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H2020-SC1-2019-Single-Stage-RTD

VANGUARD - New Generation Cell Therapy: Bioartificial Pancreas to Cure Type 1 Diabetes

Deliverable 2.1

ELSA training manual

Work package 2

Ethical, Legal and Social aspects

(ELSA)

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Revision History

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E. Massey, E. Bunnik, D. de Jongh, EMC; A. Cronin, KCL	Draft deliverable	31/12/2022
E. Berishvili, UNIGE	Revision 1	22/01/2023
E. Massey, EMC	Final version	30/01/2023

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Abbreviations

H2020	Horizon 2020
WP	Work Package

Project Partners

ACCEL	accelopment AG
EMC	Erasmus University Medical Centre
ESOT-ELPAT	European Society for Organ Transplantation
UNIGE	University of Geneva

1 Introduction

The development of bioartificial organs is a new and innovative area in medicine technology which crosses boundaries of cell therapy, regenerative medicine, transplantation, and bioethics. Research groups around the world are using regenerative medicine technologies to develop bio-artificial organs for transplantation into human patients. While most of this research is still at the preclinical stage, bio-artificial organ technologies are gearing up for first-in-human clinical trials in the not-too-distant future. Given the novelty of the area there has been little exploration of the ethical challenges involved. What are the ethical conditions under which early-phase clinical research of bio-artificial organs can be conducted safely and responsibly? What lessons can be learned from prior experiences with early-phase clinical trials in adjacent fields of research?

This deliverable was designed to promote awareness and knowledge of these ethical challenges when conducting early phase clinical trials with bioartificial organs among researchers carrying out regenerative medicine projects within the H2020 call SC1-BHC-07-2019 (Regenerative medicine: from new insights to new applications). In this deliverable, we summarize the content and outcomes of the online international VANGUARD Ethics Workshop that was held on the 3rd of February 2022.

The event was jointly organized by EMC, ESOT-ELPAT, accelCH, and UNIGE. 102 people registered and 74 people attended the online workshop. In addition to the VANGUARD project, two other EU-funded project under the same call were invited to contribute by presenting their projects and ethical considerations and participate in the panel discussion (Brav3 and OrganTrans).

2 Workshop Programme

KEYNOTE SPEAKER	Professor Jonathan Kimmelman, McGill University Director of Biomedical Ethics Unit Author of Gene Transfer and the Ethics of First-in-Human Trials: Lost in Translation
SHOWCASES OF REGENERATIVE MEDICINE APPLICATIONS	Insights from 3 projects funded through Horizon 2020 'Regenerative medicine: From new insights to new applications' presented by junior researchers: - VANGUARD: Dide de Jongh, E MC - OrganTrans: Ary Marsee, Utrecht University - Brav3: Olalla Iglesias García, University of Navarra
PANEL DISCUSSION	Moderated by Eline Bunnik & Emma Massey, EMC *Panel members* Jonathan Kimmelman, McGill University Antonia Cronin, King's College London Ekaterine Berishvili, University of Geneva Anne-Floor de Kanter, Utrecht University Mariana Pacheco Blanco, Amires S.r.o. Manuel M. Mazo Vega, University of Navarra

3 Key points of the meeting

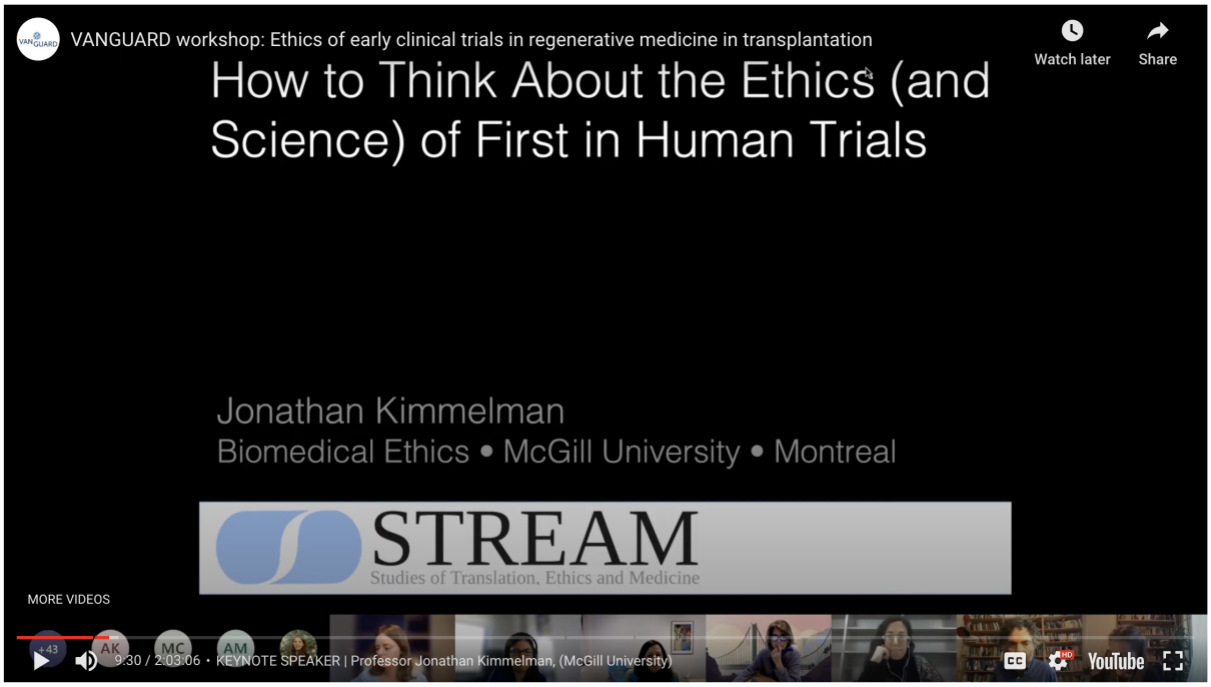

Figure 1: Screenshot of the event

- Kimmelman highlighted that researchers involved in regenerative medicine should aim to maximize **'moral efficiency'** and minimize welfare loss, thus minimising the number of patients exposed to risks and harms.
- Efficient and cost-effective medicine must be promoted by understanding when and how to use medical technology, as well as the incremental value compare to alternative treatments.
- There is a moral requirement for participants in research trials to be able to **trust** researchers and the collaborative networks for clinical translation. Factors influencing this trust include risk assessment, patient assessment and informed consent.
    - **Risk-benefit assessment**: rigorous pre-clinical evidence is required in order for research ethics committees to be able to evaluate potentials harms.
    - **Patient selection**: this entails seeking a balance between maximizing moral efficiency and generating scientific evidence. Patients with a progressive illness may have less to lose but also less to gain. Researchers should also consider the impact of patient selection on trust in the collaborative research networks.
    - **Informed consent**: participants of early clinical trials often hope for gain in the form of health improvement however the welfare gain is for society rather than for the individual. Informed consent should make clear that welfare loss and experience of side-effects are more likely than individual welfare gain.
- While many ethical considerations are not novel, there are some unique aspects of bioartificial organs which generate new questions. Transplantation of a bioartifical organ requires surgery and is therefore more invasive than a trial of a pharmaceutical agent. Bioartifical organs contain biologically active material which may integrate into

the body rendering the treatment irreversible. They are often complex products with various cell sources (autologous, allogeneic, xenogeneic), each of which raising their own ethical issues. Finally, bioartifical organs have the potential to be personalized. This makes testing of safety and efficacy as well as large scale production more difficult. Personalized technologies may need to be evaluated—and regulated—not as medicines, but as health services.

- A principle shared by attendees was the idea of **social value**: that research on bioartifical organs should lead to improvements in health or wellbeing for future patients. Social value depends not only on safety and efficacy of the novel technology but also on contextual factors within a given disease setting, including the presence or absence of effective and acceptable alternative treatment options. The potential to add social value also depends on access to and affordability of the new technology whereby patients in developing countries are likely to be disadvantaged. This is an issue that will need to be addressed during clinical translation.
- Anticipating ethical issues at a later stage of clinical translation, **trial design** was discussed. While randomized controlled trials are the gold standard for generating evidence, in surgery, procedures are usually refined gradually over time and trials may be limited by the practical and ethical difficulties in determining a comparator group (eg. sham surgery). In order for research ethics committees to be able to adequately assess such trial designs they may need to enlist experts in the area of regenerative medicine and ethics.
- Engagement with the general public through **dialogue** was seen as essential in order to maintain (or restore) trust and promote willingness to engage in (trials of) this technology and societal support for this scientific endeavor. Communication should neither fuel hype nor crush h ope. Transparency, comprehensible language and patient involvement are key.

4 Outcomes

- Publication of video recording within ESOT's TranspantLive educational space: ESOT (esottransplantlive.org)
- Publication of the video recording on the VANGUARD project website: Ethics of early clinical trials in regenerative medicine in transplantation – VANGUARD (vanguard-project.eu)
- Publication of the meeting report in *Transplant International*:
  Bunnik, E., de Jongh, D., Massey, E., and the VANGUARD Consortium. Ethics of Early Clinical Trials of Bio-Artificial Organs. *Transpl Int*, 2022 Jul 6;35:10621. doi: 10.3389/ti.2022.10621

5 Next steps

Further exploration of the ethical, legal and psychosocial aspects of bioartifical organs including empirical studies among patients and professionals.