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The law for mini-organ prototypes in a dish. Mapping the legal status options for organoids in Swiss law

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ABSTRACT

Advances in generating human mini-organ prototypes will further improve fundamental research,[1] disease modeling,[2] drug screening[3] and the development of personalized medicine.[4] Currently, there is no legal definition, identified legal status, or existing regulatory framework for organoids. Ethical discussions regarding brain and embryo-like mini-organ models leave researchers uncertain about the extent to which work on any organoids is legally permissible. The legal protection of human embryos, many other

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1 Y. Li, et al., *Organoid based personalized medicine: from bench to bedside*, 9 Cell Regen (2020).

2 Jihoon Kim, Bon-Kyoung Koo, Juergen A Knoblich, *Human organoids: model systems for human biology and medicine*, 21 Nature Reviews Molecular Cell Biology (2020); Smriti Mallapaty, *The mini lungs and other organoids helping to beat COVID*, News Nature, 26 May 2021.

3 Lisa Liu, et al., *Patient-derived organoid (PDO) platforms to facilitate clinical decision making*, 19 Journal of Translational Medicine (2021).

4 Li, Cell Regen (2020); H. C. Clevers, *Organoids: Avatars for Personalized Medicine*, 68 Keio J Med (2019). Marie-Anne Meier, et al., *Patient-derived tumor organoids for personalized medicine in a patient with rare hepatocellular carcinoma with neuroendocrine differentiation: a case report*, 2 Communications Medicine (2022).

separated human body parts[5] as well as organoids is more complex than the application of the traditional rules of rights *in rem* or of the law of personality alone. The paper's focus is to examine whether the legal status of organoids or lack thereof, could influence their concrete regulatory framework, or whether a legal status in private law is necessary for their regulation. This paper deliberately chooses not to attempt a unifying theory of law but rather to argue for a possible regulation of organoids using the example of Swiss law.[6] While, at present, there is no comprehensive research addressing either the status or the regulation of organoids, we believe that the argumentation presented could improve the overall understanding of how a potential organoid regulation could be set out within national legal frameworks.

KEYWORDS: legal status, organoids, cerebroids, embryoids, embryo, embryo surrogates

I. INTRODUCTION

The scientific world is excited about the potential of mini-organ prototypes, or organoids. These three-dimensional (3D) models are generated from embryonic stem cells (ESCs); from artificially created cells, ie, induced pluripotent stem cells (iPSCs); from organ-specific adult stem cells (ASCs);[7] or from culturing biopsied, aspirated, or surgically resected tissue used, for instance, to generate tumor organoids.[8] Organoids used in research represent certain aspects of the human system (eg lungs or intestine). This gives organoids a privilege over animal experimental matter, as non-human animals do not always share the same histological and biological characteristics as humans. However, the use of organoids encounters several limitations, including a lack of the development, behavior, and health of living beings, and therefore remain suitable only for a particular organ or its part. Still, organoids, could contribute to the 3 Rs principle (refine, reduce, replace)[9] as defined by Russel and Burch.[10]

From a legal perspective, we would prefer to address not only scientific understandings but also the legal definition of organoids in Swiss law. The legal definition is important because it could impact legal status as well as define which laws

5 Philippe Ducor, *Statut juridique des parties détachées du corps humain Une approche anatomique fonctionnelle*, 135 Zeitschrift für Papyrologie und Epigraphik, 256 (2016).

6 We use Switzerland as a reference country not only because Switzerland is a major player in organoid research (please refer to J. Y. Shoji, et al., *Global Literature Analysis of Organoid and Organ-on-Chip Research*, 13 Adv Healthc Mater (2024).) but also because its private law is influenced by both German and French (Roman) traditions (please refer to André Brunschweiler Sandrine Giroud, Noémie Raetzo, *Switzerland*, in International Civil Procedure SW1 (Christian Campbell Dennis Campbell ed. 2019). It could therefore be a potential example for other European countries. Regarding the regulatory aspects, the authors refer to Swiss law, as most of the issues addressed in this paper are regulated not on the international or the European Union but at the national level.

7 T. Sawai, et al., *Mapping the Ethical Issues of Brain Organoid Research and Application*, 13 Ajob Neurosci (2022).

8 Zhen Fang, et al., *The role of organoids in cancer research*, 12 Experimental Hematology & Oncology (2023).

9 Wageningen University and Research, *Mini Intestines Replace test animals*(2020), available at https://www.wur.nl/en/research-results/research-institutes/food-safety-research/show-wfsr/mini-intestines-replace-test-animals.htm

10 R. L. Burch W. M. S. Russell, The principles of humane experimental technique [1959 (as reprinted 1992)].

are applicable for their regulation. There is, however, no appropriate legal definition[11] of organoids as a whole or their types, and even scientists working in this field have a different opinion of what organoids should constitute. The main features of organoids that scientists mostly agree upon are their multicellular structure, their recapitulation of cell types, their organ structure and organ function, their 3D structure, and the necessity of an extracellular matrix.[12]

Not only do organoids lack a definition, but also their legal status is likewise unclear. Organoids could be classified as a legal subject (persona, person) and (or) as a legal object [res(es), things] under private law. The reason for potential duality is rooted in the mixed character of organoids. On the one hand, the status of organoids could be compared to that of their starting material, ie, cells and tissues. On the other hand, organoids, specifically those akin to the brain or the embryo, could display some elements reminiscent of a person. Embryo-like organoids have the potential ability to create an early-stage human-like organism, and brain-like organoids may manifest an ability to have a consciousness. The key question here is whether these features suffice as a basis for establishing that organoids should have the status of a person or whether they can be classified as things. Accordingly, they would either be treated as persons with their own rights or obligations, or they would be regarded as property. We emphasize, however, that the legal status of organoids may become less relevant as the boundaries between persons and things become blurred from a regulatory perspective and that it is possible that the organoid's regulatory framework might function independently of their defined legal status.

II. ORGANOID STATUS FROM A PRIVATE LAW PERSPECTIVE

The Swiss private law system is based on the distinction between persons, things, and animals.[13] Organoids as a whole or different organoid types may be found in different legal categories or in none of them at all. This largely depends on organoid features.

II.A. Organoids as Persons

Persons or legal subjects is a legal category assigning all persons as the bearers of rights and obligations having a right to personality *(die Persönlichkeit)*.[14] The right to personality[15] begins at birth, ie when the child has completely left the mother's body.[16] Legal

11 Please refer to: Jochen Taupitz, *Organoide: die deutsche Rechtslage*, *in* Organoide: ihre Bedeutung für Forschung, Medizin und Gesellschaft, herausgegeben von Sina Bartfeld, Hannah Schickl, Cantas Alev, Bon-Kyoung, Koo, Anja Pichl, Angela Osterheider, Lilian Marx-Stölting (2020); Hybrida, *Regulating organoid research. Embedding a comprehensive ethical dimension to organoid-based research and related technologies*(2020–2023), available at https://hybrida-project.eu/. Hybrida project, however, does not encounter legal questions of definition and status of organoids.

12 cf. Clémentine Le Magnen, Organoid Interview Nr. 4 Pos. 44–45, 51 (Inesa Fausch & Daniel Zeyer-Iyengar ed., 2023); cf. Prisca Liberali, Organoid Interview Nr. 2 Pos. 16 (Alfred Früh & Daniel Zeyer-Iyengar ed., 2023); cf. Amiq Gazdhar, Organoid Interview Nr. 3 Pos. 47 (Inesa Fausch & Daniel Zeyer-Iyengar ed., 2023);

13 Although animals are not things, the rules applicable to things apply to animals, pursuant to Art. 641 a Swiss Civil Code. Please refer to the Section II.B of this paper.

14 Art. 11 Swiss Civil Code.

15 Ivo Schwander, *Art. 11 N 1*, in ZGB Kommentar, Schweizerisches Zivilgesetzbuch (Jolanta Kren Kostkiewicz; Stephan Wolf; Marc Amstutz; Roland Fankhauser ed. 2021).

16 Art. 31 Swiss Civil Code; Peter Breitschmid, *Art. 31 N 2*, in Personen und Familienrecht Art. 1 bis 456 ZGB. Partnerschaftsgesetz (Ruth Arnet; Peter Breitschmid; Alexandra Jungo ed. 2023);

doctrine grants personhood to all born human beings guided by moral reasons[17] and do not confer personality rights on individual body parts. Because organoids are not born humans, but miniature human organ prototypes generated from separated human body parts,[18] they are not legal persons and thus cannot acquire rights and obligations. Exceptions are, however, possible. Regarding organoids, the status of, embryo- and brain-like organoids is particularly controversial, and their right to personhood needs to be discussed in detail.

II.A.1. Embryoids

There is no legal definition of embryoids. In scientific literature, one can find that embryoids are also called stem cell-based embryo models[19] or synthetic embryos[20] and are defined as a multilayered cluster of differentiating ESCs (or iPSCs)[21] that resembles an embryo at certain stages of early development.[22] To date, embryoids, cannot develop to the equivalent of postnatal-stage[23] humans.[24] With relation to human embryo, we need to distinguish different embryo and alike organisms, which play role in comparing them to embryoids. These are embryo in vivo, embryo in vitro, embryonic stem cells, and induced pluripotent stem cells, which are starting materials for embryoid generation. Embryoids share similarities with all of the above categories.

Embryoids as embryo in vivo and embryo in vitro To compare the status of embryoids to a human embryo, we need to define the status of the human embryo both in vitro and in vivo.

There is no unanimous understanding of embryos in vivo regarding their legal status.[25] Swiss law defines a human embryo by way of fertilization to the completion of organ development,[26] ie embryo in vivo means *'the offspring, from the fusion of the cell*

Hans Michael Riemer, Personenrecht des ZGB Studienbuch und Bundesgerichtspraxis. 2. Auflage N 120 (2002).

17 Anja J. Karnein, A Theory of Unborn Life. From Abortion to Genetic Manipulation 18 ff. (Oxford University Press. 2012).

18 Mélanie Mader, Le don d'organes entre gratuité et modèles de récompense. Quels instruments étatiques face à la pénurie d'organes? 380 (Helbing Lichtenhahn Verlag. 2010).

19 International Society of Stem Cell Research ISSCR, *The ISSCR Statement on New Research with Embryo Models* (June 26, 2023), available at https://www.isscr.org/isscr-news/isscr-statement-on-new-research-with-embryo-models.

20 See, for example, N. C. Rivron, et al., *An ethical framework for human embryology with embryo models*, 186 Cell (2023).

21 Opinion of the Conseil d'orientation: stem cell-based embryo models. (21 September, 2023); ISSCR. June 26, 2023.

22 M. Simunovic & A. H. Brivanlou, *Embryoids, organoids and gastruloids: new approaches to understanding embryogenesis*, 144 Development (2017).

23 The postnatal period begins immediately after the birth of the baby and extends up to 6 weeks (42 days) after birth. Please refer to World Health Organisation, *Technical Consultation on Postpartum and Postnatal Care* (2010), available at https://www.ncbi.nlm.nih.gov/books/NBK310595/.

24 ISSCR. June 26, 2023.

25 See, for instance, Andrea Büchler, Reproduktive Autonomie und Selbstbestimmung. Dimensionen, Umfang und Grenzen an den Anfängen menschlichen Lebens 21 f. (2017); Clausen Sandro Büchler Andrea, *Pränataler Kindesschutz*, FamPra.ch, 655 (2018).

26 The definition of an embryo, and therefore its regulation, varies in different European countries and is not harmonized. For example, 'legally, an embryo is not the same in Germany—where only the fertilized ovum is considered as such after the fertilization process has been completed—as it is in Spain—where

nuclei (karyogamy) to the completion of organ development'.[27] Some legal scholars suggest that despite the lack of a clear legal status, only embryos in vivo, those that can actually develop into human beings, are normatively significant and subject to legal protection[28] due to the sacred value[29] attached to them and considering their nature.[30] This line of argument finds support, for instance, in inheritance law, where only a fetus, once born, has a right to inherit.[31] Organoids, in turn, could not be compared to embryos in vivo and not be subject to the same legal protection, as they are generated and grow outside of the human body.

An in vitro embryo, as opposed to an in vivo one, is created during in vitro fertilization, ie the sperm fertilizes the eggs outside of a human body. In Swiss law, the embryo in vitro is called a *surplus embryo,* which means *'an embryo produced in the course of an in vitro fertilization (IVF) procedure that cannot be used to establish a pregnancy and therefore has no prospect of survival'*.[32] Similarly, there is no consensus neither in the literature nor in case law as to whether embryos in vitro fall into the category of legal subjects, objects, or a legal tertium[33] and the scope of their dignity protection is debatable.[34] In contrast to embryos in vivo, to date, embryos in vitro cannot develop into a human.[35]

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a distinction is being made between embryo and pre-embryo—or in the Netherlands where it is a cell or group of cells with the potential to develop into an embryo' *Iñigo De Miguel Beriain, et al., Re-defining the human embryo, 25 EMBO* reports *(2024).*

27 Art. 2 lit. a Federal Act on Research Involving Embryonic Stem Cells. Precise clarification of what is exactly meant by 'completion of organ development' is not provided in the Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA), 1168 (2002). More precise is the medical embryo definition, where a human embryo is usually understood to be from the fertilized egg or from implantation in the uterus to the completion of organogenesis. The latter has a precise timeframe, as completion of organogenesis usually is due by week eight when the fetus appears human-like and is prepared to undergo further growth and differentiation. For more information, please refer to: Cascella M. Donovan MF, *Embryology, Weeks 6–8* (10 October, 2022), available at https://www.ncbi.nlm.nih.gov/books/NBK563181/.

28 See analysis provided by Karnein, 282012; See for example, Art. 19 Para. 2 Federal Constitution of the Swiss Confederation; Brigitte Tag, *Art. 30 Entwicklung von Embryonen ausserhalb des Körpers der Frau, in* Fortpflanzungsmedizingesetz (FMedG) N 2 (Andrea Büchler; Bernhard Rütsche ed. 2020); Breitschmid, Art. 31N 8. 2023; Marcus Düwell, *Human Dignity and the ethics and regulation of technology*, in The Oxford Handbook of Law, Regulation and Technology 177–178 (Roger Brownsword; Eloise Scotford; Karen Yeung ed. 2017).

29 Eric Rakowski, *The Sanctity of Human Life*, 103 The Yale Law Journal, 2069 (1994); Ronald Dworkin, Life's dominion: an argument about abortion, euthanasia, and individual freedom (Harper Collins 1993).

30 Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA), 1187–1199 2002; Federal Council Dispatch concerning the amendment of the constitutional provision on reproductive medicine and gene technology in the human sphere (Art. 119 of Swiss Constitution) and the Reproductive Medicine Act (Preimplantation genetic diagnosis), 5946 (2013).

31 Art. 480 Para. 1; Art. 545 Para. 1 and Art. 311 Para. 3 Swiss Civil Code.

32 Art. 2 lit. a Federal Act on Research Involving Embryonic Stem Cells.

33 Vagias Karavas, Körperverfassungsrecht. Entwurf eines inklusiven Biomedizinrechts 87 ff. (Dike Verlag 2018).

34 Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA), 1187–1199 2002.

35 Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA) 1164. 2002.

They are neither persons nor 'things';[36] however, they encounter use restrictions. For example, embryo research is limited to 7 days[37] of embryo development, after which it is no longer possible to derive stem cells from it.[38] Moreover, it is forbidden to create an embryo in vitro for research purposes, to import or export them, or to implant them in a woman for the purpose of stem cell derivation, etc.[39]

We can compare embryos in vitro to embryoids. The main reason for this is the fact that both show similar features and structure as well as the inability to develop into human beings[40]. So far, scientists have been able to create embryoids that show an early stage of human development equivalent to that of natural embryos in vitro about 14 days after fertilization. This is already 7 days longer than the allowed research duration on human embryos in Switzerland[41] and gives rise to a discussion about whether embryoids are 'more' than only an embryo-like model. It is currently not known whether embryoids have the exact same potential of development as a human embryo in vitro. At the same time, we also need to take into consideration the main difference between embryos in vitro and embryoids. Both are created in a different way. While embryoids are created from stem cells, either embryonic or induced pluripotent, the human embryos in vitro are a result of fertilization,[42] the fusion of female and male

36 Lenke Wettlaufer, Mensch und Tier in Transzendierung, Eine rechtliche Auseinandersetzung mit der Bildung und Nutzung von Mensch-Tier-Mischwesen unter Einbeziehung biologischer ethischer und christlich-theologischer Aspekte 376 (Zürich/St. Gallen 2018); Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA), 1187–1199 2002; Federal Council Dispatch concerning the amendment of the constitutional provision on reproductive medicine and gene technology in the human sphere (Art. 119 of Swiss Constitution) and the Reproductive Medicine Act (Preimplantation genetic diagnosis), 5946 2013; Andrea Büchler & Margot Michel, Medizin Mensch Recht (PrintPlu§), Eine Einführung in das Medizinrecht der Schweiz 23 (Schulthess).

37 Most EU countries have a 14-day rule, according to K. R. Matthews & D. Moralí, *National human embryo and embryoid research policies: a survey of 22 top research-intensive countries*, 15 Regen Med (2020); Art. 3 Para. 2 lit. c Federal Act on Research Involving Embryonic Stem Cells.

38 It is also prohibited to create embryo outside of women body or implant human embryo into animal, please refer to Art. 3 Para. 1 lit. a, Art- 3 Para. 2 lit. c Federal Act on Research Involving Embryonic Stem Cells; Art. 29 Para. 1 and Art. 30 Federal Act on Medically Assisted Reproduction.

39 Art. 3 Para. 1 lit a, Art. 3 Para. 2 lit. b and d Federal Act on Research Involving Embryonic Stem Cells.

40 Thus far, both embryoids and in vitro embryos have been unable to develop into human beings outside the human body, including the technology of ectogenesis. While there have been some successful outcomes with ectogenesis technology on a live lamb fetus that has been preserved for 4 weeks, there has been no research conducted on a human being to date. Furthermore, while embryoids are more comparable to the characteristics of embryo development, ie before the 11th week of pregnancy, the subjects of ectogenesis are more comparable to the fetus, ie the development of a human being after the 11th week of pregnancy. It is therefore possible that, in the future, when embryoids demonstrate similarities to a human fetus, their status may be comparable to that of a subject of ectogenesis. Nevertheless, at this time, this does not appear to be a scientifically feasible proposition and is therefore not elaborated upon in the article. Francesco Maria Bulletti, et al., *The artificial uterus: on the way to ectogenesis*, 31 Zygote (2023); Nick Colgrove, *Subjects of ectogenesis: are 'gestatelings' fetuses, newborns or neither?*, 45 Journal of Medical Ethics (2019); Emily A. Partridge, et al., *An extra-uterine system to physiologically support the extreme premature lamb*, 8 Nature Communications (2017); John P. Cunha Melissa Conrad Stöppler, *Embryo vs. Fetus: Differences Between Stages Week by Week*, available at https://www.medicinenet.com/embryo_vs_fetus_differences_week-by-week/article.htm.

41 Most EU countries have a 14-day rule, according to Matthews & Moralí, Regen Med (2020); Art. 3 Para. 2 lit. c Federal Act on Research Involving Embryonic Stem Cells.

42 Philip Ball, *Most advanced synthetic human embryo models yet spark controversy*, Nature (16 June 2023), available at https://www.nature.com/articles/d41586-023-01992-0.

gamete nuclei.[43] This suggests that embryoids and human embryos in vitro are not comparable from a biological or legal point of view.[44] Here, the biological creation of an embryo in vitro is still strictly linked to the legal protection of human dignity.[45] It would therefore be premature to grant the same legal protection to embryoids as to human embryos created in vitro. This alone does not mean that embryoids could not encounter protection and fall under special regulations. One possibility would be that embryoids are subject to the same legal restrictions as similar technological processes that allow the development of organisms without fertilization, such as *parthenotes*.[46] The technological processes even if they have some similarities, however, are not identical. With relation to parthenotes, parthenotes, in contrast to embryoids, could show only very early development, ie the development into a blastocyst-like structure.[47] Another possibility would be to consider a special legal protection for embryo surrogates, like embryoids, according to completeness, from partial to complete organism, as well as a scaling[48] according to how advanced the developmental stage of an organism is.[49] The more advanced the technology is in the development of an organism, the stricter the regulation will be.

To conclude, embryos in vivo and embryos in vitro, while showing similar features, are not identical to embryoids. While, *de lege lata*, embryoids cannot be compared to embryos in vivo, they are closer to in vitro embryos. Whether embryoids could encounter the same protection as embryos in vitro is debatable from biological and legal perspectives and therefore depends on a social and political agreement. Ultimately, it is for the Swiss legislator to decide on how to regulate embryoids. While, *de lege ferenda*, granting embryoids the same legal protection as embryos in vitro might be premature, it may be unavoidable to consider similarities to other technological processes as well as separate legislation for embryo surrogates.

Embryoids and stem cells There are also good reasons to argue that embryoids are not legal persons, not 'embryos' but actually things and to compare embryoids to ESCs or iPScs, ie the starting materials they are generated from. In our opinion, the explanation of their similarities could be found, in the nature of embryoids. First of all, ESCs, iPScs, and embryoids have the ability to differentiate into various cell types but

43 Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA), 1187–1199 2002; Federal Council Dispatch concerning the amendment of the constitutional provision on reproductive medicine and gene technology in the human sphere (Art. 119 of Swiss Constitution) and the Reproductive Medicine Act (Preimplantation genetic diagnosis), 5946 2013.

44 R. Lovell-Badge, et al., *ISSCR Guidelines for Stem Cell Research and Clinical Translation: The 2021 update*, 16 Stem Cell Reports (2021); International Society for Stem Cell Research ISSCR, *Guidelines for Stem Cell Research and Clinical Translation* (May, 2021), available at https://www.isscr.org/guidelines.

45 Federal Council Dispatch concerning the Federal Act Research involving Surplus Embryos and Embryonic Stem Cells (Embryo Research Act, ERA), 1187–1199 2002.

46 A parthenote is an organism derived from an unfertilized oocyte, whose development in Switzerland is prohibited, despite lack of consensus on its similarity to conventional embryo definition. Art. 2 Para. d and Art. 3 Para. d Federal Act on Research Involving Embryonic Stem Cells.

47 International Stem Cell v Comptroller General of Patents, C-364/13 (CJEU).

48 ISSCR, 10–11. May, 2021.

49 See for example, Paola Nicolas, et al., *The ethics of human-embryoids model: a call for consistency*, 99 Journal of Molecular Medicine (2021).

not to develop into a human being. Secondly, embryoids are artificially generated cell-based 'products' from either ESCcs or iPScs and not cells *per se*, that occur in nature. For this reason, we further compare embryoids to iPScs. To clarify, embryoids and iPSc are similar as both could be generated from adult cells[50] as their starting materials and both are mainly used as research tools. Thus, embryoids, like iPScs, are not clearly identified in law, but because of the way of their creation and use, they could be classified as biological materials[51] separated from the human body, ie things (III.A). As things, the regulation of embryoids could largely depend on the materials from which they are generated. If embryoids are generated from ESCs, they might fall under the same strict regulation of ESCs under the Stem Cell Research Act.[52] This means that in order to carry out any research on domestically available or imported ESCs, a license *(die Bewilligung)* from the Federal Office of Public Health is required, as well as approval from an ethics committee.[53] A licensee is also subject to numerous duties with relation to derivation of ESCs.[54] However, if embryoids are created from iPScs, their regulation is less strict, in accordance with the provisions for human biological material in the Human Research Act.[55] If iPScs are anonymized, they are not subject to the Human Research Act, and, if they are pseudonymized or coded, only the consent of donors of biological material as well as the approval for the research project from an ethics committee in order to conduct a research project shall be required[56] (III.A).

The Swiss legislator as well as scholars remain silent as to whether embryoids shall be regulated the same as the starting materials they are generated from. This, in turn, leaves room for interpretation and the possibility of applying legal provisions on the regulation of human embryoids. The main problem is that human embryos in vitro, ESCs, and other biological materials (like iPScs) have different legal protections, allowing for stringent regulation of embryoids being interpreted and assigned to one of the categories. In discussing the Swiss situation, we see a clear need to re-evaluate the legal status of the human embryo in vitro and human embryo surrogates, highlighting the need for clarity for embryoids, especially as they are not only cell-generated prototypes of organ models but also coming closer and closer to the actual human embryo in vitro.

II.A.2. Cerebroids or brain organoids

Brain-like organoids are organoids that can recreate many features of the fetal human brain.[57] This raises an ethical question as to the moral value[58] of manipulating such organoids, leaving us a need to clarify their status from a legal perspective.

50 *The promise of organoids and embryoids*, 20 Nature Materials (2021).

51 Inesa Chmurec, *iPS cells and iPS cell-based therapies - Swiss and UK perspective on definition and regulation*, *in* Stammzellen - iPS-Zellen - Genomeditierung. Stem Cells - iPS Cells - Genome Editing (Henning Rosenau Susanne Müller ed. 2018).

52 Art. 1 Para. 1 Federal Act on Research Involving Embryonic Stem Cells.

53 Art. 8 Federal Act on Research Involving Embryonic Stem Cells.

54 Art. 9 Federal Act on Research Involving Embryonic Stem Cells.

55 Chmurec. 2018; Please compare Section 1 and Section 2 of the Federal Act on Research involving Human Beings.

56 Art. 2 Para. 2 lit. b and Art. 45 Federal Act on Research involving Human Beings.

57 Ilaria Chiaradia & Madeline A. Lancaster, *Brain organoids for the study of human neurobiology at the interface of in vitro and in vivo*, 23 Nature Neuroscience (2020).

58 Joshua Jowitt, *On the Legal Status of Human Cerebral Organoids: Lessons from Animal Law*, Cambridge Quarterly of Healthcare Ethics 575 (2023).

Organoids based on the human brain, being generated in a laboratory and not coming from born human beings, are not persons. Any special protection for brain organoids could be provided only by the legislator, which is currently not in case in Swiss law. We suggest that the protection is necessary only if organoids exhibit features that could identify organoids with a person. For instance, if a brain organoid were sapient (have moral worth[59]), had consciousness, and specifically minimal sentience with respect to the basic experiences of pain and pleasure[60] or had the ability to 'coordinate' and 'integrate' the entire human being,[61] or human body as a whole,[62] they could arguably be treated as a human being. This would entail formulating desires and possessing the capacity to act with purpose and volition.[63] However, to date, cerebroids show only limited *'appearance of discrete, regionally specified brain regions'*[64] and have not shown any characteristics consistent with a comprehensive, functioning human adult brain in vitro,[65] Taking all the aforementioned into account and considering that brain-like organoids could not 'survive' a day without a professional's supervision and cultivation in lab, granting them right to personality or special protection[66] is rather premature. To date, and in contrast to embryoids, cerebroids do not require a special protection regime. While embryoids show an early stage of human development that is equivalent to natural embryos in vitro at about 14 days after fertilization, human brain organoids, have not yet acquired a consciousness similar to that of natural persons. Therefore, at this stage, they can only be considered as brain models that mimic very limited and specific brain regions and can therefore be regulated like other organoid model types.

59 The legal status of brain-like organoids has to be considered if they have passed the moral threshold of sentience, please refer to Jowitt, Cambridge Quarterly of Healthcare Ethics (2023); H. C. Stoeklé, et al., *Ethical Issues of Brain Organoids: Well Beyond "Consciousness"*?, 13 AJOB Neurosci (2022).

60 A. Lavazza & F. G. Pizzetti, *Human cerebral organoids as a new legal and ethical challenge*, 7 J Law Biosci (2020).

61 Federico Gustavo Pizzetti, *Embryos, Organoids and Robots: "legal subjects"*?, BioLaw Journal - Rivista di BioDiritto Artificial Intelligence e Diritto - Focus on (2021); Lavazza & Pizzetti, J Law Biosci (2020).

62 Masanori Kataoka, et al., *The legal personhood of human brain organoids*, 10 Journal of Law and the Biosciences (2023).

63 Please compare to J Jowitt, *Agency, moral worth and the legal status of human cerebral organoids [version 1; peer review: 2 approved]*, 2 Molecular Psychology: Brain, Behavior, and Society (2023); Alan Gewirth, Reason and Morality 48–54 (The University of Chicago Press 1981); Deryck Beyleveld & Roger Brownsword, Human Dignity in Bioethics and biolaw 70–77 (Oxford University Press 2001). *Jowitt in particular* elaborates on the *Gewirth* Principle of Generic Consistency (PGC). PGC states that agents contradict that they are agents if they do not accept that the PGC is the supreme principle governing the permissibility of actions. Human agency is the capability of humans to act independently, making voluntary choices according to their free will. For this, human agents have generic needs, requirements that need to be fulfilled to facilitate successful action toward a purpose. PGC is a moral principle; however, some consider that so far as judgements concerning human dignity are made in bioethics and biolaw, the validity and scope of those judgements must conform with the PGC and considerations that are essentially connected with it.

64 Theresa S P Rothenbücher and Alberto Martínez-Serrano, *Human cerebral organoids and neural 3D tissues in basic research, and their application to study neurological diseases*, Future Neurology (25 January, 2019), available at https://www.futuremedicine.com/doi/10.2217/fnl-2018-0043.

65 Abigail Presley, et al., *Media portrayal of ethical and social issues in brain organoid research*, 17 Philosophy, Ethics, and Humanities in Medicine (2022).

66 Please compare to J. Taupitz, *What Is, or Should Be, the Legal Status of Brain Organoids?*, in Brain Organoids in Research and Therapy. Advances in Neuroethics (HG. Dederer, Hamburger, D., ed. 2022).

II.A.3. Organoids as animals

Under Swiss law,[67] animals are granted, if not an exact status,[68] definitely a special place. We need to consider whether and under which circumstances organoids can fall under the animals' category. According to the statutory provisions, animals are not property (pursuant to Art. 641a para. 1 of Swiss Civil Code). Thus, animals are not things, but their further exact status is until now unclear.[69] This means that animals enjoy special protection across private, public, and criminal law,[70] with an emphasis on protecting their dignity.[71] However, the provisions applicable to things apply to them unless special rules exist (Art. 641a para. 2 Swiss Civil Code), which means they are being treated 'like' things and are property and not beings in their own right.[72] Like animals, organoids, have no clear legal category that they fit into. Essentially declaratory in nature, this regulation *'takes account of the new sensitivity of the population towards animals and the fact that they form a special legal category'*.[73] The legal status of pets thus differs, albeit modestly, from that of things governed solely by rights *in rem* because of the emotional bond that attaches them to their keeper and the respect that is due to them.[74] They therefore form a special legal category, which some scholars compare to the separated human body parts,[75] which despite being things are excluded from commercialization[76]. A parallel could be drawn here with organoids, whose sensitivity could be recognized by granting them a special status, which would not necessarily lead to a special protection regime. However, the Swiss legislator has not yet recognized a special place for organoids in its legislation. Therefore, we must consider the possibility of assigning organoids to the classical categories of either persons or things.

II.A.4. Organoids as things

Swiss legislators, despite providing rules on movable property, have refrained from providing a definition for legal objects or things under property law.[77] Legal doctrine defines things as impersonal, physical objects that exist in their own right and can be

67 Similarly, in Civil Codes of Germany, Austria, France, Czech Republic animals are recognized as not being equal other legal things or goods. The provision, similarly to Swiss one, has mainly declarative meaning, ie §90a BGB1.IS.42, 2909 (2002). Art. 285a BGBl. I Nr. 33/2024 (2024). §494 Zákon č. 89/2012 Sb. (2012). Art. 515–14 (2024). Please refer also to Eva Bernet Kempers, *Neither Persons nor Things: The Changing Status of Animals in Private Law*, 29 European Review of Private Law, 39–70 (2021).

68 Stephan Wolf, *Art. 641 N 3; BSK-Wolf/Wiegand vor ZGB 641 ff. N 17 f*, in ZGB Kommentar, Schweizerisches Zivilgesetzbuch Art. 641a N 3 (Jolanta Kren Kostkiewicz; Stephan Wolf; Marc Amstutz; Roland Fankhauser ed. 2021).

69 Wolf, Art. 641a N 3. 2021.

70 Peter V Kunz, *Tier(schutz)recht zwischen Ideologie und Ökonomie*, AJP, 994 ff. (2022).

71 See for example, Nora Flückiger, Tierschutzrechtliche Schranken der Tierzucht - Auslegung und Umsetzung von Art. 10 TSchG 132 (Schulthess Verlag 2021).

72 Margot Michel, *Moving Away from Thinghood in Law. Animals as a New Legal Category*, Journal of Animal Law, Ethics and One Health (LEOH) (2023); Stephan Wolf & Wolfang Wiegand, *Art. 641 ff. ZGB*, in Basler Kommentar Zivilgesetzbuch II (Thomas Geiser & Stephan Wolf eds., 2023); WETTLAUFER, 94. 2018; Michel, Journal of Animal Law, Ethics and One Health (LEOH), (2023); Art. 80 Federal Constitution of the Swiss Confederation; Art. 641a Swiss Civil Code.

73 Ducor, Zeitschrift für Papyrologie und Epigraphik 263 (2016).

74 Ducor, Zeitschrift für Papyrologie und Epigraphik 263 (2016).

75 Please compare to Ducor, Zeitschrift für Papyrologie und Epigraphik 263 (2016).

76 Please refer to II.C.

77 Wolf & Wiegand, N 4. 2023.

subject to human control.[78] The fact that the thing has a monetary value or that it can be legally disposed of is not necessary for the definition.[79] A proper interpretation would be that organoids fulfill all the requirements for a thing, but this does not mean that organoids are or should be treated as things. However, whether something is to be regarded as a thing depends not only on the physical properties thereof but also above all on its economic function, on public opinion, and on ethical considerations.[80] The closest example to organoids is the human body or the separated parts thereof from which such organoids are generated. In Swiss law, the human body and any integral part thereof are not property or things.[81] While body parts separated from the body are legal things that can be owned or possessed,[82] they are excluded from their commercialization. This means that separated human body parts have a special property regime as their trade as well as donation in return for payment are prohibited.[83] Organoids, in contrast, are created 'artificially' and are not *per se* separated human body parts or human organs, cells, or tissues, which appear in nature, meaning that their comparison to separated human body parts could be inaccurate and lead to a special property regime including limitation on their commercialization. Thus, up until now, we could not state that organoids are things based solely on their comparison to separated human body parts.

As complex as organoids' status might appear, we will further show that it is not decisive whether organoids are or are not things but rather, how organoids, depending on their function, are regulated by public law. We will compare organoids to organs, cells, and tissues, whether modified or not, not from a private but from a public law perspective as even if organs, cells, and tissues do have the classical characteristics of property, they are primarily subject to specific legislation[84].

III. DEVELOPING A LEGAL STATUS FOR ORGANOIDS

As organoids cannot be categorized precisely as persons, animals, or things in private law, it therefore seems sensible that organoids either fall under existing legal frameworks or special laws for the specific problems connected to organoids are developed, if needed. This does not necessarily have to lead to the fact that organoids will be granted a legal status. An independent legal status for organoids would require extensive

78 Wolf & Wiegand, N 4. 2023.

79 Barbara Graham-Siegenthaler, *Berner Kommentar. Zweiter Abschnitt Sachen und andere Rechtsobjekte / I. - II. N 243*, *in* Das Eigentum - Allgemeine Beziehungen - Art. 641-654a ZGB (Christoph Müller Regina E. Aebi-Müller ed. 2022).

80 Graham-Siegenthaler, 2022.

81 Graham-Siegenthaler, 2022; Wolf & Wiegand, N 16 f. 2023.

82 Ladina Zegg, *Das Verbot der Kommerzialisierung des menschlichen Körpers – Ausdruck einer Wertvorstellung im Recht*, *in* Werte im Recht - Das Recht als Wert 51 (Morand Anne-Sophie Vasella Juana ed. 2018); Hans-Joachim Weitz, Nutzung menschlicher Körpersubstanzen: Verbietet das Recht die Einholung der Erlaubnis? 242 ff. (Medizin – Recht – Wirtschaft, Bd. 4. 2008). Wolf & Wiegand, N 182023; Hans Ekkehard Schnorrenberg, *Zur Kommerzialisierung menschlicher Körpersubstanzen: Verstößt die Vereinbarung der Zahlung eines Entgelt an den Substanzspender gegen die Menschenwürde?*, *in* Wem gehört der menschliche Körper? Ethische, rechtliche und soziale Aspekte der Kommerzialisierung des menschlichen Körpers und seiner Teile 226 (Beate Herrmann Thomas Potthast, Uta Müller ed. 2010).

83 Art. 119 Para. 2 lit. e and Art. 119a Para. 3 Federal Constitution of the Swiss Confederation.

84 Graham-Siegenthaler. 2022.

legal, ethical, and philosophical analyses. Considering the sensitivity of the topic, especially regarding an embryo status discussion, the question of individual status is rather challenging. It is also conceivable that specific regulations for organoid research, manufacturing, storing, transferring, or use in different areas of practical life could be issued in different areas of law. Organoids generated from human material consist of tissues and cells and are already subject to special protection under public law.[85] In terms of classification, organoids raise several questions related to the application of several federal laws and numerous ordinances. Organoids may be regulated as biological materials to be used for research purposes, transplantation, in the development of transplant (medicinal) products, ie advanced therapy medicinal products,[86] medical devices, or in vitro diagnostic tools.

III.A. Organoids as Biological Material

In Switzerland, biological material is defined in the legal framework for human research.[87] Biological materials consist of bodily substances derived from living persons, including living human organs, cells, and tissues as well as fluids of human origin, such as blood or urine,[88] excluding substances taken from embryos or fetuses.[89] Neither Swiss legislators, nor academics provide a clear opinion on whether materials that do not occur in nature, such as organoids, iPScs,[90] or even 3D-bioprinted organs[91] qualify as biological materials.

Whether organoids qualify as biological material may be clarified by looking at their purpose in the relevant regulation. The purpose of biological material is the use in

85 For example, in Switzerland in the Federal Act on Medically Assisted Reproduction.

86 The definition of transplant product as defined in Art. 2 Federal Act on the Transplantation of Organs, Tissues and Cells; and Advanced therapy medicinal products as defined in Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 (2007); both definitions are used in by Swiss authorities as synonyms and describe somatic cell therapy products, tissue-engineered products, and gene therapy products (please refer to Swissmedic, *Advanced Therapy Medicinal Products (ATMPs)*, available at www.swissmedic.ch/atmp-en.

87 For comparison to the Swiss Human Research Act, in the EU, Directive 2004/23/EC establishes the standard quality, donation safety, harvesting, tests, processing, preservation, storage, and distribution for human tissues and cells and provides the definition of body parts like cells and tissues but remains silent with the common definition of biological material. However, biological material definition is provided in Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, which in its Art. 2 Para. 1 lit a, defines biological material as any material containing genetic information and capable of reproducing itself or being reproduced in a biological system. As of 7 August 2027, the Regulation (EU) 2024/1938 will provide a definition and regulation of quality and safety of 'substance of human origin' or 'SoHO', which means any substance collected from the human body, whether it contains cells or not and whether those cells are living or not, including SoHO preparations resulting from the processing of such substance. However, research on organoids as research tools, if those are perceived SoHO, is applicable only if research does involve human application and does not apply, for example, in vitro research or research in animals [Art. 60 of Preamble to Regulation (EU) 2024/1938].

88 Art. 3 lit. e Federal Act on Research involving Human Beings; Bernhard Rütsche, Stämpflis Handkommentar zum Humanforschungsgesetz (HFG) 133, para. 41 (Stämpfli Verlag AG Bern 2015).

89 Rütsche, 134, para. 41. 2015.

90 Chmurec, 64. 2018.

91 Sereina Anais Kuster, 3D Bioprinting von Organen - eine Beurteilung ausgewählter rechtlicher und ethischer Fragestellungen 67–71 (Schulthess Juristische Medien AG 2023).

research[92] as defined in the Human Research Act. This law prohibits commercialization,[93] albeit with some exceptions.[94] Organoids are therefore biological materials that fall under the Human Research Act if they are used as 'research products'[95] or 'research tools'[96] for basic research, a model for a novel disease, eg bladder cancer[97] or interstitial lung fibrosis, or a potential drug screening prototype. Organoids appear to be used quite often as research tools, for instance, to study leprosy,[98] different cancer types,[99] NeuroHIV,[100] and many more. Although they are significantly more 'complex' than cell lines, they may serve the same purpose. This interpretation of the law is in line with the International Guidelines for Human Stem Cell Research (ISSCR), which have already classified organoids as 'research tools' (Category 1),[101] being exempted from a specialized oversight process.[102]

The generation of organoids should be considered in the context of their intended use. By this, we mean that the generation of organoids, even though it requires a substantial manipulation (processing)[103] of biological material, could still qualify organoids as 'research products' rather than medicinal products, meaning that the process of 'substantial manipulation' involved is an essential factor that could lead to the classification of an organoid as a transplant (medicinal) product in case it is used for treatment purposes[104] (D). However, despite being substantially manipulated, organoids could still be qualified as biological materials but only in case their purpose is to serve as 'research products' or 'research tools'.[105]

If organoids used for research are classified as biological materials, their regulation will depend on whether the biological materials used to generate the organoids are (i)

92 Federal Council Dispatch concerning the Federal Act on Research involving Human Beings (Human Research Act, HRA), 8046–8047 (2009).

93 Art. 9 Federal Act on Research involving Human Beings.

94 Art. 17, Art. 18, Art. 32 and Art. 41 Federal Act on Research involving Human Beings.

95 Swissethics, Basic Research: Guidance for researchers 3.

96 Swissethics, Basic Research: Guidance for researchers 3., ISSCR. May, 2021.

97 Martina Minoli, et al., *Bladder cancer organoids as a functional system to model different disease stages and therapy response*, 14 Nature Communications (2023).

98 Keshav Sharma, et al., *Neuro-Vascularized Skin Organoids': Novel Exploratory Research Tools in Leprosy*, 13 Indian Dermatology Online Journal (2022).

99 S. El Harane, et al., *Cancer Spheroids and Organoids as Novel Tools for Research and Therapy: State of the Art and Challenges to Guide Precision Medicine*, 12 Cells (2023); Nina Maenhoudt, et al., *Developing Organoids from Ovarian Cancer as Experimental and Preclinical Models*, 14 Stem Cell Reports (2020).

100 A. Premeaux Thomas, et al., *Next-Generation Human Cerebral Organoids as Powerful Tools To Advance NeuroHIV Research*, 12 mBio (2021).

101 International guidelines for human stem cell research there typically use three categories of concern, from Category 1, which is least problematic and does not require full ethical review, to Category 3, which comprises prohibited research (like the breeding of chimeras, the transfer into the uterus of a modified human embryo, etc.). While organoid research would traditionally have been in Category 1, there is now a question as to whether we should move it to Category 2 because of the special features that make it more complex than established cell lines. Please refer to ISSCR, 52. May, 2021.

102 ISSCR, 52 May, 2021.

103 Swissethics, Basic Research: Guidance for researchers, 3–4. 2021.

104 Substantial manipulation is one of the decisive factors for biological material to be classified as a transplant product. According to the position of Swissmedic: 'Tissues and cells that have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved are therefore classified as transplant products'. Please refer to: Swissmedic, Legal framework governing the use of tissues and cells of human origin.

105 Swissethics, Basic Research: Guidance for researchers, 3. 2021; ISSCR, 9. May, 2021.

coded or pseudonymized,[106] ie linked to a specific person via a code, or anonymized, ie in which case they cannot (without disproportionate effort) be traced to a specific person.[107] In Switzerland, only coded biological material falls under the scope of the Human Research Act. This means that the consent of donors of biological material as well as approval for the research project from an ethics committee is required.[108] The Human Research Act does not apply if the material is anonymized, meaning that a third party could not, due to life experience or technical possibilities, easily de-identify personal information from the biological material.[109] In such a situation, only the donors' consent for biological materials donation to generate organoids is necessary.

Although the definition of biological materials does not include organoids, they could be considered and regulated as such when used as a 'research product' or 'research tool'. Except for embryoids, there is little indication that the creation of organoids, however complex, substantially differs from any other existing research-oriented technology (eg cell lines) and thus does not need a specific legislative category. In fact, an additional category would create confusion rather than clarity.[110]

III.B. Organoids as Transplants

Attempts at organ transplantation started as early as 600 BC, but the first successes came only in the mid-20th century.[111] Transplantation offered the hope of saving, prolonging, and improving the quality of life. However, the shortage of donor organs, difficulties raised by its distribution for transplantation,[112] and the illegal trafficking of human organs are just a few of the problems scientists had to face, so they were forced to look for alternatives. In the following, we will analyze whether organoids could potentially be alternatives to human organs and fulfill the criteria to be considered transplants under Swiss law.[113] There are two main criteria that organoids have to fulfill to be regarded as transplants. First, they have to fall into the category of bio-artificial or

106 If organoids are developed from coded, ie pseudonymized biological material, the respective research is subject to Human Research Act regulation. In practice, this means that such research is subject to mandatory authorization by ethics committees. Please refer to Art. 45 Federal Act on Research involving Human Beings.

107 Art. 3 lit. e, Art. 3 lit. h, Art. 3 lit. i Federal Act on Research involving Human Beings.

108 Art. 2 Para. 2 lit. b and Art. 45 Federal Act on Research involving Human Beings.

109 Beat Rudin, *4. Kapitel: Weiterverwendung von biologischem Material und gesundheitsbezogenen Personendaten für die Forschung, Art. 32–35*, in Humanforschungsgesetz (HFG) (Bernhard Rütsche ed. 2015).

110 It should be noted that organoids represent one of numerous novel technologies. Consequently, the creation of a specific legislative category for them would be considered unnecessary if their regulation is possible within existing law. This is particularly the case for new technologies, which are subject to rapid development and therefore require 'no or as few technology-related regulations as possible and to formulate requirements independently of possible technical solutions'. Please refer to Alexander Roßnagel, *"Technikneutrale" Regulierung. Möglichkeiten und Grenzen*, in Innovationsfördernde Regulierung 323–325 (Martin; Hoffmann-Riem Eifert, Wolfgang ed. 2009);Herbert Zech, Einführung in das Technikrecht 34 § 2 (Digital Recht 2021).

111 David Hamilton, et al., A History of Organ Transplantation. Ancient Legends to Modern Practice xiii-xx (University of Pittsburgh Press 2012).

112 Thomas Gutmann & Bijan Fateh-Moghadam, *Rechtsfragen der Organverteilung. Verfassungsrechtliche Vorgaben für die Verteilung knapper medizinischer Güter am Beispiel der Organallokation*, *in* Grundlagen einer gerechten Organverteilung 59 ff. (Ursula Schmid Bijan Fateh-Moghadam, Eva Wunderer ed. 2002).

113 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act), 132–133 (2001).

biological[114] organs, cells, and tissues. Second, they have to be intended to be used for transplantation into humans.

To start with, bio-artificial organs, according to the Swiss legislator, are medical devices or machines (E) that perform the functions of certain organs and contain biological components, such as cells.[115] The Swiss legislator rarely mentions bio-artificial organs, and the only example thereof can be found in the field of xenotransplantation, with bio-artificial liver support systems.[116] Such bio-artificial liver support systems are used for acute liver failure and are basically an extracorporeal device. They contain pig liver cells and are perfused with the patient's blood in a similar way to a dialysis machine.[117] Similarly to such bio-artificial organs, organoids contain a vital biological component, such as cells. However, in contrast to the bio-artificial organs, organoids are not used in combination with technological devices. Therefore, organoids do not fulfill one of two requirements for bio-artificial human materials and could not be qualified as such.

Another possibility for organoids to be classified as transplants exists if organoids were treated as human biological organs, cells, or tissues that are being intended to be used for transplantation. We have already discussed that organoids could be considered as biological materials within the meaning of the Human Research Act when used for research purposes. It is now necessary to consider whether organoids could fall within the categories of cells, tissues, or organs used for transplantation purposes as defined in the Swiss Transplantation Act. We will address the meaning behind definition of cells, tissues, and organs if it is suitable for organoid understanding based on grammatical, historical, and teleological interpretation.

The grammatical interpretation starts by looking at the wording of the definitions used for organs, cells, and tissues in the Swiss Transplantation Act in precise detail and seeing how they would fit organoids. Firstly, the Act defines 'cells' as *'an individual cell, an unstructured cell mass or a cell suspension that consists exclusively of the same type of cell'*.[118] Cells are understood as the basic components or building blocks of a living being, in contrast to organoids, which are a more complex mechanism generated from cells and may contain one or more tissue types.[119] Thus, organoids cannot, according to the wording of the definition used for cells, be considered a 'cell'. Similarly, they cannot be matched to the definition of tissue. Tissues are *'a structured association of cells, consisting of the same or different types of cells, that have a common function in the body'*,[120] which could be interpreted as a representation of a tissue-specific cell type isolated from a patient's organ, organoids represent a mere model of that organ's

114 'Bio-artificial organs are … containing vital cells'; please refer to: Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act) 1352001.

115 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act) 200. 2001.

116 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act) 39. 2001.

117 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act) 51, 132–133. 2001.

118 Art. 3 Federal Act on the Transplantation of Organs, Tissues and Cells.

119 Isabelle Hautefort, et al., *Everything You Always Wanted to Know About Organoid-Based Models (and Never Dared to Ask)*, 14 Cellular and Molecular Gastroenterology and Hepatology (2022).

120 Art. 3 Federal Act on the Transplantation of Organs, Tissues and Cells.

epithelial niche.[121] This means that the language used to describe tissues does not cover organoids. Lastly, the Act states that organs are *'any part of the body whose cells and tissues together comprise a unit with a specific function; organ parts whose function is similar to that of an organ and parts of the body that consist of different types of tissue and which have a specific function are regarded as equivalent to organs'*.[122] Organs are understood here as full human organs or as a representation thereof, whereas organoids are a miniature, simplified version of these organs,[123] sometimes mimicking only their separate parts. To conclude, organoids do not fall under the cell, tissue, or organ categories as defined in the Swiss Transplantation Act from a grammatical perspective. However, we may have to look at historical and teleological interpretations that might justify a broader interpretation of the legal text.

The historical interpretation shows that the organs used for transplantation purposes were non-modified donor organs given from donor to recipient for transplantation. The first modern organ transplantation was renal and completed in 1954,[124] following the most common organ used for transplantation—the kidney—completed in 1959.[125] Parallel to that, the use of tissues, especially for grafting skin and muscles, for transplantation has developed.[126] In Switzerland, organs, tissues, and cells used for transplantation were understood as separated and non-modified, non-manipulated body parts.[127] The statistics from 1992 reveal that this was the year when classical transplants of the heart, lungs, liver, kidneys, pancreas, bone marrow, or blood cells began to be done in Switzerland.[128] Historically, transplants tissue and organ transplants were therefore understood as non-modified living human materials. In this sense, organoids, as products consisting of cells or tissues, historically do not fall into the category of organ or tissue transplants.

The teleological interpretation suggests that the law must distinguish products derived from cells, tissues, and organs from non-modified organs, cells, and tissues. The separation of these categories has been implied during the discussion for the implementation of the first version of the Transplantation Act.[129] A federal communication regarding a constitutional provision on transplantation medicine has allowed the legislator to separate organs, tissues, and cells, named transplants, from products consisting of or containing human organs, tissues, or cells.[130] The former are standardized products, ie, products derived from organs, cells, or tissues, which have to be prepared or processed

121 Kim Bak Jensen & Melissa Helen Little, *Organoids are not organs: Sources of variation and misinformation in organoid biology*, 18 Stem Cell Reports (2023).

122 Art. 3 Federal Act on the Transplantation of Organs, Tissues and Cells.

123 Fang, et al., Experimental Hematology & Oncology (2023).

124 Sir Roy Y. Calne, *A Brief History of Clinical Organ Transplantation*, *in* Textbook of Organ Transplantation (2014).

125 Kenneth J. Dery, et al., *New therapeutic concepts against ischemia–reperfusion injury in organ transplantation*, 19 Expert Review of Clinical Immunology 124–128 (2023).

126 Thomas Schlich, The Origins of Organ Transplantation Surgery and Laboratory Science, 1880–1930 14–20 (Boydell & Brewer NED - New edition ed. 2010).

127 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act) p. 135–136. 2001.

128 Federal Council Dispatch concerning a constitutional provision on transplantation medicine, 656 (1997).

129 Federal Council Dispatch concerning a constitutional provision on transplantation medicine, 656 (1997).

130 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act), p. 135–136 (2001).

in one or more steps after the collection or harvesting of the appropriate biological materials. The legislator has stated that even if those cells, tissues, and organs maintained their name of 'organs, tissues, and cells', upon their preparation and processing, they should rather fall under separate regulation.[131] The exact separation of the two categories took place in the Transplantation Act and the Transplantation Ordinance. The latter category of transplants, ie unmodified human organs, tissues, and cells, are defined as 'transplant products',[132] which are to be regulated simultaneously by the Therapeutic Products Act and the Transplantation Act.[133] The intent to create two different governing mechanisms shows that substantially processed materials are not organs, tissues, and cells. Organoids are processed cells or tissues, ie as they undergo substantial manipulation,[134] before they can be used on a human being. Moreover, they lack some essential organ transplant characteristics, namely, fibroblasts and blood vessels.[135] Thus, they cannot be categorized as cells, tissues, and organs under the Transplantation Act.

As a result, organoids do not fit into the classification of bio-artificial and biological organs, cells, and tissues. Therefore, they are not transplants and are not governed accordingly by the Swiss Transplantation Act.

III.C. Organoids as Artificial Human Materials

The process of engineering organoids could mean that, if they are not transplants, they could instead be classified as artificial human materials. Legally, those are not transplants but medical devices.[136]

Artificial, or in other words, devitalized organs, cells, or tissues, are distinguished from biological ones by the fact that they no longer contain any living material. Indeed, their main feature is the absence of living material, which increases their compatibility with the recipient and excludes the transmission of pathogens.[137] Artificial or devitalized organs could include human or animal heart valves, tendons, or bone spongiosa.[138]

In contrast to artificial materials, which contain only non-living or devitalized material, organoids do contain living material. Therefore, there are fundamental differences between the two technologies insofar as their nature is concerned. As a result, organoids could not be artificial organs, tissues, or cells.

131 Federal Council Dispatch concerning a constitutional provision on transplantation medicine, 6781997.

132 Art. 2 Para. 1 lit. c Ordinance on the Transplantation of Human Organs, Tissues and Cells.

133 Federal Council Dispatch concerning a constitutional provision on transplantation medicine, 6781997. Art. 2 Para. 1 lit. c Ordinance on the Transplantation of Human Organs, Tissues and Cells.

134 The process that defines cells, tissues, and organs to fall into Transplant products category, please refer to Art. 2 Para. 1 lit. c Ordinance on the Transplantation of Human Organs, Tissues and Cells.

135 X. Jiang, et al., *Graft microvascular disease in solid organ transplantation*, 92 J Mol Med (Berl) (2014).

136 Swissmedic, *Meldung devitalisiertes menschliches Gewebe*, available at https://www.swissmedic.ch/swissmedic/de/home/medizinprodukte/marktzugang/meldung-devitalisiertes-menschliches-gewebe.html.Bundesamt für Gesundheit, Totalrevision der Medizinprodukteverordnung und Verordnung über klinische Versuche mit Medizinpro-dukten (neue Medizinprodukte-Regulierung), 7 (2020).

137 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act), 135. 2001.

138 Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act) 134. 2001.

III.D. Organoids as a Transplant (Medicinal) Product

Scientists expect organoids to serve a therapeutic purpose.[139] Examples of organoids-based therapies already exist. Starting with some limited or potential therapeutic application examples of organoids from corneal 3D tissue and insulin-producing islets to treat diabetes,[140] organoids are making their way into medicine. One such example could be the successful colonic organoid transplantation therapy performed for intractable ulcerative colitis in Japan in 2022.[141] For organoids to be classified as a transplant product, they must consist of or contain human organs, tissues, or cells and fulfill several requirements.[142] First of all, the organs, tissues, or cells in question must be substantially modified. Here substantial modification or manipulation means: *'multiplication of cells via cell culture, the genetic modification of cells, the differentiation or activation of cells'*.[143] Second, the organs, cells, and tissues in question must not be intended to perform the same function in the receiving person as in the donor.[144] In addition to the human starting materials, transplant products could consist of or contain cells, tissues, or organs of animal origin.[145] Under Swiss law, the purpose of a transplant product is its transplantation,[146] but it is also intended to have a medical effect on the human or animal organism, ie, the diagnosis, prevention, or treatment of diseases, injuries, and handicaps.[147] For this reason, they are subject to regulation by both the Swiss Transplant and the Swiss Therapeutic Product Act. Transplant products have to be standardized,[148] with proven safety, quality, and efficacy, and have the approval of the relevant authorities.[149]

The process of colon organoid transplantation therapy that has already been developed and put into clinical use may serve as an example. By analyzing it step by step, we will be able to see whether the aforementioned requirements were observed and to determine whether the organoid therapy named above could possibly be viewed

139 Stian Kogler, et al., *Organoids, organ-on-a-chip, separation science and mass spectrometry: An update*, 161 TrAC Trends in Analytical Chemistry (2023).

140 Fanny Lebreton, et al., *Insulin-producing organoids engineered from islet and amniotic epithelial cells to treat diabetes*, 10 Nature Communications (2019).

141 Emily Henderson, *World's first-in-human research using organoid transplantation yields good results* (2022), available at https://www.news-medical.net/news/20220822/Worlds-first-in-human-research-using-organoid-transplantation-yields-good-results.aspx.

142 Art. 2 Para. 1 lit. c and d Ordinance on the Transplantation of Human Organs, Tissues and Cells.

143 Art. 2 Para. 1 lit. d Ordinance on the Transplantation of Human Organs, Tissues and Cells.

144 Art. 2 Para. 1 lit. c Ordinance on the Transplantation of Human Organs, Tissues and Cells.

145 Art. 2 Para. 1 lit. c and d Ordinance on the Transplantation of Human Organs, Tissues and Cells.

146 Art. 2 Para. 1 and 3 Federal Act on the Transplantation of Organs, Tissues and Cells.

147 Art. 4 Federal Act on Medicinal Products and Medical Devices.

148 Federal Act on the Transplantation of Organs, Tissues and Cells. does not, however, specify what is meant by 'standardized'. This concept must therefore be defined precisely in order to permit firms to classify their products. Swissmedic and the Federal Office of Public Health have therefore decided to follow the European Regulation 1394/2007/EC on Advanced Therapy Medicinal Products intended for advanced therapies. Tissues and cells that have been subject to substantial manipulation to attain the biological characteristics, physiological functions, or structural properties relevant for the intended regeneration, repair, or replacement are therefore classified as transplant products. Cultivation with cell expansion, for instance, is considered to be a substantial manipulation· For more information, please refer to: Swissmedic, Legal framework governing the use of tissues and cells of human origin.

149 Art. 4 Federal Act on Medicinal Products and Medical Devices; Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act), 134–136. 2001.

as a transplantation product under Swiss law.[150] First of all, scientists collected some healthy colon mucosa from the patient and cultured it for about a month to form spherical organoids. Thus, the first step covers the two main requirements, in that the products contained human cells (colon mucosa) and the cells were substantially manipulated (cultured). Afterward, the scientists transplanted these spherical organoids into the colon of the same patient by means of a colonoscopy.[151] Later still, the transplanted organoids were integrated into areas where the epithelium was damaged, and the cultured cells displayed an ability to engage in tissue regeneration in vivo and to reconstitute a functional epithelial barrier.[152] Thus, the final criterion for a transplant product is also fulfilled, as organoids perform the function of regeneration, but not in the same way as the cells of the colon mucosa or intestinal epithelial cells (IECs), which contribute to the digestion and absorption of dietary nutrients.[153] Therefore, the function of the starting material is different from the one processed and transplanted back into the human body. In this case, one can conclude that organoids can potentially serve a therapeutic purpose[154] as they fulfill all the criteria set for transplantation products.[155]

III.E. Organoids as Medical Devices

A product is a medical device if it is *'an instrument, apparatus, appliance, software, implant, reagent, material or other article which has to fulfill specific one or more medical purposes'*.[156] The medical purposes, which a medical device has to meet, are the diagnosis, prevention, monitoring, prediction, prognosis, treatment, or alleviation of an illness (medical condition), as well as providing information by means of an in vitro examination of specimens derived from the human body, including organ, blood, and tissue donations.[157] Importantly, to be considered a medical device, it must not

150 Cell or gene-based therapies are approved as transplantation products. For example, the CAR-T cell therapy is gene-based therapy, which was approved as transplantation product and subject to reimbursement in Switzerland. For example, please refer to:Swissmedic, *KymriahTM, Zellsuspension zur Infusion (Tisagenlecleucelum)*, available at https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/authorisations/new-medicines/kymriahtm_zellsuspensionzurinfusiontisagenlecleucelum.html; Federal Office of Public Health FOPH, *CAR-T cell therapies*, available at https://www.bag.admin.ch/bag/en/home/versicherungen/krankenversicherung/krankenversicherung-leistungen-tarife/hta/hta-projekte/carttherapien.html.

151 Henderson, 2022.

152 Please refer to: Satoshi Watanabe, et al., *Transplantation of intestinal organoids into a mouse model of colitis*, 17 Nature Protocols (2022).

153 J. A. Jankowski, et al., *Maintenance of normal intestinal mucosa: function, structure, and adaptation*, 35 Gut (1994); Shanshan Kong, et al., *Regulation of Intestinal Epithelial Cells Properties and Functions by Amino Acids*, 2018 BioMed Research International (2018).

154 Bundesamt für Gesundheit BAG, Ergebnisbericht der Vernehmlassung Genehmigung des Übereinkommens des Europarats gegen den Handel mit menschlichen Organen (Organhandelskonvention) und seine Umsetzung (Änderung des Transplantationsgesetzes) 5 (2018).

155 Please compare it to CAR-T cell therapy Richard Dissmann & Sarah Somboonvong, *Die Unionsgewährleistungsmarke*, GRUR 657; Dissmann & Somboonvong, GRUR (2016). They have a standardized function as well as an established manufacturing process. Federal Council Dispatch concerning the Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act). 2001. BAG, 5. 2018.

156 Art. 3 Medical Devices Ordinance.

157 Art. 3 Medical Devices Ordinance provides an exhaustive list of purposes medical devices have to fulfill. The same regulation, with some exceptions, applies to in vitro diagnostic medical devices and provides an exhaustive list of purposes medical devices have to fulfill.

contain, incorporate, or be derived from viable tissues or cells of human or animal origin or consist of viable biological materials or other viable organisms.[158] Therefore, as organoids are generated from a viable biological material, they cannot be classified as medical devices.

IV. CONCLUSION

The legal status of organoids is not clearly defined. Nevertheless, organoids are subject to regulatory oversight.

We argued that organoids do not fall within the category of legal persons or animals. Organoid classification as things is a potential way for consideration, particularly if organoids are compared to separated human body parts. However, such a comparison could cause several legal issues. First of all, organoids, in contrast to human body parts, do not occur in nature. Rather, they are lab-generated human mini-organ prototypes. Therefore, comparing organoids to separated human body parts will result in limitations, for instance, on their commercialization. Secondly, there may be controversy surrounding the classification of cerebroids or embryoids as things. Despite the fact that organoids are only brain- or embryo-like models, currently, they are the subject of public debate. Therefore, there needs to be a social and political agreement to apply to the traditional rules of rights *in rem.* In light of the numerous potential issues with organoids' legal status, our aim has been to examine whether and how, despite these challenges, potential organoid regulation could be shaped by public laws.

Swiss legislation does not specifically address organoids. With this in mind, we examined a number of laws that could potentially be used to regulate organoids. Our aim was to identify those that best meet two criteria: the features of the organoids themselves and the way in which they are used. We argued that organoids fall into two categories: biological materials and transplantation (medicinal) products. First, organoids used for research purposes could be regulated as biological materials under the provisions of the Swiss Human Research Act. Secondly, organoids used for therapeutic purposes must be considered transplantation (medicinal) products or, in other words, advanced therapy medicinal products. They must therefore be regulated by the Swiss Transplantation Act, the Swiss Human Research Act, and the Human Therapeutic Products Act. We have concluded that organoids should not be categorized as transplants, medical devices, or bio-artificial human materials. We have clarified that organoids are not transplants, as they are substantially processed materials and not organs, tissues, or cells intended for transplantation. Organoids are also not medical devices. Unlike medical devices, they do not contain non-living or devitalized materials. Moreover, organoids cannot be used in combination with medical devices and therefore do not qualify as bio-artificial human materials.

This paper has shown that organoids are, at least to some extent, subject to the existing Swiss legal framework, although they are not directly addressed by the legislator. Nevertheless, legal questions remain regarding human brain organoids and embryoids. While embryoids require legislative attention, brain organoids can currently be compared to other types of organoids. However, this could change with future developments in organoid research.

158 Art. 1 Para. 3 lit. c and d, Art. 2 Para. 1 lit. h and j, Art. 3 Medical Devices Ordinance.

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CONFLICTS OF INTEREST

The author declares that the research was conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.