REGEN MED HCT CENTERS

FREQUENLY ASKED QUESTIONS

Confidential
March 2016

In a separate document, we review the concepts of Regenerative Medicine Procedures ("RMP's"), as well as a Clinical Human Cell/Tissue Center ("HCT") which supports the delivery of such RMP's in a manner designed to obtain consistent clinical results.. See "Regen Med Standard Turn-Key HCT Center Proposal with Appendices".

That document also provides a pro-forma financial model for an illustrative HCT Center; it details how Regen Med works with hospitals and clinics ("Affiliates") in establishing such a Center; and it provides a generic use case.

Below, we identify and answer frequently asked questions relating to HCT Centers.

Why do you recommend a physically separate HCT Center to deliver RMP's? Why can't we simply purchase one or more of the proprietary product platforms (PRP machines, etc.) which already exist on the market?

In short, a dedicated HCT Center ensures (i) reproducible and consistent clinical results, (ii) efficiency, flexibility and adaptability across a range of RMP's and indications, (iii) the ability substantially to grow the nature and volume of clinical offerings, (iv) regulatory and data maintenance peace-of-mind, and (v) the opportunity to participate in third-party sponsored individual or multi-center RMP studies and trials, among other benefits. More specifically:

Safety, Legal and Regulatory. Dealing clinically with HCT's involves critical sterility, environmental, therapeutic, scientific, data maintenance and other considerations, while requiring consistency in the expected results. By definition, one is dealing ex-vivo with human cells, which are processed and placed back in body. The HCT legal and regulatory environment is increasingly, and understandably, severe.

Stand-alone HCT equipment cannot be truly "push-button". The clinician must be conscious of the likely need for cellular characterization protocols, endotoxins testing, batch recording, sterile fields, regular training, detailed documentation demonstrating conformance to recommended manufacturers' SOP's and other matters.

A key function of the HCT Center and its dedicated technician is to maintain proper records on equipment calibration and maintenance, HCT processing/characterization for each RMP,

environmental and other controls for biologics, follow-up records for each RMP, updated RMP protocols (tissue extraction, HCT processing/characterization) and similar matters. These are all matters addressed in a facility conforming to Good Manufacturing Practices ("GMP"), and are increasingly expected by patients and regulators alike in dealing with HCT's.

Flexibility and Adaptability. Science's understanding of the immuno-modulatory, regenerative, trophic (e.g. angiogenic, anti-scarring, proliferative and anti-apoptotic) and other effects of cells, tissue, platelets, growth factors etc. is evolving at a fast rate. Similarly, best practices regarding biological matrices, dosages, nature of injection (single or multiple; local, intravenous, intrathecal) and other matters are constantly developing.

No single equipment manufacturer, research institute or clinician can possibly keep abreast of the enormous and dynamic field of regenerative medicine. Conversely, the HCT Center, through its relationship with Regen Med's scientific/clinical associates, provides the opportunity to adapt to this rapidly-evolving environment. At the same time, an HCT Center offers the flexibility to innovate, and thus contribute to advances in the field of regenerative medicine.

Moreover, purportedly "push-button solutions" to processing HCT's are necessarily limited to one or a few indications, are unable properly (if at all) to count and characterize cells, are limited regarding tissue sources and output types and volumes, require careful and regular maintenance/certification, and are at real risk of early clinical and scientific obsolescence in the fast-evolving world of RMP's.

An HCT Center provides a controlled, purpose-designed location to process properly a wide variety of HCT's. It can begin supporting one or two indications commonly presented to the clinic – e.g., Osteoarthritis (OA), wound care -- and then economically expand to accommodate additional indications.

Economics of Time and Money. It is ultimately uneconomical for a physician to spend the time necessarily to calibrate, maintain, prepare, use and clean stand-alone HCT equipment and related biologics. (As indicated above, not doing so, and not taking the time to document that all necessary protocols have been followed, can negatively effect efficacy, safety and reproducibility/reliability, leading to increased regulatory and legal exposure.)

The HCT Center allows the surgeon to do what he does best – engage with the patient, extract tissue and inject HCT's (whether as a primary or adjunct therapy), while a trained technician handles and documents HCT processing, characterization, equipment maintenance, tissue banking, and other matters.

Practice Growth. The purchase of a single piece of equipment – regardless of how "turn-key" it claims to be -- allows the clinic to expand its revenues only to the extent the clinic can successfully market the particular procedure associated with it. Moreover, the time which the practitioner must dedicate to the proper maintenance and use of the equipment, and documentation of all related procedures, is time which cannot be spent on procedures and with patients.

Conversely, a dedicated HCT Center allows the clinic to sensibly expand the number and type of RMP's it performs. It can support, initially, specific procedures performed by a single surgeon, and subsequently many more types of RMP's performed by surgeons in the clinic, as well as visiting practitioners utilizing the HCT Center to support their own practices. Moreover, it can support research studies and trials, leading to additional revenue sources.

Why do I need Regen Med to help us set up an HCT Center? Why can't we do so ourselves?

Regen Med assists its Affiliates with one or more of the following in connection with an HCT Center. A busy clinic typically has neither the expertise nor the time properly to execute on such items.

- Co-investment (if desired by the Affiliate).
- Equipment specification and acquisition at favorable pricing.
- Technician selection/training.
- Data collection and management.
- RMP outcomes follow-up.
- Association with international scientific and clinical thought-leaders.
- Professional and patient educational materials.
- Best practices in RMP's (surgical and cell processing aspects) from Affiliates around the world.
- Legal/regulatory compliance.
- Sponsored research studies and trials (including preparation of material for IRB, medical ethics committee approvals).
- Business plan development, including developing equity value for HCT shareholders.

Importantly, Regen Med's principal compensation -- unlike that of a product distributor or consultant -- is aligned with the success of the HCT Center.

How does Regen Med help ensure the financial success of the HCT Center?

In addition to scientific and clinical credibility in the field of RMP's, Regen Med makes available for its Affiliates decades of business and legal experience. Regen Med is a for-profit business, and it works with its Affiliates to help ensure that an HCT Center is a profitable business as well. (Always in the context of evidence-based and safe patient care provided at a reasonable, transparent price.) This is one of the reasons we recommend that an Affiliate set up an HCT Center not only as a physically segregated space, but as a separate legal entity with its own profit and loss accountability.

Many practices suffer from the inability to build true equity value which can be sold or otherwise monetized upon the retirement of the individual practitioner(s). An HCT Center will be a strong boost to an existing practice but, even more importantly, it represents a revenue source independent of any individual practitioner and therefore a foundation for building monetizable equity value.

Unlike a device or product company, Regen Med is prepared – if desired by the Affiliate -- to co-invest with the Affiliate in the set-up and operations of an HCT Center. Regen Med's interests are thus closely aligned with those of the Affiliate in building a profitable and enduring business. Also, as described below, Regen Med takes advantage of centralized economies of scale wherever possible for the benefit of the HCT Centers at all Affiliates.

An HCT Center seems intriguing, but we are a busy practice, and have no time for or interest in additional administrative burden. How do you address this concern?

Regen Med was co-founded, and is closely advised, by clinical surgeons with deep experience in large academic hospital settings, as well as in smaller practices. Rather than imposing additional non-clinical burdens on our Affiliates, we seek to reduce them. Centralized capabilities and benefits we offer to Affiliates in the context of RMP's include:

- HCT Center lay-out design, legal structure, business plan.
- Organization of equipment specification, procurement at best available prices (no mark-up), training, in-servicing.
- Technician selection, training, on-going interaction.

- Professional and patient marketing and education materials.
- Development of patient flow for RMP's locally and, where relevant, from outside the country.
- Protocol development, documentation.
- Clinical trial, study design; submissions to IRB's, Medical Ethics Committees and similar groups.
- Data maintenance, collection.
- Patient follow-up.
- Local and regional workshops for other healthcare professional interested in RMP's for their practices.
- Assistance with regulatory authorities.
- Professional collaboration, including multi-center studies, conference presentations and journal articles.

We are worried that there is currently insufficient data to support RMP's. Can you convince us that today's scientific environment supports a clinical focus on regenerative medicine?

Many RMP's are performed today across a variety of indications – fat grafting, PRP, bone marrow aspirate; bone marrow transplants; micronized fat; pancreatic islet cells; various biological matrices and gels, growth and other factor injections, etc.

A growing body of peer-reviewed literature exists supporting, in-vivo and ex-vivo, the safety as well as trophic (e.g.: angiogenic, anti-scarring, proliferative and anti-apoptotic), immuno-modulatory and regenerative effects of mesenchymal stem cells (MSC), stromal vascular fraction (SVF), hematopoietic stem cells (HSC), endothelial progenitor cells (EPC) contained in SVF and a number of other HCT's for many indications. (Of course, as with all medicines, diagnosis is critical to select the appropriate RMP.) For other indications, there is scientific plausibility and encouraging anecdotal evidence, but a shortage of well-designed clinical datasets. (This is of course the case with a substantial percentage of non-RMP clinical procedures currently considered "standard of care".)

At the same time, a broad base of clinicians, patients and legislators are pushing back against the expense, lack of transparency, delays and other limitations inherent in today's clinical trial process. As a result, there are strong movements for open registries and other streamlined approaches to testing safety and efficacy of drugs, devices and biologics. Japan, for example, has instituted recently a revolutionary approval mechanism favoring the early clinical use of

RMP's. Regen Med believes that patient-centered medical knowledge advances, today as in the past, through the careful collection and analysis of relevant clinical data.

Accordingly, Regen Med recommends commencing with established RMP's for the specific indications most relevant to the Affiliate's patient flow. This is accompanied by careful data (including outcomes) collection. It is in the discretion of the clinic whether – and if so how -- to pursue RMP's for other indications. In such contexts, Regen Med can assist with, for example, IRB-approved study designs.

We are aware of various "Stem Cell Centers" in a number of countries. Many of these seem to overcharge patients for procedures based on questionable science, and/or ignore regulatory requirements. How does an HCT Center, as proposed by Regen Med, differ from such "Stem Cell Centers"?

Regen Med, and any Affiliate with which we work, are emphatically committed to patient safety, reproducible therapeutic benefits, transparency, and reasonable pricing. Regen Med's Clinical/Scientific Board of Advisors and other affiliated surgeons and scientists enjoy strong reputations for clinical and academic excellence, and are committed to the highest level of medical ethics.

We do believe that ethically-delivered RMP's will play an important role in obtaining positive outcomes for a large number of patients, as both primary and adjunct therapies. We and all healthcare providers with whom we work are committed to providing such RMP's in a fully transparent and ethical manner.

Indeed, it is through HCT Centers that Regen Med and Affiliates will be able, jointly, to generate evidence-based medicine through well-designed and executed clinical trials and studies. A central theme of the Regen Med philosophy is to replace **experience**-based practice with **evidence**-based medicine.

We are a large teaching hospital, with sophisticated laboratories and many departments already engaged in various forms of "Regenerative Medicine". Why do we need Regen Med?

It is not unusual for a hospital system to announce a "Regenerative Medicine Center of Excellence", or equivalent. It is unusual, however, to find actual execution of all the positive

patient-care and financial opportunities which are implied in such an announcement. Challenges can include one or more of the following:

- Inter-departmental rivalries or other obstacles preventing cross-disciplinary training, specific RMP procedure codes and privileges, development of "beginning-to-end" RMP protocols for patients and healthcare professionals alike, and other internal hurdles to the efficient delivery of RMP's.
- Insufficient budget allocation to forming a true center of excellence. The issue is not investing in bricks-and-mortar, but rather in the integration of disparate parts of the system to make a regenerative medicine "whole" which is greater than the sum of the parts.
- Inability to genuinely translate in-house cell research to clinical use.
- Lack of an ombudsman to define and obtain medical ethics committee approvals for RMP's.
- Lack of a business plan to ensure the profitability and growth of the center.
- Absence of a "lead" department committed to providing scientific and clinical RMP education across all departments/specialties.
- Absence of coordinated patient and physician marketing and other communications.

These are all areas where Regen Med can assist. For a large hospital system, as for a smaller surgery center, Regen Med believes that the establishment of a dedicated HCT Center is the most sensible way to begin addressing the foregoing challenges, and exploiting the patient care and financial opportunities inherent in regenerative medicine.

We are a small practice with a specific practice area. Regenerative Medicine seems too large and unfocused a concept for us. Is there a sensible way to enter into the market conservatively?

Yes. As indicated in the more detailed description of a generic HCT Center, a small practice can begin delivering evidence-based and regulatorily-compliant RMP's with a modest investment, on a small physical footprint. Regen Med Affiliate status brings many advantages typically available only to larger providers, which in turn allow the smaller practice to begin and then grow in the dynamic field of Regenerative Medicine.
