The Focal Point: Advocacy & Legislative Update
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World's First Corneal Transplant Made from Reprogrammed Stem Cells

In July, a Japanese woman in her forties received the first-ever corneal transplant made from extremely thin sheets of induced pluripotent stem cells (iPSCs) — adult skin cells that have been reprogrammed into stem cells — to treat a disease of the cornea. The team of researchers from Osaka University in Japan, led by ophthalmologist Dr Kohji Nishida, reported that over the past month the woman's cornea has remained clear and her vision has improved.

"We have only conducted the first operation and we are continuing to monitor the patient carefully", Nikida said at the press conference. The Japanese health ministry has given approval for a total of four patients to receive a corneal transplant made from stem cells and the second procedure will be performed later this year.

Although stem cells are less prone to immune rejection, doctors will cautiously monitor the patient to fully determine the safety and efficacy of the treatment. Potential tumor growth is the main risk associated with stem cell therapies.

Video : https://eyewire.news/videos/japan-conducts-worlds-first-transplant-for-corneal-disease-using-ips-cells/

HHS Seeks Comments on Proposed Revisions to the 2013 PHS Guideline for Reducing HIV, HBV, and HCV Through Organ Transplantation

The Office of the Assistant Secretary for Health in the Department of Health and Human Services (HHS) seeks public comment regarding proposed revisions to the 2013 PHS Guideline for Reducing Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV) Through Organ Transplantation.

HHS is considering the following revisions to current recommendations in the 2013 Guideline:

1. Test all organ donors for HIV, HBV, and HCV using serological tests (including total antibody to hepatitis B core antigen [total anti-HBc], hepatitis B surface antigen [HBsAg], and hepatitis C antibody [anti-HCV]) and NAT.

- For living potential donors, testing should continue to be performed as close as possible to the surgery, but at least within the 7-day time period prior to organ recovery.
- For deceased donors, the donor specimen should be collected within 72 hours prior to organ recovery with results of these screening tests available at the time of organ recovery. If the donor sample used for testing was collected more than 24 hours prior to

organ recovery, an additional donor specimen should be collected in the immediate 24 hours prior to organ recovery and tested for HIV, HBV, and HCV by NAT. Results of these screening tests should be made available as soon as possible, even if these results might not be available at the time of organ recovery.

2. Regardless of donor risk profile for HIV, HBV, or HCV, transplant programs should test all organ recipients:

- Before transplantation for HIV, HBV, and HCV using NAT and serologic tests including total anti-HBc, HBsAg, anti-HCV, and hepatitis B surface antibody (anti-HBs);
- At 4-6 weeks following transplantation for HIV, HBV, and HCV (with NAT); and
- At 12 months following transplantation for HBV (with NAT).

3. OPOs should ascertain whether any of the following medical or social risk criteria were present in potential organ donors within 30 days prior to organ recovery:

- Sex with a person known/suspected to be HIV, HBV, or HCV infected
- Being a man who has had sex with another man
- Sex in exchange for money/drugs
- Non-medical drug injection
- Sex with a person with history of non-medical drug injection
- Incarceration for >72 consecutive hours
- Child breastfed by a mother with HIV
- Child born to a mother with HIV, HBV, or HCV

OPOs should identify donors for whom medical and social history is unknown at the time of organ recovery, which is also considered a risk criterion.

4. When donors with ≥1 of the criteria as specified under #3 are identified, OPO's should communicate this information to the appropriate transplant centers. Transplant centers should discuss this information with transplant candidates and families as part of transplantation-related informed consent discussions. Transplant centers should make efforts to contextualize these discussions and should include the following:

- The risk of undetected HIV, HBV, or HCV infection is very low
- Recipients are universally tested for HIV, HBV, and HCV after transplantation and should transmission occur, effective therapies are available
- Recipients may have a higher chance of survival by accepting organs from donors with risk factors for HIV, HBV, and HCV compared with waiting for an organ from a donor without recognized risk factors

5. Remove any specific label (*e.g.,* “increased risk donor”) to describe donors with risk factors for undetected HIV, HBV, or HCV infection, with inclusion of additional strategies to enhance recipient safety.

6. No requirement for specific informed consent with recipients who are considering acceptance of these organs, though recipients would still be informed of certain donor risk factors.

7. All organ transplant candidates should be vaccinated for HBV per previous recommendations (*https://doi.org/10.1111/ctr.13563*).

8. HHS proposes no additional substantive changes to the following sections of the 2013 PHS Guideline

- Collection and/or storage of donor and recipient specimens

- Tracking and reporting of HIV, HBV, and HCV infection in donors or recipients

HHS seeks informed feedback regarding this proposed approach to revising the recommendations in the 2013 Guideline, including the feasibility of the recommended timing of testing for living and deceased donors. Comments must be received no later than 5:00 p.m. ET on September 26, 2019 to be considered.

FDA Finalizes HDE Guidance

The FDA has issued final guidance on its Humanitarian Device Exemption (HDE) program , further clarifying the criteria to determine "probable benefit" related to its decision-making process for humanitarian use devices (HUDs).

HUDs are medical devices intended to help treat or diagnose diseases or conditions that affect or are manifested in not more than 8,000 individuals in the US per year, a number which was increased by the *Cures Act* from 4,000 individuals per year.

The guidance addresses commonly asked questions about HDEs and Humanitarian Use Devices (HUDs), including FDA actions on HDE applications, post-approval requirements, and special considerations for devices marketed under the HDE Program.

When FDA Can Accept Greater Premarket Uncertainty for Medical Devices

The Center for Devices and Radiological Health (CDRH) at FDA finalized guidance that explains when agency review staff may be able to accept greater premarket uncertainty about a device's benefit-risk profil e .

The guidance informs industry of the process FDA follows for considering acceptable levels of uncertainty about a device in making benefit-risk determinations for premarket applications, de novo classification requests or humanitarian device exemption applications.

The guidance provides illustrative examples on how the principles for considering uncertainty could be applied in the context of clinical evidence and when greater uncertainty could be appropriate in the PMA context, such as PMAs for Breakthrough Devices and PMAs for devices intended for small patient populations.

FDA Announces Clinical Investigator Training Course

CDER Small Business and Industry Assistance (SBIA) announced that a Clinical Investigator Training Course will be held November 12-14, 2019 in College Park, MD.
This course provides a study of clinical trial principles with in-depth coverage of clinical trial design, issues in safety and efficacy, investigator responsibilities, understanding the investigator brochure, and FDA requirements across Centers. Upon completion, attendees should understand pre-clinical research, clinical trials, and FDA submissions for licensure of medical products.

Draft Guideline Recommends Hepatitis C Screening for All US Adults

A draft recommendation from the US Preventive Services Task Force calls for adults ages 18 to 79 to be screened for the hepatitis C virus, and the draft will be open for public comment until Sept. 23. The recommendation is a departure from 2013 guidelines, which endorsed HCV screening for baby boomers and high-risk individuals.

Since the 2013 recommendations, new evidence suggests the number of new HCV cases per year is now approximately 3.5 times higher compared with 10 years ago. Rates have rapidly increased among younger people — especially women, those who inject drugs, and those who live in rural areas. And as baby boomers age, HCV infections in individuals older than 79 years are expected to increase.

FDA Issues Warning Letter to Marketer of Unapproved Stem Cell Products

The FDA sent a letter to Stemell warning against the marketing of unapproved stem cell-based products derived from umbilical cords and umbilical cord blood. Stemell manufactures and markets two stem cell-based products, StemL UCB-Plus and StemL UCT-Plus, for allogenic use as regenerative cellular therapies to treat specific conditions such as arthritis. These products should be regulated as drugs and biologics.

The warning letter also details 11 citations for GTP and GMP violations, including failing to document donor eligibility determinations; failing to maintain donor screening procedures; process and laboratory controls issues; and lacking appropriate written procedures for validating aseptic and sterilization processes.

Google to Ban Ads for Stem Cell Therapies

Google has announced a new Healthcare and medicines policy that bans advertising for "unproven or experimental medical techniques, such as most stem cell therapy, cellular (non-stem) therapy, and gene therapies" that have not been tested in rigorous clinical trials.

The company said it has seen "a rise in bad actors" attempting to take advantage of people "by offering untested, deceptive treatments." Google will continue to allow advertising for clinical trials and for clinicians to promote research findings to the public.

CMS Releases Final Rule to Address Fraud in Medicaid, Medicare, CHIP

The CMS issued a final rule, " Medicare, Medicaid, and Children's Health Insurance Programs; Program Integrity Enhancements to the Provider Enrollment Process ," to address fraud and other vulnerabilities in the CMS Medicare and Medicaid programs.

Medicare, Medicaid and CHIP providers will have to disclose any current or previous affiliation with an organization that has uncollected debt, has had a payment suspension under a federal healthcare program, has been excluded from those programs, or has had billing privileges denied or rescinded.

The final rule creates a new authority that allows CMS to revoke or deny health care provider eligibility for Medicare, Medicaid and the Children's Health Insurance Program if they were previously affiliated with a banned entity or if they exhibit a wasteful or fraudulent pattern of ordering treatments or services, among other scenarios. The rule will take effect Nov. 4.

FDA Recalls Sterile Products from Pacifico National Inc. dba AmEx Pharmacy

The FDA is alerting patients and health care professionals not to use drug products intended to be sterile made by Pacifico National Inc., an outsourcing facility doing business as AmEx Pharmacy , in Melbourne, Florida. The drugs—which include Avastin and other compounded ophthalmic products— pose unnecessary risks due to significant quality and sterility concerns.

Following an inspection of the pharmacy's production facility, the FDA requested in a letter not only that the company immediately initiate a recall of all unexpired drugs intended to be sterile, but also stop production of all drugs intended to be sterile until remediation actions have been taken.

The FDA has received reports of adverse events associated with the use of AmEx Pharmacy's drugs. Health care professionals are encouraged to report adverse events to the FDA's MedWatch Adverse Event Reporting program online at www.fda.gov/medwatch/report.htm .

Upcoming Events & Deadlines

September 11: Keeping Track of Your Training Program: Best Practices in QA
October 10: 2019 EBAA Fall Leadership Meeting
October 10: 2019 Medical Advisory Board: Live Audio Broadcast
October 11: 2019 Cornea and Eye Banking Forum
October 13: Run for Vision 5k (San Francisco)
October 14: Slit Lamp Microscopy Seminar Registration Deadline