



May 29, 2019

UPS EXPRESS MAIL

A New Way Clinic
9320 SW Barbur Blvd, Suite 165
Portland, OR 97219

To Whom It May Concern:

R3 Stem Cell, LLC (R3) has identified you as a R3-affiliated clinic or center on its website, available at www.r3stemcell.com. For that reason, the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) is enclosing for your attention a copy of an Untitled Letter issued to R3 on May 28, 2019.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research



May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

Dear Dr. Greene:

The Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) has reviewed the website for R3 Stem Cell, LLC, available at www.r3stemcell.com (R3 Stem Cell website, or website), which offers “regenerative stem cell therapies” at affiliated centers or clinics throughout the United States.

R3 Stem Cell promotes these stem cell therapies for numerous diseases or conditions, such as dementia and Parkinson’s disease, see <https://r3stemcell.com/conditions/dementia/>, and directs patients with amyotrophic lateral sclerosis (ALS), diabetes, kidney failure, Lyme disease, Parkinson’s disease, and stroke to certain “R3 Stem Cell Centers of Excellence” for stem cell treatment. For example, the website states:

- “R3 Stem Cell is now offering stem cell therapy for ALS at several Centers of Excellence.” See <https://r3stemcell.com/conditions/als/#>.
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In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

The above-referenced stem cell therapies appear to be human cell, tissue, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

HCT/Ps that do not meet all the criteria in 21 CFR 1271.10(a), and when no exception in 21 CFR 1271.15 applies, are not regulated solely under section 361 of the PHS Act [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Such products are regulated as drugs, devices, and/or biological products under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and/or the PHS Act, and are subject to additional regulation, including appropriate premarket review.

Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

We note that your products are intended to treat a variety of serious or life-threatening diseases or conditions. 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. We direct your attention to FDA’s comprehensive regenerative medicine policy framework for HCT/Ps, which is intended to spur innovation and efficient access to safe and effective regenerative medicine products. The policy framework is outlined in a suite of four guidance documents available on FDA’s website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

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Sincerely,

Mary A.
Malarkey -S

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cn=Mary A. Malarkey -S
Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
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Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



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Advanced Stem Cell Institute - Beverly Hills Ca
5757 Wilshire Blvd, Suite 490
Los Angeles, CA 90036

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



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Advanced Stem Cell Institute - Encino CA
16952 Ventura Blvd, #100
Encino, CA 91316

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



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Advanced Stem Cell Institute - Rancho Cucamonga Ca
8599 Haven Ave, Suite 103
Rancho Cucamonga, CA 91730

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13847 E 14th St
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Sincerely,

Mary A.
Malarkey -S

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ou=FDA, ou=People,
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cn=Mary A. Malarkey -S
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Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Align Medical - Surprise AZ
15278 W Bell Rd, #114
Surprise, AZ 85374

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Director
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May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Atlas Medical Center
3401 W Airport Fwy, Suite 101
Irving, TX 75062

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

BOD RX
710 Tennent Rd, Suite 104
Manalapan, NJ 07726

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Bothell Regenerative Medicine
18920 Bothell Way NE, Suite 100
Bothell, WA 98011

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Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

CRMC
7901 Santa Monica Blvd
West Hollywood, CA 90046

To Whom It May Concern:

R3 Stem Cell, LLC (R3) has identified you as a R3-affiliated clinic or center on its website, available at www.r3stemcell.com. For that reason, the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) is enclosing for your attention a copy of an Untitled Letter issued to R3 on May 28, 2019.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research



May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

Dear Dr. Greene:

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R3 Stem Cell promotes these stem cell therapies for numerous diseases or conditions, such as dementia and Parkinson’s disease, see <https://r3stemcell.com/conditions/dementia/>, and directs patients with amyotrophic lateral sclerosis (ALS), diabetes, kidney failure, Lyme disease, Parkinson’s disease, and stroke to certain “R3 Stem Cell Centers of Excellence” for stem cell treatment. For example, the website states:

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In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

The above-referenced stem cell therapies appear to be human cell, tissue, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

HCT/Ps that do not meet all the criteria in 21 CFR 1271.10(a), and when no exception in 21 CFR 1271.15 applies, are not regulated solely under section 361 of the PHS Act [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Such products are regulated as drugs, devices, and/or biological products under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and/or the PHS Act, and are subject to additional regulation, including appropriate premarket review.

Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

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Del Mar Integrative Medicine
1349 Camino Del Mar, Suite B
Del Mar, CA 92014

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May 29, 2019

UPS EXPRESS MAIL

Freedom Healthcare - Independence MO
4200 Little Blue Parkway, Suite 320
Independence, MO 64057

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10074 Woodland Rd
Lenexa, KS 66220

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Malarkey -S

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Director
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Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Freedom Healthcare - St Joseph MO
1802 N Woodbine Rd.
St Joseph, MO 64506

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May 28, 2019

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David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

FRID Institute of Regenerative Medicine
151 East 62nd St., Ste 1A
New York, NY 10065

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Genesis Medical
9780 N 56th St
Tempe Terrace, FL 33617

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23813 La Cadena Dr, Suite 103
Laguna Hills, CA 92653

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ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=1300054353
cn=Mary A. Malarkey -S
Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Green Sports Medicine
2021 Herndon Ave, #101
Fresno, CA 93611

To Whom It May Concern:

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Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
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May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

Dear Dr. Greene:

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In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

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Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

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May 29, 2019

UPS EXPRESS MAIL

IE Stem Cell Institute
3333 Concourse St., Building 4, Suite 4200
Ontario, CA 91764

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Innovative Medical Center
55 Caren Ave, Suite 360
Worthington, OH 43085

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

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Integrative Medical Center
11111 N. Scottsdale Rd, Suite 105
Scottsdale, AZ 85254

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Magnificat Wellness Center
17833 Kuykendahl Rd
Spring, TX 77379

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Sincerely,

Mary A.
Malarkey -S

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ou=FDA, ou=People,
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Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
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Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

MD Pain - Greenwood Village CO
6950 East Bellview Ave, Suite 300
Greenwood Village, CO 80111

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May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

MD Pain - Parker CO
11960 Lioness Way, Suite 130
Parker, CO 80134

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

MD Pain - Thornton CO
3655 East 104th Ave
Thornton, CO 80233

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May 29, 2019

UPS EXPRESS MAIL

Nirvana Med Spa
Salaman Hashmi
14524 Cantrell Rd, Suite 130
Little Rock, AR 72223

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Digitally signed by Mary A. Malarkey -S
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ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=1300054353
cn=Mary A. Malarkey -S
Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

NYC Stem Cell Institute
22 W 48th St, Suite 300
New York, NY 10036

To Whom It May Concern:

R3 Stem Cell, LLC (R3) has identified you as a R3-affiliated clinic or center on its website, available at www.r3stemcell.com. For that reason, the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) is enclosing for your attention a copy of an Untitled Letter issued to R3 on May 28, 2019.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research



May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

Dear Dr. Greene:

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R3 Stem Cell promotes these stem cell therapies for numerous diseases or conditions, such as dementia and Parkinson’s disease, see <https://r3stemcell.com/conditions/dementia/>, and directs patients with amyotrophic lateral sclerosis (ALS), diabetes, kidney failure, Lyme disease, Parkinson’s disease, and stroke to certain “R3 Stem Cell Centers of Excellence” for stem cell treatment. For example, the website states:

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In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

The above-referenced stem cell therapies appear to be human cell, tissue, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

HCT/Ps that do not meet all the criteria in 21 CFR 1271.10(a), and when no exception in 21 CFR 1271.15 applies, are not regulated solely under section 361 of the PHS Act [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Such products are regulated as drugs, devices, and/or biological products under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and/or the PHS Act, and are subject to additional regulation, including appropriate premarket review.

Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

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May 29, 2019

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Optilux Wellness Center
706 Stevenson Blvd.
New Kensington, PA 15068

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Optimal Medical Group - Fresno
7206 North Milburn Ave, Suite 106
Fresno, CA 93722

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May 29, 2019

UPS EXPRESS MAIL

Orthopedic Center for PRP & Stem Cell
2690 Pacific Ave
Long Beach, CA 90806

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Prescott Functional Wellness
1151 Iron Springs Rd, Suite F
Prescott, AZ 86305

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Sincerely,

Mary A.
Malarkey -S

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Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

R3 Stem Cell - Austin TX
4611 Guadalupe St, Ste 200
Austin, TX 78751

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Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
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May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

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Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

R3 Stem Cell - Cedar Park TX
715 Discovery Blvd, Suite 102
Cedar Park, TX 78613

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

R3 Stem Cell - Lakeway
5329 Serene Hills Dr, Suite 202
Austin, TX 78738

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8962 East Desert Cove Avenue #115
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May 29, 2019

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R3 Stem Cell - Oakton VA
2915 Hunter Mill Rd, #11
Oakton, VA 22124

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Malarkey -S

Digitally signed by Mary A. Malarkey -S
DN: c=US, o=U.S. Government, ou=HHS,
ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=1300054353
cn=Mary A. Malarkey -S
Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Regenerative Medicine of Columbus
8621 Columbus Pike
Lewis Center, OH 43035

To Whom It May Concern:

R3 Stem Cell, LLC (R3) has identified you as a R3-affiliated clinic or center on its website, available at www.r3stemcell.com. For that reason, the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) is enclosing for your attention a copy of an Untitled Letter issued to R3 on May 28, 2019.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
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May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

Dear Dr. Greene:

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R3 Stem Cell promotes these stem cell therapies for numerous diseases or conditions, such as dementia and Parkinson’s disease, see <https://r3stemcell.com/conditions/dementia/>, and directs patients with amyotrophic lateral sclerosis (ALS), diabetes, kidney failure, Lyme disease, Parkinson’s disease, and stroke to certain “R3 Stem Cell Centers of Excellence” for stem cell treatment. For example, the website states:

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In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

The above-referenced stem cell therapies appear to be human cell, tissue, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

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Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

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8962 East Desert Cove Avenue #115
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May 29, 2019

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Santa Monica Physical Medicine
2232 Santa Monica Blvd, #101
Santa Monica, CA 90404

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Stem Cell Clinics of America - Arlington Heights
415 W Golf Rd, Suite 3
Arlington Heights, IL 60005

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1283 W. Dundee Rd
Buffalo Grove, IL 60089

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810 S. McLean Blvd
Elgin, IL 60123

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Sincerely,

Mary A.
Malarkey -S

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ou=FDA, ou=People,
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Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Stem Cell Clinics of America - McHenry
202 South Route 31
McHenry, IL 60050

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Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
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May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

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Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Stem Cell Clinics of California
1575 N Lake Ave, Suite 100
Pasadena, CA 91104

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cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Total Health Rejuvenation - Atlanta
2941 Piedmont Rd NE, Suite C
Atlanta, GA 30305

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May 29, 2019

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Tulsa Pain Care Group
817 S Elm Place, Suite 106
Broken Arrow, OK 74012

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Malarkey -S

Digitally signed by Mary A. Malarkey -S
DN: c=US, o=U.S. Government, ou=HHS,
ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=1300054353
cn=Mary A. Malarkey -S
Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Venturis Clinic
7917 N. May Ave
Oklahoma City, OK 73120

To Whom It May Concern:

R3 Stem Cell, LLC (R3) has identified you as a R3-affiliated clinic or center on its website, available at www.r3stemcell.com. For that reason, the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (FDA) is enclosing for your attention a copy of an Untitled Letter issued to R3 on May 28, 2019.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research



May 28, 2019

UPS EXPRESS MAIL

David Greene, MD, MBA, Chief Executive Officer
R3 Stem Cell, LLC
6042 East Brianna Road Cave
Creek, AZ 85331

Dear Dr. Greene:

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R3 Stem Cell promotes these stem cell therapies for numerous diseases or conditions, such as dementia and Parkinson’s disease, see <https://r3stemcell.com/conditions/dementia/>, and directs patients with amyotrophic lateral sclerosis (ALS), diabetes, kidney failure, Lyme disease, Parkinson’s disease, and stroke to certain “R3 Stem Cell Centers of Excellence” for stem cell treatment. For example, the website states:

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In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

The above-referenced stem cell therapies appear to be human cell, tissue, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

HCT/Ps that do not meet all the criteria in 21 CFR 1271.10(a), and when no exception in 21 CFR 1271.15 applies, are not regulated solely under section 361 of the PHS Act [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Such products are regulated as drugs, devices, and/or biological products under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and/or the PHS Act, and are subject to additional regulation, including appropriate premarket review.

Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

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8962 East Desert Cove Avenue #115
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May 29, 2019

UPS EXPRESS MAIL

Wellness Rejuvenation - Henderson
1681 Horizon Ridge Parkway
Henderson, NV 89012

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8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Wellness Rejuvenation - Las Vegas
311 North Buffalo Dr, Suite A
Las Vegas, NV 89145

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Scottsdale, AZ 85260



May 29, 2019

UPS EXPRESS MAIL

Donald Plance, DO
2520 Honolulu Ave.
Montrose, CA 91020

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May 29, 2019

UPS EXPRESS MAIL

Zhenghong Yuan, MD
416 W Las Tunas Dr, #303
San Gabriel, CA 91776

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- “R3 Stem Cell is now offering stem cell therapy for stroke at several Centers of Excellence.” See <https://r3stemcell.com/conditions/stroke/>.

In addition, your website lists a variety of “conditions treated at R3 Stem Cell Clinics,” including, among numerous others: rheumatoid arthritis, spinal stenosis, and trigeminal neuralgia. See <https://r3stemcell.com/faq/>.

The above-referenced stem cell therapies appear to be human cell, tissue, or cellular or tissue-based products (HCT/Ps) as defined in 21 CFR 1271.3(d) that would be subject to regulation under 21 CFR Part 1271, issued under authority of section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

HCT/Ps that do not meet all the criteria in 21 CFR 1271.10(a), and when no exception in 21 CFR 1271.15 applies, are not regulated solely under section 361 of the PHS Act [42 U.S.C. 264] and the regulations in 21 CFR Part 1271. Such products are regulated as drugs, devices, and/or biological products under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and/or the PHS Act, and are subject to additional regulation, including appropriate premarket review.

Based on a review of your website, it appears that R3 Stem Cell, LLC does not qualify for any exception in 21 CFR 1271.15 and the stem cell therapies offered by R3 Stem Cell, LLC are intended for nonhomologous uses and would be regulated as drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)] and biological products as defined in section 351(i) of the PHS Act [42 U.S.C. 262(i)]. 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].

We note that your products are intended to treat a variety of serious or life-threatening diseases or conditions. 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. We direct your attention to FDA’s comprehensive regenerative medicine policy framework for HCT/Ps, which is intended to spur innovation and efficient access to safe and effective regenerative medicine products. The policy framework is outlined in a suite of four guidance documents available on FDA’s website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Manufacturers and health care professionals who have any uncertainty regarding the regulatory status of their products are encouraged to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P. For more information in this regard, or to obtain further information about IND requirements for biological products, please see pages 23 and 24 of the guidance entitled, Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products:

Minimal Manipulation and Homologous Use at the link to FDA's webpage provided above.

This letter addresses certain issues regarding some of the products your website offers at affiliated centers or clinics and is not intended to be an all-inclusive review of those products. You and your firm are responsible for ensuring that all your products fully comply with the PHS and FD&C Acts and all applicable regulations. Any response to this letter should be sent to the following address: U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, 10903 New Hampshire Avenue, Bldg. 71, Silver Spring, MD 20993. If you have any questions regarding this letter, please contact the Division of Case Management, CBER at (240) 402-9155. Please be advised that only written communications are considered official.

Sincerely,

Mary A.
Malarkey -S

Digitally signed by Mary A. Malarkey -S
DN: c=US, o=U.S. Government, ou=HHS,
ou=FDA, ou=People,
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Date: 2019.05.28 14:46:58 -04'00'

Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: David Greene, MD, MBA, Chief Executive
Officer R3 Stem Cell, LLC
8962 East Desert Cove Avenue #115
Scottsdale, AZ 85260