



Nebraska Department of Health and Human Services
HEALTH ALERT NETWORK
Advisory



TO: Nebraska Primary Care Providers, Infection Preventionists, Infectious Disease, Orthopedics, Ophthalmologists, and Public Health

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RE: Risk Associated with Unapproved Products Derived from Stem Cells, Placenta, and Umbilical Cord Blood

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Recent events in our state and others have highlighted the risks to patients treated with unapproved stem cell, placental and umbilical cord blood-derived products. A recent incident involved individuals treated in Nebraska who became ill after receiving a product derived from C-section placentas, a subset of whom became bacteremic. The FDA recently issued a warning regarding unapproved products derived from stem cells.¹ Today, the FDA has issued a patient safety notification warning of risks associated with products derived from stem cells and placentas, especially a product termed exosomes.² These therapies are administered through intravenous injection, inhalation, or injection into joints or soft tissue. Nebraska DHHS continues to actively assess this situation along with our federal partners at the FDA and CDC.

FDA and CDC Warnings Regarding Unapproved Stem Cell Derived Therapies

According to the FDA, stem cell therapies offer the potential to repair, restore, replace, and regenerate cells, and could *possibly* be used to treat many medical conditions and diseases for which few therapies currently exist. The New England Journal of Medicine has published articles further clarifying the benefits and risks of these therapies.^{3, 4} For almost all of these products, it is not yet known whether the product has any benefit—or if the product is safe to use. The FDA is concerned that some patients seeking cures and remedies may resort to stem cell treatments that are potentially harmful.² The CDC and FDA report that clinics are marketing stem cell-derived therapies for conditions ranging from arthritis, injury-related pain, chronic joint pain, and anti-aging.^{1, 2, 5} According to the FDA certain clinics across the country “deceive patients with unsubstantiated claims about the potential for these products (exosomes) to prevent, treat or cure various diseases or conditions”.²

The only FDA-approved stem cell-based products consist of blood-forming stem cells (hematopoietic progenitor cells) derived from cord blood. These products are approved for limited use in patients with hematologic disorders or malignancies. There are currently no FDA-approved exosome products. The FDA states that some clinics “claim that these products do not

fall under the regulatory provisions for drugs and biological products – that is simply untrue.”² However, stem cell-derived therapies can be offered in clinical trials under an Investigational New Drug Application (IND). An IND is a clinical investigation plan submitted and approved by the FDA. When clinical trials are not conducted under an IND, the FDA has not reviewed the experimental therapy to help make sure it is reasonably safe. (Learn more on the [FDA’s clinical trials page](#).)

Because of a number of reported adverse events, the FDA is increasing its oversight and enforcement to protect people, while continuing to encourage innovation so that the medical industry can properly harness the potential of stem cell products.¹

The FDA has the authority to regulate stem cell products in the United States. When stem cell products are used in unapproved ways—or when they are processed in ways that are more than minimally manipulated, which relates to the nature and degree of processing—the FDA may take (and has already taken) a variety of administrative and judicial actions, including criminal enforcement, depending on the violations involved.¹

Health care providers and their patients should be aware of potential risks related to unproven and unapproved stem cell treatments, placental and umbilical cord blood derived products including exosomes as noted by the FDA^{1,2} and CDC³:

- Failure of the cells to work as expected
- Injection site reaction
- Growth of tumors
- Infections
- Potential for contamination of the product
- The ability of cells to move from placement sites and multiply or change into inappropriate cell types

These above concerns exist even for the use of the patient’s own cells.

How You Can Protect Your Patients: Clinicians should consider the possibility of procedure-related infection following administration of these types of therapies. Patients with symptoms consistent with infection (fever, chills, etc.) should be cultured and treated empirically. Reported bacteremias in such patients have been caused by *E.coli*, *Enterobacter cloacae* and polymicrobial agents.

Patients with infections or other complications following treatment with such products should be reported to Nebraska DHHS Division of Public Health and the FDA, even if this has occurred in the past Contact Dr. Maureen Tierney with Nebraska DHHS, at the phone number above or email her at Maureen.Tierney@Nebraska.gov, and report the event to the FDA via [MedWatch](#).

Educate your patients of the risks of receiving unapproved products used in therapies and refer them to the FDA and CDC links below.

What Patients Can Do to Protect Themselves: The CDC and FDA offer the following advice for patients if you are considering stem cell treatments^{2,3}:

- Check to make sure the product you are considering is on the [FDA’s approved list of stem cell treatments](#).

- If the stem cell product is not on the approved list, ask the provider to show you that they have FDA permission to research a new drug, which requires an IND application number and acknowledgment communication issued by FDA.
- Request the facts and ask questions if you don't understand. To participate in a clinical trial that requires an IND application, you must sign a consent form that explains the experimental procedure. The consent form also identifies the Institutional Review Board (IRB) that assures the protection of the rights and welfare of human subjects. Make sure you understand the entire process and known risks before you sign. You also can ask the study sponsor for the clinical investigator's brochure, which includes a short description of the product and information about its safety and effectiveness.
- Ask for this information before getting treatment—even if the stem cells are your own.

Patients considering treatment using an exosome product in another country should:

- Learn about regulations that cover products in that country.
- Know that FDA does not have oversight of treatments done in other countries. FDA typically has little information about foreign establishments or their products.
- Be cautious. If you're considering an exosome product in a country that may not require regulatory review of clinical studies, it may be hard to know if the experimental treatment is reasonably safe.

1. <https://www.fda.gov/consumers/consumer-updates/fda-warns-about-stem-cell-therapies>
2. <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>
3. Blau, HM, Daley, GQ. Stem Cells in the Treatment of Disease. N Engl J Med 2019; 380:1748-1760.
4. Marks, PW, Witten, CM, Califf, RM. Clarifying Stem-Cell Therapy's Benefits and Risks. N Engl J Med 2017; 376:1007-1009
5. <https://www.cdc.gov/hai/outbreaks/stem-cell-products.html>