



February 11, 2020

UPS EXPRESS MAIL

Jason Bailey, DC
Owner
Bailey Health Solutions
224 Southpark Circle East
St. Augustine, FL 32086

Dr. Bailey:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 09:27:22 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Melodie Darvish, JD
Clinic Director
Create Wellness
8950 Villa La Jolla Drive, Suite C117
La Jolla, CA 92037

Dr. Darvish:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and Research

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=130005435
3, cn=Mary A. Malarkey -S
Date: 2020.02.11 16:01:52 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Christopher M. Sharp
CEO
Skye Orthobiologics, LLC
2255 Campus Drive
El Segundo, CA 90245

Mr. Sharp:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 16:11:13 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Christian J. Renna, DO
Founder
LifeSpan Medicine
2311 Cedar Springs Rd., Suite 150
Dallas, TX 75201

Dr. Renna:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 16:12:09 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Pejman Bady, DO
Medical Director
Cellaxys
5741 S Fort Apache Rd., Suite 100
Las Vegas, NV 89148

Dr. Bady:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

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,
0.9.2342.19200300.100.1.1=1300054353,
cn=Mary A. Malarkey -S
Date: 2020.02.11 16:13:04 -05'00'

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

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Gary S. Gillheeney, Sr.
President, CEO
Organogenesis, Inc
150 Dan Rd.
Canton, MA 2021

Mr. Gillheeney, Sr.:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³


Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

 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: 2020.02.11 16:14:04 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Phillip Yoo, DC
Founder, CEO
21st Century LaserSTEM Pain & Regenerative Medicine Institute
12665 Garden Grove Blvd., Suite 311
Garden Grove, CA 992843

Dr. Yoo:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 16:15:17 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Matthew G. Thorson, MD
Advanced Spine & Pain Clinics of MN
7373 France Ave., Suite 606
Edina, MN 55435

Dr. Thorson:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

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: 2020.02.11 16:16:24 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Angelo Reyes, MD
Medical Director
Affinity Integrated Healthcare
736 Florsheim Dr., Suite 13
Libertyville, IL 60048

Dr. Reyes:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.


FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

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,
0.9.2342.19200300.100.1.1=1300054353,
cn=Mary A. Malarkey -S
Date: 2020.02.11 16:17:26 -05'00'

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

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Kyle Alexander , MD
Alexander Center for Muscle and Joint Therapy
3998 Indianola Avenue
Columbus, OH 43214

Dr. Alexander :

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 09:28:24 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Charles Mok, DO
Allure Medical
8180 26 Mile Road, Suite 300
Shelby Township, MI 48316

Dr. Mok:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and Research

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: 2020.02.11 10:21:20 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Anju Mathur, MD
Medical Director and Owner
Angel Longevity Medical Center
12840 Riverside Dr., Suite 402
Studio City, CA 91607

Dr. Mathur:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 10:24:45 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Shayla Porter
Founder, CEO
Arborvitae Biologics LLC
6975 Union Park Center
Cottowood Heights, UT 84047

Ms. Porter:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³


Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

 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: 2020.02.11 12:42:19 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Frank B. Hatch, DC, FIACA
Clinic Director
Array Medical Center
18761 North Reems Rd., Suite 400B
Surprise, AZ 85374

Dr. Hatch:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 12:43:15 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Aref Karbasi, MD
Avicenna Medical Clinic
18445 Vanowen St.
Reseda, CA 91335

Dr. Karbasi:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and Research

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: 2020.02.11 12:45:01 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Simon Voitanik, MD, PhD
Avicenna Spine & Joint Care
8706 South 700 East, Suite 206
Sandy, UT 84070

Dr. Voitanik:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

**Mary A.
Malarkey -S**

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

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: 2020.02.11 12:46:19 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Roth Riley, MD
Medical Director
Balanced Well Health Center
26-01 Pellack Drive, 2nd Floor
Fair Lawn, NJ 7410

Dr. Riley:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 15:58:14 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Michael Repik, DO
Medical Director
Beverly Hills New Life Medical Group
Huntington Hospital, 100 W California Blvd
Pasadena, CA 91105

Dr. Repik:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

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,
0.9.2342.19200300.100.1.1=1300054353,
cn=Mary A. Malarkey -S
Date: 2020.02.11 15:59:20 -05'00'

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

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Bal M. Rajagopalan, MD, FRCSC
CEO
Beverly Hills Orthopedic Institute
8501 Wilshire Blvd., Suite 316
Beverly Hills, CA 90211

Dr. Rajagopalan:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.

Malarkey -S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and Research

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=130005435
3, cn=Mary A. Malarkey -S
Date: 2020.02.11 16:00:52 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Naveed Shafi, MD
BioCure Regenerative Medicine
2731 Executive Park Drive, Suite 7
Weston, FL 33331

Dr. Shafi:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

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,
0.9.2342.19200300.100.1.1=1300054353,
cn=Mary A. Malarkey -S
Date: 2020.02.11 16:03:08 -05'00'

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

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Matthew Cook, MD
Founder, President
BioReset Medical
3803 Bascom Avenue, Suite 203
Campbell, CA 95008

Dr. Cook:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³


Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

**Mary A.
Malarkey -S**

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

 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: 2020.02.11 16:05:06 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Bradley Aylor, MD
Director
Bozeman Sport, Spine, Regenerative Medicine
925 Highland Blvd, Suite 1130
Bozeman, MT 59715

Dr. Aylor:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and Research

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: 2020.02.11 16:06:21 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Cheryl Johnson, MD
Medical Director
Campbell Medical Clinic
1012 Campbell Rd.
Houston, TX 77055

Dr. Johnson:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

<https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A. Malarkey

-S

Mary A. Malarkey

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and Research

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: 2020.02.11 16:07:37 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Dean Jones, DC
Colorado Medical Solutions
621 17th Street #701
Denver, CO 80293

Dr. Jones:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 16:09:04 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.



February 11, 2020

UPS EXPRESS MAIL

Ryan Helms, DC
Colorado Regenerative Health
1 Oakwood Park Plaza, Suite 206
Castle Rock, CO 80104

Dr. Helms:

It has come to the attention of the United States Food and Drug Administration (FDA or the Agency), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ) that you appear to be offering regenerative medicine products to treat certain diseases or conditions. FDA generally regulates such products under the Public Health Service Act (PHS Act) as human cells, tissues, or cellular or tissue-based products (HCT/Ps), as defined in 21 CFR 1271.3(d). Although generally regulated as HCT/Ps, such products may also be regulated under the PHS Act and the Federal Food, Drug, and Cosmetic Act (FD&C Act), as biological products, drugs, and/or devices, and may require pre-market review.¹

In order to lawfully market an HCT/P that is also a biological product and a drug, a valid biologics license must be in effect. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products intended for clinical use in humans, generally require an investigational new drug application (IND).²

FDA's November 2017 comprehensive regenerative medicine policy framework is intended to spur innovation and efficient access to safe and effective regenerative medicine products, including HCT/Ps. An overview of the framework is outlined in a suite of four guidance documents that are available on FDA's website at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

¹ Secreted body fluids (e.g., amniotic fluid) are generally not considered HCT/Ps; see 21 CFR 1271.3(d), however, such products are subject to premarket review and approval as drugs and biological products when they are intended to treat diseases or conditions in humans.

² Please be advised that, as a general matter, exosomes for clinical use in humans are regulated as drugs and biological products under section 351 of the PHS Act and the FD&C Act, and are subject to premarket review and approval requirements. We also direct your attention to FDA's Public Safety Notification on Exosome Products, issued on December 6, 2019, and available at <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-exosome-products>.

FDA's final guidance, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*, issued in November 2017, informed manufacturers, health care providers, and other interested parties about the Agency's compliance and enforcement policy for these products. The guidance outlined FDA's intent to exercise enforcement discretion for the first 36 months following issuance of the guidance for certain products with respect to FDA's IND and premarket approval requirements when the use of the product does not raise reported safety concerns or potential significant safety concerns. This period provides manufacturers time to comply with the IND and premarket approval requirements and engage with FDA to determine whether they need to submit an IND or marketing authorization application, and if so, to submit their application to FDA.

FDA is currently applying a risk-based approach to enforcement, accounting for how products are being administered and the diseases and conditions for their use, and reminds you that the 36-month period during which FDA intends to exercise enforcement discretion will end in November 2020.³

Manufacturers, health care providers, and other interested parties who have any uncertainty regarding the regulatory status of their products, and who have not already done so, are encouraged to contact FDA well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements.

For more information on how to contact FDA to obtain a recommendation or decision regarding the classification of an HCT/P, or for 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*, available at <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm585218.htm>.

Sincerely,

Mary A.
Malarkey -S

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

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: 2020.02.11 16:10:12 -05'00'

³ Please be advised that FDA has not evaluated the application of the compliance and enforcement policy to your firm or its products. You and your firm are responsible for ensuring full compliance with the PHS and FD&C Acts and all applicable regulations.