Human cells, tissues, and cellular and tissue-based products (HCT/Ps) such induced pluripotent stem cells (iPSC) and haematopoietic stem cells (HSCs) have been used for decades and still have expanding potential.[1] But the use of naturally occurring materials, and patient derived materials complicate the regulatory landscape for this area of technology. [2]

The FDA has approved some cellular and gene therapy product treatments.[3] However, there are applications of HCT/Ps that evade or escape the FDA regulations.[4] And there is conflict within case law that questions the FDA's ability to regulate.[5]

Currently HCT/Ps are regulated through various means. Under a regulatory route of "same function," HCT/P are regulated by Section 361 of the Public Health Service Act. [6] Section 361 applies to homologous cell or tissue applications in which "an HCT/P … preforms the same basic function or functions in the recipient as the donor."[7] These HCT/Ps are still expected to follow the good tissue practices, but the regulation under section 361 and 21 CFR part 1271 is limited, with no premarket authorization required.[8]

If the requirements of section 361 do not apply because more substantial cellular changes occurred, a doner was used, or function changed, then the product is regulated under Section 351. Under section 351 these products must obtain FDA approval, among other regulatory requirements. [9]

Additionally, there is a same day surgical procedure exception for some HCT/P s use.[10] This exception is justified by the risk of communicable disease in same day same patient HCT/P use being on par with the risks already associated with surgical procedures.[11]

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[1] Kimbrel, E.A., Lanza, R. Next-generation stem cells — ushering in a new era of cell-based therapies. *Nat Rev Drug Discovery* 19, 463–479 (2020) https://doi.org/10.1038/s41573-020-0064-x. Lomax GP, Torres A, Millan MT. Regulated, reliable, and reputable: Protect patients with uniform standards for stem cell treatments, Stem Cells Transl Med. 2020 May;9(5):547-553. doi: 10.1002/sctm.19-0377.

[2] FDA has approval for some stem cell treatments but warns of the dangers of unapproved treatments. FDA Warns About Stem Cell Therapies, U.S. Food and Drug Administration, https://www.fda.gov/consumers/consumer-updates/fda-warns-about-stem-cell-therapies (last visited March 26,2023).

[3] Approved Cellular and Gene Therapy Products, U.S. Food and Drug Administration, https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products (last visited March 26, 2023).

[4] Megan Stride, Potential Upheaval For FDA Regulation Of Stem Cell Clinics, Law360, https://www.law360.com/articles/1561200/potential-upheaval-for-fda-regulation-of-stem-cell-clinics (last visited March 26, 2023).

[5] *Id.*

[6] *Id.*

[7] 21 C.F.R. § 1271.3(c) (2023).

[8] U.S. Food & Drug Admin., Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Small Entity Compliance Guide (2022).

[9] *Id.*

[10] *Id.*

[11] U.S. Food & Drug Admin., Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception (2017).

FDA regulation has both costs and benefits. Exemptions for minimally altered materials are logical, and lower regulatory hurdles are often beneficial. But simultaneously the uncertainty and complexity of future regulation could slow and deter future advancements. While cutting edge treatments can be helped by the speed of market entry that comes from exceptions from FDA regulation, it lacks the confidence and relative transparency that eventually comes from FDA approval.