The Focal Point: Advocacy & Legislative Update
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FDA Announces TRG Rapid Inquiry Program

FDA is announcing the TRG Rapid Inquiry Program (TRIP) program, for regulated industry to rapidly obtain a preliminary assessment from FDA as to how their HCT/Ps are appropriately regulated. The TRIP is a temporary program of FDA's Tissue Reference Group (TRG), effective June 12, 2019, to December 31, 2019.

The TRIP will help manufacturers of human cells, tissues, and cellular and tissue-based products (HCT/Ps), including those stakeholders that market HCT/Ps to physicians or patients (hereafter referred to collectively as regulated industry), obtain a rapid, preliminary, informal, non-binding assessment from FDA regarding how specific HCT/Ps are regulated. As resources permit, FDA intends to provide preliminary, informal, non-binding responses within 3 business days after receiving an inquiry that contains sufficient detail for evaluation.

FDA Obtains Permanent Injunction Against US Stem Cell

A US District Court granted a permanent injunction requiring US Stem Cell Clinic to stop marketing unapproved adipose-derived stem cell treatments, which have been associated with severe complications in patients, including loss of sight.

US District Judge Ursula from the Southern District of Florida ruled that stromal vascular fraction (SVF) cells can be a drug and subject to the *Federal Food, Drug, and Cosmetic Act*'s (FDCA) adulteration and misbranding provisions.

US Stem Cell Clinic LLC of Weston, FL and US Stem Cell, Inc. of Sunrise, FL failed to comply with the requirements of current good manufacturing practices (CGMP) and current good tissue practice (CGTP) requirements, and that the company had also refused to allow FDA investigators entry, except by appointment, and denied access to employees, which is a violation of federal law.

By siding with FDA, the court ruling marked a new win in the agency's campaign to crack down on stem cell clinics offering stem cell treatments that are unproven and could potentially cause serious patient harm. The only stem cell-based products that are FDA-approved for use in the United States consist of blood-forming stem cells (hematopoietic progenitor cells) derived from cord blood.

FDA Sends Untitled Letter to Arizona Stem Cell Company

FDA issued an untitled letter to R3 Stem Cell, LLC for unlawfully marketing stem cell therapies for numerous diseases or conditions, such as dementia and Parkinson's disease and directing patients with amyotrophic lateral sclerosis (ALS), diabetes, kidney failure, Lyme disease, Parkinson's disease, and stroke to its more than 50 affiliate centers or clinics.

"Such unapproved uses raise potential significant safety concerns. Additionally, because the products are administered by various higher risk routes of administration, including IV, their use, if contaminated could cause a range of adverse events," FDA said.
In order to lawfully market a drug that is also a biological product, a valid biologics license must be in effect [42 U.S.C. 262(a)]. Such licenses are issued only after a demonstration that the product is safe, pure, and potent. While in the development stage, such products may be distributed for clinical

use in humans only if the sponsor has an investigational new drug (IND) application in effect as specified by FDA regulations [21 U.S.C. 355(i); 42 U.S.C. 262(a)(3); 21 CFR Part 312].
The letter is part of a wider crackdown on dubious stem cell clinics that have cropped up across the US. FDA has issued almost 50 warning and untitled letters to such companies and is involved in two pending court cases.

New Guidance on Organ and Tissue Donation After Medical Assistance in Dying (MAiD)

A new publication in CMAJ (Canadian Medical Association Journal) aims to help health care teams navigate clinical and ethical issues that arise when patients choose to donate organs or tissue after medical assistance in dying (MAiD) or withdrawal of life-sustaining measures. Deceased organ donation is a common practice that saves or improves lives worldwide, and accounts for more than 3 in 4 of all transplanted organs in almost 2,000 Canadians every year.

KEY POINTS:

- First-person consent for organ donation after medical assistance in dying (MAiD) or withdrawal of life-sustaining measures (WLSM) should be an option in jurisdictions that allow MAiD or WLSM and donation after circulatory determination of death.
- The most important ethical concern — that the decision for MAiD or WLSM is being driven by a desire to donate organs — should be managed by ensuring that any discussion about organ donation takes place only after the decision for MAiD or WLSM is made.
- If indications for MAiD change, this guidance for policies and the practice of organ donation after MAiD should be reviewed to ensure that the changes have not created new ethical or practical concerns.

FDA Workshop to Explore Randomized Trials Using RWE for Regulatory Decisions

FDA announced that it will host a 2-day public workshop on leveraging randomized clinical trials to generate real-world evidence (RWE) for regulatory decisions on July 11 and 12, 2019. There will also be a live webcast for those unable to attend the meeting in person.

The Duke-Margolis Health Policy Center will convene the workshop under a cooperative agreement with FDA to explore how randomized clinical trial designs, including those that incorporate pragmatic design elements, can use real-world data (RWD) to generate RWE in clinical settings. Considerations noted in the discussions will inform the potential usefulness of RWE to support regulatory decision-making.

Considerations for discussion include: (1) selection of interventions appropriate in clinical care settings, (2) study design elements and study populations, (3) capturing outcomes in clinical care settings, and (4) addressing potential challenges around blinding, randomization, and bias. The workshop will also explore regulatory considerations for randomized clinical trials using RWD, such as safety and product monitoring and maintaining data integrity.

FDA Drafts Guidance on Enhancing Diversity in Clinical Trial Populations

FDA issued a draft guidance aimed at increasing diversity in clinical trial populations as part of its efforts to encourage drugmakers to enroll populations that more closely reflect the populations that will take the drugs in the real world.

The guidance entitled "Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs" recommends approaches that sponsors of clinical trials to support a new drug application [NDA] or a biologics license application [BLA] can take to broaden eligibility criteria, when scientifically and clinically appropriate, and increase enrollment of underrepresented populations in their clinical trials.

USP Updated Chapter 797 Now Available

The United States Pharmacopeia (USP) has released its updated General Chapter <797> on Sterile Compounding including FAQs. USP develops standards for preparing compounded sterile medications to help ensure patient benefit and reduce risks such as contamination, infection or incorrect dosing. This revised chapter contains important information on safe compounding and will become official on December 1, 2019.

Research News

Trump Administration Restricts Fetal Tissue Research

The Department of Health and Human Services (HHS) announced June 5 that it will no longer allow government scientists working for the National Institutes of Health (NIH) to conduct studies that use fetal tissue. Such intramural studies received about $31 million last year.

HHS also said university scientists who want NIH funding for such studies must now have each proposal examined by an ethics advisory board. The new policy will not affect currently funded extramural projects but will apply to researchers who apply for a renewal of a current grant or for new grants.

The government has already decided against renewing its contract with a laboratory at the University of California, San Francisco (UCSF), that uses fetal tissue to develop humanized mice for HIV drug testing.

New Laser Eye Surgery Promises to Double the Number of Donor Corneas

A new laser corneal transplant technique has been successfully performed in the UK for the first time, in an advance that promises to double the number of available donor corneas. Known as the Femto LDVZ8, the technique is so precise it can split corneal tissue in two, increasing the number of uses and patients it can benefit.

Doctors at University Hospital Southampton, where the operation was performed, said the machine pulses at one quadrillionth of a second. The procedure allows one corneal donor tissue to be used in two recipients and, therefore, a single eye donor could restore sight in up to four patients. In the UK, the sight of 4,000 people was restored through a transplant last year but there is a shortage of suitable donors, with some patients waiting four to six months for corneal transplant tissue.

Researchers 3-D Print First Human Cornea in U.S.

Florida A&M University (FAMU) College of Pharmacy & Pharmaceutical Sciences (COPPS) researchers have, for the first time in the United States, created corneas using a high throughput 3D printer. The corneas will eventually be entered into an artificial blinking eye, which was also printed in 3D, tear fluid and all. That way, products can be tested in a simulated atmosphere, reducing the need for animal testing.