FDA-Compiance-Enforcement-Letter-SENT-1-23-2018: updated 2-4-2018

-------- Original Message --------

Subject:	RegeneXX Case 1:10-cv-01327-RMC "Advisory panel" and "Clinical Trials" COMPLIANCE ENFORCEMENT
Date:	2018-01-23 20:06
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[BEGINNING OF DOCUMENT]

TO: USA FDA Commissioner Dr. Scott Gottlieb, M.D. (and, FDA "CBER" Ombudsman's office agents) ALSO: Manufacturer's Assist., Product Deviations, CBER(Peter Marks, M.D.- Ph.D.), Product Surveillance (CBER), DIRECTOR-OFFICE OF COMPLIANCE AND BIOLOGICS QUALITY – CBER

FROM: USA Citizen – Susan Marie [Cassady] – Neuhart

Subject: RegeneXX Case 1:10-cv-01327-RMC "Advisory panel" and "Clinical Trials" COMPLIANCE ENFORCEMENT

Date: 1-23-2018

Dear USA FDA Commissioner Dr. Scott Gottlieb, M.D. (and, FDA "CBER" Ombudsman's office agents: Ms. Sheryl Lard-Whiteford, Ph.D. and Mr. Howard S. Balick, J.D.), (CBER Compliance Director: Ms. Mary Anne Malarkey) et al

Thank you! for your recent statement regarding (the) *"FDA's comprehensive new policy approach to facilitating the development of innovative regenerative medicine products to improve human health" AND cell-based therapies and their use in regenerative medicine."* (made January 16, 2018 - Reference 1)

Sir, I read your "comprehensive new policy" announcement with great interest. As, I am exactly the person that you were referring to in your January 16, 2018 announcement. I am very hopeful of the success of "regenerative therapies"! And,

I would like to contribute – to their successful implementation and offering to the American public – if I can.

You see, I have been recently diagnosed – by a MRI procedure (performed 10-23-2017) – that I have a "*Supraspinatus Tendon Tear*" in my right shoulder. The MRI files and the radiologist's report which documents this "tear" can be accessed & downloaded through my personal web site (Reference 2) PLEASE NOTE: I DO NOT SELL ANYTHING UTILIZING MY "PERSONAL" WEB SITE. Rather, its sole purpose is to facilitate communications – with professionals – in the USA Government, my large family – and, my acquaintances. In fact, to review my personal medical documents, you will require a password and a username – which, I will gladly supply (these) – to your FDA agents. Please REPLY email your request to me – OR, use my personal web site CONTACT form. In fact, to produce these important medical documents, the US Government (and I) paid over $5,000 US dollars to the identified "radiologist" – who also (BTW) identifies himself as an M. D. – on his company web site. (Reference 5)

My "Google Research" performed thus far (Reference 6) indicates that a "conventional surgical repair" – of this tendon tear – will require the "sacrifice" of my right shoulder's Deltoid muscle – so that a conventional orthopedic surgeon may gain access to the underlying tendon area of interest – to perform surgery. Then, I must endure a 4 to 6-week period of an "immobilized" right arm.

This stated, my reasons for contacting you today are varied (totaling four items):

First, a SW Ohio "Medical Doctor" – states (on his web site) – that he is a "licensed representative" for a product called "RegeneXX". This seems odd – as, (in fact) the FDA did file and win a Court action related to this very product in 2012 and 2014. [Case 1:10-cv-01327-RMC Document 47 Filed 07/23/12] FDA vs REGENERATIVE SCIENCES, LLC, REgeneXX Procedure]. (Reference 12 – Results & COMPLAINT) The legal results (as I understand them) was full "enjoinment" [PROHIBITION] of the sale of the product "RegeneXX" & ALL related medical services– to the American public. This was (then) "upheld" – in a later & higher USA Court [2014]. (Reference 15) Now, just in case – this "*unscrupulous actor*" (Reference 1) reacts to my inquiries (already made directly to his company) by removing the "advertisements" – that I did see, I have posted his "WWW statements"- for your convenient viewing - onto my personal web site. (Reference 3) Or, you can just go (directly) to his web site: (Reference 4) This

person's full name and Medical License number are: Henry Stiene, M.D. Medical License #1063402949

Second, Sir, your announcement (Reference 1) makes it clear – that you are trying to implement an "innovative policy" – related to "regenerative scientific products and services." Thus, I realize, that it is possible that Mr. Stiene – has obtained the necessary "special standing" with the FDA (via your announced procedures) to administer the "RegeneXX procedure" – to SW-Ohio persons. [that is, he may have a "**RMAT designation**" (Reference 8)] However, the public presentation – at his web site (that I saw) – does not seem appropriate for a FDA "Clinical Trial" paradigm – with "fully divulged" patient scientific risk involved. Rather, he poses the "trial" product & service (to me) – as the "unscrupulous actor" you anticipate in your announcement (Reference 1). That is (to me), I perceive (the) *huckster* element of "*hurry & See If You Qualify*" to an unsuspecting public; Then, Mr. Stiene (M.D.) also attempts to obtain personal medical information – from potential clients (via a web form OHSAA link) and, further infers (all on his web site) that he will accept referrals – from other USA Medical Doctors – in the SW Ohio area. (References 43 & 3)

Third, I want to congratulate you on your FDA employee "Pat H.". She took my call – at the CBER toll-free number (1 800 835-4709) circa 1-18-2018. She answered my questions – with thoroughness and patience. She directed me to portions – of the FDA web site – that were useful and related. And, Pat also suggested a role, that I may wish (to play) – in the safe implementation of "regenerative technology"- to the greater American public. That is, after we discussed (briefly) my formal education, work experience and knowledge of molecular genetics – Pat stated, how this knowledge & experience *may* make me a possible "candidate" – to serve on an FDA "Advisory panel". (References **17-21)**

In short, I told Pat: "… (that) my private company [Hans and Cassady, Inc., Westerville, Ohio – operating 1985-1996] was the first studio (in America, circa 1986) to provide "digital" textbook art services to College Textbook publishers. The text book titles - which H&C provided "digital art programs" for – included, Klug Genetics, Weaver-Hedrick Genetics, Tamarin Genetics, Zubay Biochemistry, Fishbane Physics, etc. That is, typically based on a PhD author's input [to us] of *scribbles* and *stick figure* drawings – we worked with a reputable publisher's team of textbook developers, to create scientific and medical illustrations (to accompany the educational text) including all phases of genetic material [DNA] inheritance & replication, gene expression and protein synthesis. In fact, updated versions of these text books are still used in colleges and

universities throughout the world today (1-23-2018)…" My husband (of 35+ years) Mr. Hans Neuhart – is a Medical and Scientific artist." (Reference 9).

The details of my formal education and professional experience appears on my personal web site (Reference 13). In brief, I formally studied the (then) very new field of molecular genetics (in an inter-disciplinary environment) – at the University of Wisconsin [during the 1970s]. I was intensely interested in answering the question(then): **HOW can a lizard regrow his lost tail?** My time (at UWGB) coincided with "Geneticist" Dr. Charles irhke, "Microbiologist" Dr. Alice Goldsby, "Environmental Scientists" Dr. Keith White & Dr. Joe Moran, "Physicist" Dr. Nancy Sell – and, many other important and early contributors – to the fields of Molecular Biology/Physics/Chemistry and, Environmental Science. (Reference 14).

I am retired – at this time – mostly related to a stroke – that I suffered – in 2012: (SAH at my MCA). Initially, I was completely paralyzed – from the stroke event; But – today (now 5 years later) - I perform (27+) YOGA poses daily (at the YMCA) and I am constructing a personal web site (Reference 3) – (all) at the suggestion – of my Medical Doctors. I take one hyaluronic acid capsule (200 mg) daily. Finding out – only recently – that HA is being investigated (Reference 41)– relative to its role in mammal "nerve"- and, green lizard appendage and organ regeneration. This is a happy coincidence (only)! – In fact, I began taking HA – after reading about the success of YOGA + HA – in helping USA Veterans – suffering from chronic aging symptoms – such as arthritis. (Reference 42) In fact, my current Orthopedic Surgeon (Jennifer Jerele M.D.), has cautioned me (recently) – that, daily "Yoga poses" are not likely to fully "heal" my torn (and painful) supraspinatus tendon tear – without surgical intervention. However, trying to remain optimistic [**and, hoping to be included in a safe "clinical trial"** – under the auspices of the FDA] – I am delaying (this) surgery – despite my discomfort.

Fourth – and finally: **A)** My formal education and experiences – in the employ of the USA military (through GE), scientific writing and software systems development may be useful - if applied to (the) research, investigation, package tracking, protocol development - and, enforcement method documents needed- for FDA CBER/public health inspector implemented protocols - insofar as the *extraction*, *packaging*, *shipment* and *tracking* of human genetic materials-related to regenerative products and services. **B)** As my personal resume' (Reference 13) shows, I created reporting and training systems (such as this) for the USA-Simulations Systems Division of General Electric and Battelle Memorial Institute – under the auspices of (their) USA Military Contracts. **C)** Thus, unlike

many of the "clinical trial" participants, you can "assume", (that) I would have an "informed opinion" about the experimental protocols and documentation – that I (personally) would want to see utilized – in my treatment. **D)** In fact, it may be very helpful- to other participating Americans (that) I am (still) very detail oriented. In fact, this aspect (of my personality) assisted Dr. [PhD] Jiayuan Fang (of SIGRITY Software) – to realize 83 million US dollars- on the sale of his EDA software tools – to USA Cadence EDA Software. In small part (this USA technology "sale") was a result of the Speed 2000 End User's Manual – that I created – in partnership with my co-workers – from China, Pakistan, India and Mexico (Reference 45). **E)** I paid for 100% of my college education; AND, earned much of my USA "Work-Study Program" award, through "coding software & reporting systems"– for the Professors of UWGB _ and their National Science Foundation grants (Reference 14). Thus, I would be wary and circumspect of "college students" -earning their college "Work – Study" Award Program proceeds – in perhaps "filthy labs", at Colorado State University – day-to-day handling the materials – related to my biologic stem cell therapy treatment. That is, as a UWGB student, I worked day-after-day in just such a minimal, practical & necessary laboratory environment (under the auspices of the National Science Foundation) – related to sewage waste-water treatment experiments (to recover hydrogen gas). And so, I can appreciate the areas of "Lab Protocol" – that may need "special attention". [See the district court judge's comments – related to the Regenerative Sciences case. (Reference 12 – page 2)] **F)** As I told Pat, "…there would be no charge for any small contributions - that I could make- to your good FDA work efforts." That is, I am "legally disabled" – and, I am pleased to collect my (well-earned) Social Security benefits – which, (I fear) would be put at risk – if you paid me. **G)** Moreover, although I am doing relatively well – in my daily rehabilitation program – I am (I admit) very deliberate (*slow*) in my actions. That is, I become confused - if hurried. I also surrendered my driver's license after my stroke event. Thus, I could not commit to an aggressive daily work-schedule. **H)** On the other hand, I am (obviously) – a passionate writer – **and, if permitted to be a "participant" – in a clinical trial [as I would like to be!]**– I could contribute the communications abilities - that I still have (to suggest and complain – when necessary) – by written means. **I)** My recent brain scans (MRI & angiogram – with dye) are clear – no concerns noted. I am reasonably certain, that my Neurologist (an M.D. and a Professor) would sign up – to my participation – in a clinical trial.

Thank you- again (Dr. Scott Gottlieb & your FDA team)– for your efforts – to keep the American public safe! I look forward to hearing from

you – or, your assigned FDA staff member – re: "**RegeneXX**" and Dr. Stiene M.D. – (Reference 4). Also, I hope to "serve" & "participate" in a "clinical trial".

- Very Truly, Susan Marie [Cassady]-Neuhart

Noted references AND related Links:

- 1) https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm585342.htm (Dr. Gottlieb's a Announcement Jan. 16, 2018)
- 2) http://hansandcassady.org/mri-images/index.html (Susan's MRI files and the radiologist's report.)
- 3) http://hansandcassady.org/ (Susan's personal web site "HOME" page.)
- 4) https://www.beaconortho.com/physician/henry-stiene-m-d/insights/ (Dr. Henry Stiene's web site URL.)
- 5) http://www.kriview.com/about-knri/our-team.html (Dr. Keith Bidwell, M.D. – Radiologist)
- 6) https://orthoinfo.aaos.org/en/treatment/rotator-cuff-tears-surgical-treatment-options/ (Surgical Repair – Supraspinatus Tendon Tear)
- 7) http://www.cnn.com/2017/08/28/health/fda-stem-cells-bn/index.html (news article CNN. "FDA cracks down on stem cell clinics": August 29-2017
- 8) https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm537670.htm (RMAT Designation Regenerative Medicine Advanced Therapy Designation)
- 9) https://www.scientific-illustrator.com/ (Hans' web site)
- 10) https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm106001.htm (CONTACTS at CBER)
- 11) https://www.fda.gov/AboutFDA/CentersOffices/OrganizationCharts/default.htm (organization chart USA-FDA)
- 12) https://www.gpo.gov/fdsys/pkg/USCOURTS-dcd-1_10-cv-01327/pdf/USCOURTS-dcd-1_10-cv-01327-0.pdf (USA v. Regenerative Sciences) Case 1:10-cv-01327-RMC https://www.casewatch.org/fda/court/regenexx/complaint.pdf **<COMPLAINT**
- 13) http://www.hansandcassady.org/Susan_Resume_Jan2017latest.pdf (Susan's Resume')
- 14) https://www.uwgb.edu/cst/our-people/founders-award/ (Susan UWGB Professors)

- 15) http://www.bipc.com/recent-case-upholds-fda%E2%80%99s-jurisdiction-over-cell-and-tissue-product-regulation (Law Firm Presentation: Buchanan, Ingersoll & Rooney)
- 16) https://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/default.htm (FDA Biologics License Application (BLA) – REQUEST Process information)
- 17) https://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/ucm585218.htm (FDA 4 Final Guidance Documents)
- 18) https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/default.htm (ADVISORY COMMITTEE Blood, Vaccines and Other Biologics)
- 19) https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/CellularTissueandGeneTherapiesAdvisoryCommittee/default.htm (ADVISORY COMMITTEE Cellular, Tissue, and Gene Therapies Advisory Committee)
  20) https://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/CommitteeMembership/AdvisoryCommitteeVacancies/default.htm (**NEW PROCESS:** Advisory Committee Vacancies, Qualifications, and Experience)
- 21) https://www.fda.gov/AdvisoryCommittees/Calendar/default.htm (Advisory Committee Calendar)
- 22) https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/CellularTissueandGeneTherapiesAdvisoryCommittee/default.htm (Cellular, Tissue, and Gene Therapies Advisory Committee)

- 23) https://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/CommitteeMembership/AdvisoryCommitteeVacancies/default.htm (Blood, Vaccines, Biological Products Committee Vacancies – 1 OF 2)
- 24) https://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/CommitteeMembership/AdvisoryCommitteeVacancies/ucm110164.htm(Blood, Vaccines, Biological Products Committee Vacancies - 2 OF 2)
- 25) https://www.accessdata.fda.gov/scripts/FACTRSPortal/FACTRS/index.cfm (FDA Advisory Committee Membership Application)
- 26) https://www.accessdata.fda.gov/scripts/FACTRSPortal/FACTRS/downloadConsentForm.cfm (cONSENT form pdf dOWNLOAD LINK)
- 27) https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/default.htm (Cellular & Gene Therapy Products REGULATION HOME)

- 28) https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/default.htm (Approved Cellular and Gene Therapy Products OTAT LIST)
- 29) https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/default.htm (Report a Problem to the Center for Biologics Evaluation & Research)
- 30) https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/BiologicalProductDeviations/default.htm (Biological Product Deviations)
- 31) https://www.accessdata.fda.gov/scripts/email/cber/bpdrcontact.cfm (Biological Product Deviation Reporting (BPDR) – Contact)
- 32) https://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Consumers/default.htm (Consumers (Biologics))
- 33) https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/default.htm (About the Center for Biologics Evaluation and Research [CBER])
- 34) https://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/HealthcareProviders/default.htm [Healthcare Providers (Biologics)]
- 35) https://www.fda.gov/AboutFDA/CentersOffices/ucm481936.htm < (CBER Leader Dr. Marks)
- 36) https://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Industry/default.htm (Industry (Biologics)
- 37) https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm059181.htm (Section 8000: General Information
- 38) https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/UCM350368.pdf (processing of Biologics License Applications)
- 39) https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm123224.htm (CBER Key Staff Directory)
- 40) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1129084/ (Stem cell technology)
- 41) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2853843/ (Mechanical control of tissue and organ development)
- 42) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2614414/ (Implantation of neural stem cells embedded in hyaluronic acid and collagen composite conduit promotes regeneration in a rabbit facial nerve injury model)
- 43) http://www.ajpmonline.org/article/S0749-3797(17)30290-8/fulltext (Yoga for Military Veterans with Chronic Low Back Pain)

- 44) https://www.ncbi.nlm.nih.gov/pubmed/24395315)
  (Treatment of non-traumatic rotator cuff tears)
- 45) https://www.beaconortho.com/patient-forms/ (Hiene's OHsAA PREPARTICIPATION PHYSICAL EVALUATION-patient FORM)
- 46) http://www.hansandcassady.org/Speed2000UsersGuide.pdf SIGRITY Speed2000 END UsersGuide – created (1998-2002) in partnership with: Ming Jing, Jing Ping, Raymond Chen, Ji, Sun Zhao, Parminder Devsi, Raj Raghuram, Winston, Jaime Garcia, Jiayuan Fang, etc.
- 47) https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm123224.htm (CBER Key Staff Directory)
- 48) https://www.fdli.org/wp-content/uploads/2017/12/Malarkey.pdf (15 pages - ALL about FDA-CBER Enforcement & compliance)

Related Emails & CONTACT Information:

cberombudsman@fda.hhs.gov < FDA- CBER OMBUDS-personS
:: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm122881.htm

industry.biologics@fda.hhs.gov < Manufacturers Assistance
:: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm106001.htm

bp_deviations@fda.hhs.gov < :: https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/BiologicalProductDeviations/ucm129804.htm

hctp_deviations@fda.hhs.gov < https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/BiologicalProductDeviations/ucm134534.htm

ocod@fda.hhs.gov < https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm106001.htm

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Republican, https://turner.house.gov/contact/email-me
Ohio Senator: Portman(Rob) – Republican
https://www.portman.senate.gov/public/index.cfm/contact-form
Ohio Senator: Brown(Sherrod) – Democrat

https://www.brown.senate.gov/contact/email
President of the United States (1-22-2018)
:: https://www.whitehouse.gov/contact/

(from Reference 15) "… February 3, 2014, the U.S. Court of Appeals for the District of Columbia Circuit upheld the U.S. Food and Drug Administration's (FDA's) position that Regenerative Sciences' "Cultured Regenexx Procedure" was a biological drug subject to FDA approval through the biologics licensing application (BLA) process. U.S. v. Regenerative Sciences, LLC, 2014 WL 393602 (D.C.Cir. 2014). **It also upheld the permanent injunction against the Company's use of the drug without FDA approval.** The Company asserted several alternate grounds for its position that the product was not FDA-regulated, including that: **(1)** the product is really a procedure governed by state "practice of medicine" rules rather than the Federal Food, Drug, and Cosmetic Act (FFDCA); **(2)** the product was not more than minimally manipulated, and, therefore, was included under an exemption from FDA approval; and **(3)** the product was a compounded product exempt from pre-approval. **The court rejected all (of) these arguments. …"**

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