2/23/17-Reached out to Bryan Mosley, sales rep for the Marrow Cellutions device to f/u on conversations I had with him at IOF 2017 about testing the device with our lab.

Bryan's Response:

"Dr. Centeno, Mr. Zimble, Mr. McGillicuddy

Please allow me to re-introduce all and provide the setting for direct communication regarding the Marrow Cellution device. Mr. Zimble is the Executive VP and General Manager at Ranfac and Mr. McGillicuddy is the President and CEO of Endocellutions. I will step back and allow potential details to be worked out between Ranfac, Endocellutions and Regenexx.

Regards,

Bryan, Regenacell"

My response to the group on 2/23:

"Great,

Guys, we would like to test the device as we internally test all devices before allowing their use at our 41 sites. Specifically we would like to test this device on one random side and our traditional 5 sites, low volume draw on the other. We would expect an expert rep is present to make sure the device is being used to it's fullest capabilities. We would test for CFUs, flow for MSCs and HSCs, and then culture expansion. Our goal is to see if the device can produce much higher yield (at least 50% greater). If so, we would then work on a contract for purchasing for these 41 sites. Our plan is to be at 100 sites by the end of 2019. If we pay for the study and you sample the devices, the data is ours. If you pay for us to perform the study, the data is yours. You can obviously send out an independent sample to another lab (at your expense). If you do, it likely makes sense to contract with Wayne McIlwraith's lab at CSU or Kristy Anseth at CU, both of which are close enough to easily transport samples and both of which routinely handle and grow MSCs.

Chris Centeno, M.D."

I received a letter from Barry Zimble of Ranfac on 2/27 that can't be shared "as is" due to the electronic transmission instructions on his e-mails and the fact that I have no permission from the company to share these documents. In the meantime, I will summarize their replies in my own words:

2/27/17-Barry Zimble refuses to allow the testing to go forward based on his concerns that his FDA device registration may be impacted by the testing. I respond that I spoke with our FDA counsel who has stated that he sees no issues with a private medical group performing its own

tests on the MC device (i.e. that these tests would have no bearing on the MC device 510K registration with FDA). On 2/27 Mr. Zimble replies that he needs to see additional information from us (i.e. what we would like to test), before he would agree to the testing.

My response:

"Barry, yes we are a private physician's office and in this case, I represent a large medical group practice who is making the decision whether to spend big bucks on a needle system because it's dramatically better than a $25 trocar or not. I will have my staff give you the information you need on good faith. However, this all looks like a manufacturer who is reticent to allow someone else to test their claims, which is concerning. I am trying to give you the opportunity to participate in this test and to make sure that your device is used 100% per manufacturer's spec and even to send out an independent sample. I have been flexible on timing. However, if you prefer, we will use the Ranfac devices that were are able to purchase and just produce and publish our own independent study without your involvement. If your needle passes our tests, then we will contact you. Your choice…"

I then asked my lab staff to provide Barry our testing protocols. However, given his reticence to allow testing early on, here's my response:

"So once you receive that info we'll give you two weeks to review. If we don't hear from you after 14 days, we'll just move forward with our own project without the involvement of Ranfac"

On 3/2, our Science director sends a detailed plan for testing the MC device to Barry Zimble. Mr. Zimble responds on 3/6. In addition to the data we sent, he would like more info. In particular, more info on our usual aspiration protocol and the validation work we have done on cell counting for our usual protocol. More concerning is that Mr. Zimble now seems to want to design the testing protocol to show his device in the best light, hence, here is my response:

"Barry, we will be comparing against a standard, single port jamshidi trocar (we use two plastic disposable types). The protocol will be to perform 5 ml draws x 6 sites on one side with the jamshidi and use your device and follow your protocol on the other randomly chosen side to draw the same volume. It makes no sense for us to provide you with our existing data as then this test won't be blind (i.e. that would allow you to pre-game your side, which would invalidate the study methodology). So we can't do that. The same volume of total draw will be compared between the two devices (in this example 30 ml vs 30 ml). Hence the volume issue you bring up won't be a problem. Any study protocol will need to be accepted by both parties. Finally, as discussed, to ensure that we don't lose cells to cryo or 4C storage, it would be best that if you want to use an independent lab, as I proposed last time, it should be local (CU or CSU would be good fits). Wayne McIlwraith's lab does studies with industry all the time at the CSU ORC and has extensive experience with both human and animal MSCs. However. There may be other local resources as well.

Barry, based on your prior responses, we had decided to use the devices we have to perform this test without your involvement. Neven sent the protocol completing my prior request. However, if your team wants to complete this testing, please let me know, as I hadn't gotten that impression."

Mr. Zimble then responds on 3/7 that due to the fact that we want to draw 30 ml with their system, that MC is not appropriate for our practice (i.e. it is only designed to draw 8 ml of marrow).

During this time, given Mr. Zimble's reluctance to allow testing, I began to try to source several MC devices to purchase. Time and time again, we were told that the sales reps had been instructed not to sell any devices to Regenexx providers. Hence, I finally went through a third party to purchase three MC units.

On 3/16, I sent this to Mr. Zimble:

"Barry,

Just an FYI. We will be testing the Cellution needles we have on hand as I had previously described. We would again invite you to have a rep on hand to observe the testing as well as to provide any recommendations as how to improve or optimize the performance of the device. We have yet to slot a date yet and we will make every effort to ensure that your rep can be here. Please let me know what you want to do.

Chris Centeno, M.D."

On 3/20 Mr. Zimble responds that RanFac may be interested in participating in the testing. They would still not be interested in a large volume draw.

My response:

"Barry, this test if for our own purposes to determine if this device is worth purchasing. Our goal is to draw higher concentrations of MSCs and then to further concentrate. So if a higher volume draw doesn't meet your business plan, that's not important for our test. Again, the test is for our own purposes to determine if we get higher yields than our standard draw, so what's interesting to Ranfac is not important. We will compare the same volume of marrow side to side.

You guys refused to participate once, so at this point we're moving forward. We purchased three units and hence, given that you refused to sample us, the test is on our terms. As far as everything you're now proposing, please see prior e-mails as we've already covered this ground and we got nowhere. If you want someone here to observe the test, then we are inviting a rep to

provide assistance with the device, as our goal is to evaluate the device for purchase. Hence having a rep here makes sense.

In summary, we tried hard to accommodate what you wanted and you decided not to move forward. Right now our test is designed to answer one key question for us: "Are we missing out on MSCs by not using this device when compared to our standard draw?". if the answer is a resounding "yes" then we'll be a big customer. If it's a no, then we will continue doing what we're currently doing. "

Mr. Zimble responds via e-mail on 3/20 and there seems to perhaps be some meeting of the minds on what we are trying to achieve with our tests? He wants to discuss further.

My next e-mail on 3/20:

"We have a specific multi-site bma method that uses an inexpensive disposable trocar (we use a few, but the focus in not the device). The focus is the method. So the question is whether a device (this one in particular) can improve that MSC yield. I'm in Cayman right now, so e-mail is best. "

Mr. Zimble and I connect via phone on 3/22. While we seem to agree on some issues, ultimately it is a sticking point for Ranfac that even though we will compare the first 8 ml of what we draw with their MC device to our first 8 ml drawn using our technique with an inexpensive trocar, they are not interested in a test that will ultimately pit their device used to draw a larger volume of marrow that would then be concentrated to what we usually draw and concentrate.