contrast are the cause of its dys-functioning.
- The make-up of the microbiome of an individual person is unique. Because of this individuality the human microbiome also experiences protection of personality as a human right which is governed by the Universal Declaration of Human Rights, and for the EU the European Convention on Human Rights.
- Conclusion: Ownership of a specific microbiome as part of a human being belongs to the individual, not the State (Party) and the human microbiome experiences protection of personality. Accordingly, States cannot assert sovereign rights over the microbiomes of their citizens.

1. Background

The human microbiome is essential for a human being's proper functioning of its physiology. This is true for cells living on and for those living in a human's body, especially in the digestive tract, but also the mouth and the lungs. Today it becomes even better understood that improper functioning of the human microbiome can be the cause of serious diseases, incl. neurological diseases. This is illustrated by research undertaken under the National Institutes of Health Human Microbiome project (<https://commonfund.nih.gov/hmp>) and the EU MetaHit project (<http://www.metahit.eu/>) and described, e.g., in the NBC News article by Lois Parshley (MACH: January 26, 2017). A specific example how research can give insights and help better understand specific diseases is shown by the example provided in the Annex. A second example in the Annex illustrates the relevance of the human microbiome for other areas of research, namely the development of food additives

2. Legal Considerations

The term "human" is not defined in the CBD, the Protocol or the Regulation, but must include all normal functions of the human organism, including cells that live in and on the human body which are necessary for its proper functioning, as all together play a crucial role in the metabolism and the physiology of the human being, during his entire life time. The immune system of a neonate cannot

be formed without the presence of a microbiota. The microbiome is known to be passed on from one generation to the other. This shows the importance of the close evolutionary link between the human being and his/her microbiome and supports further the essential functional link. Considerable disturbances of the microbiome will lead to disease¹.

The concept of “human” - i.e. what belongs to the human body - has also to be seen in the light of current insights about the essential function of endosymbionts in living organisms as is the case for the human microbiome. It has been estimated that there are roughly the same number of microbial cells in and on humans than “human” cells. From an evolutionary point of view, endosymbionts are common place and an inseparable part of an organism.

To better understand the difference between the human microbiome and other organisms which can live in the human body a comparison to human pathogens is helpful. In contrast to the human microbiome, human pathogens are not an essential element of the proper functioning of the human physiology but in contrast the cause of diseases which lead to a dysfunction of the human body.

Although individual microorganisms of the human microbiome may exist outside the human body, the complete microbiome of a specific person only exists as such as part of the specific human being. The specific microbiome isolated from an individual person makes it a unique human material. Because of this individuality the human microbiome also experiences protection of personality as a human right which is governed by the Universal Declaration of Human Rights.

Article 3 of the Convention reads: “States have, in accordance with the Charter of the United Nations and the principles of international law, the sovereign right to exploit their own resources [...]”. Sovereign rights, therefore, are based on ownership (property). In contrast, human rights are independent from national sovereignty, and the exercise of sovereign rights are thus limited by human rights. Human rights are protected by the Universal Declaration of Human Rights. In Europe, these are also stipulated in the European Convention on Human Rights (including article 8 on personal life, which includes the right of personal autonomy). There are no sovereign rights over humans and human material. This is recognized by Article 3 of the Convention referring to “the Charter of the United Nations and the Principles of International Law”. Article 15 of the Convention takes up this concept of sovereign rights: “Recognizing the sovereign rights of States over their natural resources ...”; Article 3 of the Nagoya Protocol explicitly refers to Article 15 of the Convention; finally, the Protocol is implemented in the EU through the Regulation. Accordingly, Article 4 of the Regulation cannot trigger compliance obligations for the human microbiome.

The concept of sovereign rights refers not only to sovereignty at the International level but addresses also the idea of a property right at the national level. The EU Regulation has direct legal effects on users in EU Member States. A comparison with civil law, shows that the human microbiome can be seen as a “separated body part” which, experiences protection of personality by the original bearer. This is an established legal principle under the national laws of EU Member States, e.g. in Germany and Belgium. This general personality right translates into the (subjective) right of self-determination (“Selbstbestimmungsrecht”) by a person over his or her body parts. This is also further implemented in more specific laws, e.g. on transplantation and tissue and blood donation. This private right supersedes and cannot be made subject to sovereign rights of a state. In the event of conflict, between the concept of sovereign rights (under the Convention, the Protocol and the Regulation) and private rights pursuant to human rights protection, the protection of personality precedes property rights protection and can therefore not be subject of sovereign (property) rights under the EU Regulation².

¹ For these and other technical statements references are available upon request.

² see also H. Zech, Anwendbarkeit des Übereinkommens über biologische Vielfalt und des Nagoya-Protokolls auf das humane Microbiom?, GRUR 9, 881- 886 (2018)

3. Consequences for users in case the EU Regulation would be applicable

Article 4.1 of the EU Regulation requires users to “*exercise due diligence to ascertain that genetic resources... which they utilize have been accessed in accordance with applicable access and benefit-sharing legislation or requirements, and that benefits are fairly and equitably shared upon mutually agreed terms, in accordance with any applicable legislation or regulatory requirements*”. For said purpose, users are required under subparagraph 3 (b) to seek, among other documents, access permits and mutually agreed terms, including benefit-sharing arrangements where applicable.

Today people are far more mobile, and participate in a global economy, traveling, sharing, moving, and emigrating. In the case of the human microbiome, it would be impossible to define the specific country of origin and in what way any Party could assert ownership, if it were recognized that States have sovereign rights over human material, like the human microbiome. Complications include current nationality (or dual nationalities) of the person harboring the microbiome and of his/her mother, the place of birth of the person itself, the countries that the person visited or lived in his/her lifetime, and even the origin of the food that the person eats. Microbes in food are a major environmental source of microbes in the human body, so food ingested locally but originating from another country may contribute to the microbial population in a human body.

As long as any legal uncertainty with respect to the human microbiome persists, it will have a chilling effect on research. Without clarity, important research by academics and companies in the EU would be significantly delayed, or not begun at all, due to the onerous and potentially impossible task of identifying a country of origin (which may be different for each microbe in a microbiome composition) and the need to enter into an ABS negotiation even before being able to obtain data that is meaningful for further research and development. Such hurdles would also be a barrier for third parties outside Europe when considering a collaboration with an entity in Europe.

4. Conclusions

The human microbiome should be considered as human material which is protected by a well-defined personality right, also explicitly recognized pursuant to human rights, which cannot be made subject to sovereign rights because the human microbiome: (1) exists in humans, (2) is essential for the proper functioning of human physiology and therefore an indispensable component of a human being, and (3) is unique for an individual person. In view of the concept of sovereign rights as confirmed by the Convention, the Protocol and the EU Regulation, the human microbiome, or its components, cannot be subject to any obligations related to access and benefit sharing.

APPENDIX

Example 1:

Microbes naturally exist in humans. Understanding the composition of these microbial communities and the abundance of different microbes relative to each other in patients might be helpful towards, for example, identifying the state of a disease, predicting which drugs will be useful for treating a disease state, or identifying bacterial compositions that may be used as a drug for treating a human disease.

In one example of this, the microbial composition from stools obtained from patients that have participated in world-wide clinical trials before and after treatment with a specific drug is analyzed in the EU (isolation and classification of the component microorganisms in patients before and after treatment, e.g. by genomic sequencing and comparison to existing sequences). From this analysis, hypotheses may arise regarding microbial compositions that could be (1) predictive of responders to the specific drug (“predictive biomarker”), (2) prognostic of the state of a disease (“prognostic biomarker”) or (3) candidates as potential drugs for treating a disease. Each of these hypotheses would then take several more years of preclinical study and further testing in clinical settings in order to be accepted by the regulatory agencies around the world. This information could also be most useful for academics and companies to help to better understand the biology of the disease itself and of a specific drug. Additionally, these isolated microbes can be used for further scientific study, including for the study of metabolites released by the microbes which, in turn, could be turned into new drugs. Finally, isolated microbes can also be genetically modified to understand the biology of the human disease or for study as a potential drug candidate.

Example 2:

Probiotics are live microorganisms which, when consumed in adequate amounts, confer a health benefit. For instance, *Lactobacillus rhamnosus* GG (LGG), a well-known probiotic lactic acid bacterium, shows beneficial effects in the prevention and treatment of antibiotic associated diarrhea, a common complication in childhood.³ Probiotics are thought to support and maintain a healthy human microflora; it is thus not surprising that the healthy human microflora itself is an important source of probiotics, be it for probiotics already on the market, or for probiotics still to be discovered or in development.⁴

Selected examples of probiotics that are already on the market, and that have been isolated from the human microbiome, include the following:

- *Lactobacillus rhamnosus* GG (LGG; see above)⁵
- *Bifidobacterium lactis* Bi-07, *Lactobacillus acidophilus* La-14, *Bifidobacterium lactis* BI-04, *Lactobacillus gasseri* Lg-36 and *Lactobacillus acidophilus* NCFM⁶
- *Lactobacillus plantarum* 299v⁷

³ For a review article, see Mantegazza et al., Pharmacol. Res. 128 [2018], 63-72.

⁴ Fernandez et al., Pharmacol. Res. 69 (2013), 1-10; Mandal et al., Can. J. Microbiol. 62 (2016), 349-359; Nami et al., J. Appl. Microbiol. 117 (2014), 498-508; Yang et al., J. Microbiol. Biotechnol. 27 (2017), 1971-1982.

⁵ <https://www.chr-hansen.com/en/probiotic-supplements-and-infant-formula/cards/product-cards/lactobacillus-rhamnosus-gg-trademark-lgg?>

⁶ <http://www.danisco.com/product-range/probiotics>

⁷ <https://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/GRAS/NoticeInventory/ucm544492.pdf>



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INTERNATIONAL CHAMBER OF COMMERCE

33-43 avenue du Président Wilson, 75116 Paris, France

T +33 (0)1 49 53 28 28 F +33 (0)1 49 53 28 59

E icc@iccwbo.org www.iccwbo.org