Health Technology Review	
Technology Ref.:	HTA23009
Technology Name:	Reverse Clinical Engineering
Approvals by International Bodies:	-
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Short Description of the Technology:	The Reverse Clinical Engineering® encompasses an in vitro chemo sensibility screening on 3D tumour models originated from primary tumour tissue of cancer patients. The tumour tissue is cultivated in the laboratory and 3D organoids are generated out of each individual patient culture. The 3D tumour models are expanded, so that multiple drugs can be tested on them and viability of the tumour models after treatment is measured using a luminescence-based commercially available assay. The drugs for screening are chosen individually for each patient, without any harm to the patient due to adverse events or possible side effects of the treatment. The concentration of the drugs is based on clinical patient plasma levels and dose response curves are measured after three days of treatment. The positive and negative predictive value of tumour organoid-based tests is up to ~80% to 100%, meaning that a positive test result for a drug on tumour organoids in the lab will also give a positive result in the patient in up to 78-100% of the cases, and a negative test result will be reflected by a negative result in the clinic in up to 67-100% of the cases (Wensink et al., 2021).

Health Technology Assessment Team Recommendation:	**Disapprove**
Summary of Review:	
The technology is a test procedure that is carried out prior to the drug-based cancer therapy. It uses a piece of tumor that is removed during a biopsy or surgery. This piece of tissue is then processed in the laboratories and tumor cells are cultivated in a petri dish, which is refer to as tumor organoids or PD3D® cell cultures. The tumor organoids serve as small copies of the individual tumor. It tests different drugs and combinations of drugs on them to identify therapies that may be effective in treating the tumor. In addition, the test shows which drugs are very likely to be ineffective – valuable information which may help avoid unsuccessful therapy, including possible side effects. The large variabilities between 3D models limit their level of standardization, reproducibility, and their use as preclinical tools for drug development. This technology has been used in preclinical phase for drug development and research but not yet well established/ introduced into clinical practice.	

Advantages	Disadvantages
Provides a promising avenue for personalized cancer treatment, with the potential to enhance the selection of effective therapies for individual patients. (Precision Medicine)	additional validation through larger, multi-center studies would be beneficial to verify the robustness and generalizability of the findings
Could be an option for patients who have very rare tumours where there is no established standard of care treatment	Lack of Standardization: There is currently no universal standard for 3D culture methodologies, leading to variability in techniques and outcomes across different studies
Beneficial In patients who have exhausted all lines of approved anti-cancer therapies and no standard of care option is left (providing that the patient is fit and willing to continue with more treatment, knowing that such treatment based on chemo-sensitivity test may not necessarily lead to a benefit).	Assessing the cost-effectiveness and feasibility of implementing this technology in routine clinical practice is crucial in determining its overall impact on patient care and healthcare systems
Unnecessary adverse effects could be avoided due to the ineffective treatments	Lack of recognition for this test within established guidelines from reputable organizations like NCCN, ASCO, and ESMO
	Such tests do not take into account pharmacokinetics or pharmacodynamics of the medicine in human body.

We recommend a **disapproval of using this technology** for clinical practice at the current time as further research and validation are necessary to fully comprehend the implications and limitations of this technology, ensuring its successful integration into clinical practice.

Technology Image