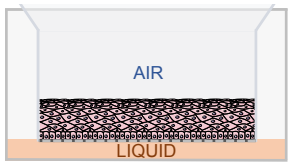
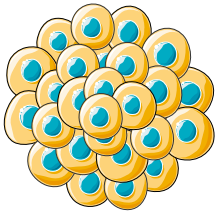
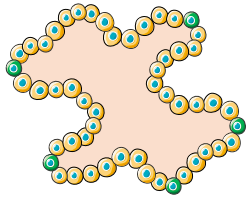
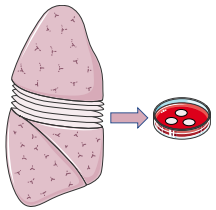
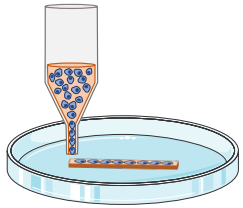
21ST CENTURY TOXICITY TESTING: HUMAN 3D TISSUE MODELS

Three-dimensional (3D) tissue models can recapitulate the organisation, morphology, functionality, and heterogeneity of human tissue, creating human-relevant models. They can be used for regulatory safety testing, product development, and basic research applications throughout the cosmetics, chemical, pharmaceutical, medical device, and household product industries. 3D tissue models may be used as standalone research tools or can be combined with other technologies.

	Reconstructed Human Tissues	Spheroids	Organoids	Precision-Cut Organ Slices	Bioprinting
					
Description	Epithelial cells grown at the air-liquid interface and with the right supplements will differentiate into different cell types representative of their original organ architecture. Reconstructed human tissues are used in several internationally accepted Organisation for Economic Co-operation and Development test guidelines (TG), including for skin corrosion (TG 431), skin irritation (TG 439), eye corrosion and irritation (TG 492), and phototoxicity (TG 498).	Clusters of one or several cell types that adhere to one another without scaffolding. Spheroids can be grown in low-adhesion culture plates or using the hanging-drop technique. Spheroids are used to study tumour microenvironments, predict drug efficacy and safety, in personalised medicine, and in stem cell research. Liver spheroids are also used to study metabolism and hepatotoxicity.	Typically derived from induced pluripotent (iPSC) or embryonic stem cells (ESC) that are usually grown in an extracellular matrix-like scaffold. Organoids are self-renewing and differentiated into multiple lineages. They reflect the functional properties of organs at the microscopic level. Organoids have several applications, including disease modelling, antitoxin production, drug discovery, and regenerative medicine.	Human precision-cut organ slices (PCOS) are ex vivo explants of tissues that are cut into thin slices with a microtome. PCOS retain the complex and multicellular histoarchitecture of the organ and can be obtained from healthy or diseased donor tissues. Human PCOS of various organs have been established and can be used for disease modelling, drug discovery, and toxicology.	Bioink, consisting of cells, growth factors, and/or biomaterials, is deposited layer-by-layer to create 3D tissue-like structures or scaffolds using 3D-printing techniques. Application areas range from drug screening and toxicology to tissue and organ fabrication and transplantation. Bioprinting offers the potential to print entire organs from patient cells.
Tissues	Skin, cornea, respiratory region (from nasal to alveolar), intestine, vagina, oral region	Liver, pancreas, bone, brain, eye, cartilage, various tumours	Intestine, lung, stomach, liver, thyroid, kidney, brain, pancreas, prostate, vasculature, retina, mammary gland, bladder, endometrium, salivary gland	Lungs, liver, kidney, brain, intestine, pancreas	Bone, heart, heart valve, cartilage, liver, lung, nervous system, pancreas, skin, vasculature
Industry Players*	Cyprotex, EPISKIN, Epithelix, ImmuONE, J-TEC, MatTek, Phenion, ZenBio	Cyprotex, InSphero, n3DBiosciences, Sanbio	Bio-Techne, Cellesce, HUB Organoids, InnoSer, Organoid Therapeutics, UPM Biomedicals	AnaBios, IIVS, Visikol	Aspect Biosystems, Cellbricks, CELLINK, Organovo

Figures modified from Servier Medical Art

For more information, see Alépée N, Bahinski A, Daneshian M, et al. t[4] workshop report: state-of-the-art of 3D cultures (organs-on-a-chip) in safety testing and pathophysiology. ALTEX. 2014;31(4):441–477.

*A number of industry players listed use animal-derived products or primary animal cells/tissues in addition to human cells. Inclusion on this factsheet does not indicate endorsement by PETA Science Consortium International e.V.

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