DG/LP

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Agenzia Italiana del Farmaco

AIFA

Il Direttore Generale

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FDA - Commissioner
Washington, DC USA

cc:

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Object: FDA role on Italian Stem Cell fraud case and possible Involvement of US based Partners

These informations are released under out mutual confidential agreement.

Dear Dr. Hamburg,

You probably remember the issue we briefly discussed in Amsterdam during the ICMRA Meeting about the Stem Cell fraud that has been going on in Italy for the past 18 months or so. The reason why I must draw your attention to it is that some U.S. Based Partner(s) falling therefore under FDA jurisdiction is/are now been involved.

The Stamina case – involvement of US based partners

The Stamina Foundation is a private organization that has been peddling fake "stem cell treatments" in Italy for several years. The operation was banned by AIFA in 2012, and a government-sponsored "trial" intended to evaluate the "method" was barred by an ad hoc Scientific Committee in 2013. Further details on the history of the case are available on request.

The Stamina case is obviously one of several instances in which US based individuals or organization support the operation of "offshore" stem cell peddlers. Professor Camillo Ricordi (University of Miami) has been actively campaigning against the scientists who have argued against any form of Government tolerance over the operation of the Stamina Foundation, which is otherwise the object of several criminal investigations. Ricordi has announced that he will be "testing" the Stamina method ("tested" already in 2012 by the Italian Health authorities and external academic labs in charge of technical expertises; evaluated again later, in detail, by the Scientific Committee appointed by the MInister of Health). The lay press has disclosed embarassing email conversations between Ricordi and Stamina staff, indicating the lack of very basic awareness about the safety and the very identity of the cell product administered to patients by Stamina, not to mention the lack of any scientific competence whatsoever. The conversation also proves the intent of Stamina to use Ricordi's support to rebut the evaluation of the Committee, of which AIFA was a part. Stamina had already appealed with an administrative Court against the ban issued by AIFA in 2012, but failed. The email conversation can be provided upon request. The Carabinieri NAS (Health Group) are intensely investigating and it is likely that the Italian fellow involved will be up to a trial soon. FBI and or Interpol should be probably alerted as well.

Indeed, it seems that Ricordi is in the Scientific advisory board of a US company called Bioheart, which commercializes two cell products, one based on myoblasts (MyoCell) and one based on adipose cells. Bioheart licenced a patent obtained by Peter Law, who was later inhibited by the FDA from treating Duchenne patients with myoblasts, and moved the operation to Singapore. Bioheart markets both products in Uganda, Kazakistan, Turkey, and in Mexico, via the Regenerative Medicine Institute in Tijuana, which was reported on by the NY Times last September. The RMI enrolls patients for a fee in "interventional", non-randomized, non-controlled trials, and pioneers the use of "cover" trials for the marketing of stem cell treatments. Ricordi also supports the operation of other stem cell peddlers elsewhere (e.g., Argentina, "Stem Cells Argentina").

Back in march, Ricordi was invited by the Italian Ministry of Health to advice on the Stamina case. His advice consisted in a) suggesting to seek the opinion of Arnold Caplan, the founder of Osiris Therapeutics and the holder of royalties on the company's patents, as well as the most proactive supporter of MSC peddling for the most improbable diseases such as autism, ALS, neurodegenerative diseases, spinal cuts, burns, liver fibrosis, renal failure and many others; b) forwarding to the Italian Minister of Health a "white paper" written by Arnold Caplan, Michael West and Andrew von Eschenbach, supporting the authorization of MARKETING of MSCs for all ailments after a phase I trial (no phase II and III), the so-called "progressive approval". The document is available on request. Based on "progressive approval", Osiris Therapeutics obtained the approval with condition for the marketing of ProchymalTM in Canada; less than one year after the approval, rather than boosting the pursuit of the missing clinical evidence for any efficacy (not proven by 2 multicenter, Osiris-sponsored phase III trials), Osiris gave up ProchymalTM rights to Mesoblast, an Australian company active in MSC peddling. Ricordi is the founder and President of a lobby called "The Cure Alliance", which states that FDA is the prime enemy of innovation and patients' access to innovative therapies. The lobby includes noted names of Italian business (pharma and non-pharma) and TV anchors and communicators. Ricordi is also a member of an organization called the MedRebels ("join the Revolution" is the motto), also proactive against drug market regulations and regulators. In response to Bianco's article in Nature Medicine, arguing against the use of MSCs for diseases that cannot be cured by MSCs, he has made public libelous statements against Bianco and other Italian Scientists. In response to Bianco's invited Nature World Views article, arguing against the marketing of unproven stem cell therapies, Ricordi and Caplan authored a libelous article in a pseudo-scientific journal

called CellR4, the official journal of "The Cure Alliance", where it i salso reiterated that indeed, MSCs can cure everything. Article available on request. Here below what was published yesterday on The Cure Alliance Facebook page and that draws in FDA and AIFA (read with attention, see how it starts and how it ends)

WHY THE CURE ALLIANCE IS AGAINST DEREGULATION AND SUPPORTS THE FDA AND AIFA MISSION TO PROTECT PUBLIC HELTH AND SAFETY

The problem of the thalidomide experience represents an excellent example of why need FDA and AIFA and why they have an essential role when they regulate the development of drugs and vaccines for mass distribution, each time public health could be at risk, but patients who want to use their own cells to try to deal with an incurable disease, which has no other therapeutic option except approved drugs that are as expensive as useless, pose no threat to public health. These patients may be deceived, exploited , cheated, but they do not endanger anyone else. The problem then becomes information on the real expectation and potential of a treatment and awareness of the risks and potential benefits. That is why it should be mandatory to publish the results and no one should escape from rigorous scientific testing and validation studies. For this reasons we have qualified hospital and laboratories, we have ethics committees, informed consent processes, data safety monitoring boards (DSMB), the oversight of professional organizations on clinical practices, like for bone marrow transplants for leukemia or in vitro fertilization. The battle should become on mandatory reporting of the results and observed side effects, in real time, without selecting what and when gets reported. This has been advocated by many, not just The Cure Alliance. Read for example what Dr. Scott Gottlieb wrote after working for the FDA as Deputy Commissioner in an article published on the Wall Street Journal titled " How the FDA can cost you your life" and indicating how excessive regulations in the exclusive pursuit of safety, with the only performance indicator being the absence of risk, should also be confronted with the mortality, the morbidity, the suffering, the costs and risks associated with the block and delay imposed to the development of cures.

Let it be known that Ricordi does not seem to me an expert in the biology of MSCs. He has repeatedly stated to the Italian lay press his intention to "verify" without prejudice the safety of the Stamina product and its properties (meaning, a trivial essential FACS analysis, with no potency assay whatsoever). However, **Nature reported on July 3rd, 2013** that the

Stamina method is a scientific and patenting fraud, and the plagiarism of **artifactual data.** And more recently Ricordi's support helps Stamina in rebutting the evaluation issued last summer by the **Minister's Scientific Committee.** Following an appeal from Stamina, an unreal ruling of an administrative Court in Italy has invalidated the evaluation issued by the **Minister's Scientific Committee.** The Minister is about to appoint a new Committee, which exlcudes AIFA; Stamina had obtained the exclusion of noted Italian experts earlier on, based on a media campaign pressuring the Minister. In this context, Ricordi's support is instrumental in keeping the Stamina case alive and his interests may be way beyond those of our national boundaries. His role in the all story so far has been covered in the last issue of **Nature** so I am sure the FDA should be aware of what is going on around this case to duly protect the health of American citizens.

Looking forward to your consideration on this matter.

Best regards,

(Luca Pani)

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