

Minutes – CHDC at YNHHS at St Raphael, Selina Lewis Building, 659 George Street, New Haven

November 16, 2016

Lisa Stump, Yale New Haven CIO and a pharmacist by trade posted. She reported that Yale New Haven Hospital system has a powerful vision with regard to genomic research with a full commitment by the organization utilizing the infrastructure and resources of Yale in order to connect the dots and fund future work. She indicated that understanding drug metabolism will be a huge aspect of the effort.

Joe McGee agreed that Yale clearly has a powerful vision of the future and that he hoped that a statewide Connecticut collaboration can help enhance the uses of the resources embedded in the labs, hospitals, and classrooms of Yale and its associated institutions. He wondered aloud how best to organize that effort. He stated that with the “state lens” that he brings to the table it is clear that the work that we are discussing will be the transformation of medicine into the future and he hopes to develop through this collaboration economic development benefits for all in the state. Joe further remarked that this group has the skill set among its organizations and people to use health informatics in order to transform the next generation of health and the related workforce that will be needed to support those efforts. The question posed, however, is where will the talent come from to drive that transformation? We have recently learned in the Brantford presentation that while UConn is leading the charge with a social genomic counseling program, the eight graduates that will launch that effort is not an extensive enough to match the needs that will be developing in Connecticut. The irony is of course that the status at the moment indicates that there is simply not enough jobs in this field in Connecticut to justify a higher graduate count.

Amy Justice added that workforce development in this field will require many levels and skill sets beyond the counselor functions. Whole teams, indeed whole cadres will be required, including physicians and data scientists. She indicated that workforce development could be a central function of this collaborative group. She added that the group has the tenant determined that a statewide audit of resources and assets is immediately necessary, which would include the UConn counseling program, the Yale clinic in this

field at Yale New Haven Hospital, and the efforts of the Veterans Administration with which she is involved. Joe can McGee added that it will be essential to set a framework for larger talks to form a collaboration beyond any one institution, i.e., the spirit of partnership must be the driver for the projects that this group will be putting together in the near future.

Mark M. We also need to map decision support tools and what organizations and individuals will be supportive of each. For instance, clinicians working on what level need to be aware of the progression through the ranks of the entire team in order for support to be available when and where it is needed to maximize productivity and effectiveness. Amy agreed that innovators are the key drivers at the initial steps, but they need to know the path into the collaboration in order to maximize returns.

Thomas Agresta (via email and conf bridge) wanted to make sure folks continue to consider the implications and needs to ensure an adequate workforce for the very interesting ideas being floated. (i.e., make sure we are training the workforce we need in CT Universities - this will require investment in targeted areas of faculty growth for example) We need undergraduate and graduate students working hand in hand. Otherwise us greybeards will be the ones who benefit - but only for a brief while :-). We in essence need to create a Silicon Valley like atmosphere where we attract the brightest of young talent (much of it home-grown in our state)

Marat introduced the topic of a NIH grant for cohort collection of samples to fill a bio bank. This grant is a time schedule stretching from today until fulfillment in the fall of 2017, this work must commence immediately. He reported that Yale will be applying for the grant, but he believes that the collaborative should partner together to help in that effort and reap the returns that could jumpstart a project of merit. Joe questioned whether or not the state of Connecticut itself should be an applicant, and one other potential grantees would be important? The discussion turned to the ways that the collaborative could partner in this effort by showing real measurable impact as a result of the work that will be proposed.

Poly Painter asked how the collaborative could demonstrate its very existence and whether that would be a determinant factor in the consideration of awarding the grant by the NIH? Marat replied that being said necessary to show the number of partners and a description of each and a profile of their role in the collaboration and project. Lisa Stump added that

each partner must be portrayed as the unique asset that each is to the group including residents programs in big Pharma. Amy pointed out that it would be extremely useful to them in straight that the state of Connecticut has skin in the game, and that the collaborative has a clear path to leveraging all funding, including that from the state. Joe pointed out that California has committed to about \$7 million for its demonstration plan regarding infectious diseases and pediatric cancer.

Matt Storegard of CT Innovations asked whether CI's commitment to to contests, similar to the project in California, would qualify as a state match? Amy speculated that it probably would not, that the funding would be targeted at infrastructure and should likewise be matched by actual infrastructure investment, demonstrating specific steps toward the involvement of the various institutions that would form the applicant group. Amy stressed that the goal of NIH is to enhance the collection of samples, thus the grant must demonstrate "what and how" steps the collaboration will take to gather patient samples and the extent of consent that is obtained. Thus, the Yale effort led by Marat to collect samples of DNA will be a key factor, and thus it is appropriate that Yale is the lead institution and preparing the grant.

Lisa pointed out that it might be necessary to frame the reasons that Connecticut has not organized in this way earlier. She observed that many states have already begun pursuit of data exchanges in obtaining contemporary consents for sample collections. She noted that a concerted effort could actually leapfrog existing activities, but that we must be flexible and have our goals set way down the road ahead.

Tom P. stated that NIH will want leaders and champions fully established in place and active, across the breadth of the organizations forming the collaborative. He stressed that established champions will go far in developing a successful application. Tom added that it might be wise to pursue incremental steps, via smaller pilots and other programs, gathering the partnerships necessary to establish true and observable relationships, in order to show the commitment that NIH will be seeking in grantees. Amy agreed and pointed out that the true heart of the application must be the demonstration that patients and their consent are the driver of the activities of the entire group. It will be groups that have access to patients and their samples, with full consent with modern forms, that will succeed.

Polly Painter teed up the question of how the Center For Precision Medicine would factor in this grant, wondering aloud whether Yale and Marat's effort should in fact be the champion to garner the support of NIH. She added that if Yale forms the bio bank and adds its existing sampling database to that, could other Connecticut-based institutions and organizations add on to this "coordinating center" through a statewide application open to all interested parties across the state? Mark M. agreed with Polly that it will be essential for a clear definition and profile of how the collaborative structure will work, what path it will pursue, and what goals it seeks to fulfill. It will be fine for the collaborative to operate under a Yale umbrella, and in fact the group could have multiple coordinating centers for the NIH people to consider.

Tom P. noted that a blanket question "who wants in?" Would lead to far more disarray than organization. Therefore, he stated that it would be important to create a "selected team" with an integrated plan and collaboration structure demonstrating partnership and common goals.

Amy agreed and feared a "broadbrush" approach that may currently be featured by the CHDC group would not be ideal for grant writing purposes. She supported the concept that the group needs to have pilot projects up and running with a clear strategy for enrollment rolling patients and obtaining their consent. She added that even TV ads would be a fine approach to market marketing and would demonstrate a highly concerted effort. She cautioned, however, that ensures pharmaceutical companies, the state itself, employers across the board remain the major players with connections to patients being the linkage that could prove success or failure. She was sure that most applications competing with the Connecticut grant request probably will not feature strong state government commitment, let alone funding.

Joe reminded the group that Tom Woodward of the Comptroller's office believes that the CHDC group has a "wow" set of players and a tightly focused set of goals and paths to success. Critelli reported on a Brigham Young hospital conference he had recently attended in which it was found that patients are beginning to decline to participate in such sampling endeavors, and that insurers are wary of genome data being used for underwriting. He reported on "grateful patients" in contrast however, being cancer recovered patients who have seen the benefits of participation. He also added that blood donors as a group are very likely to engage in

providing samples and broad consent to their use. A dialogue ensued concerning whether or not a state law could be developed in the upcoming legislative session in Connecticut that could address the potential actuarial problems faced by insurance companies in which genomic sample results could lead to greatly expanded healthcare requirements. Amy added that whatever is put in the grant would need substantive evidence and foundation demonstrating a coherent and active organization, not just fluff.

Marat profiled his Yale New Haven Hospital and Anthem insurance collaboration that is starting with 25,000 new patients, with new samples and consents, up-to-date and using the new standard form. In any case, he noted that the effort needs to start in January 2017 in order to build a case for a full-blown application in September. Tom P. added that the state employees union negotiations on healthcare are proceeding apace toward a new contract, and that that program has been very successful to date with costs having gone down, but this must be factored into state employee considerations. Polly Painter entered the Tom Woodward of the Comptroller's office had suggested that a pilot program might be possible, which would be voluntary and that it's possible no contract talks or ratification would be necessary to at least kick off a pilot, particularly around wellness. **(There are dollars available in the Wellness fund and could be utilized as long as the program works to solve a problem with and actionable benefit.)**

Amy pointed out that NIH grants often require community advisory boards, essentially independent little governments and collections of various patient groups. The CHDC partners could float a group to help with patient rights and consent discussions in the field in order to boost participation. Polly asked whether or not UConn itself could be a major player in that regard. The community address advisory boards concept was reinforced in the exchange with Gwynne Jenkins, Chief of Staff at NIH, who joined the conversation.

It became clear that the requirements will be the record a need for a bio bank first, which would be built upon data and consent collections, not attempting to jump to sequencing or genome analytics, which must build upon a well-established sampling database. He noted that the recent NIH grants have flowed to programs with thousands of patients and well-established organizations. The Indiana program with \$300 million invested

by the state was again highlighted. Amy agreed that the question with NIH is always to ask “what’s the next thing to be funded?” Marat noted that Yale has invested \$6 million some years ago which has over the ensuing. Generated hundred million dollars in grants into the University and has produced excellent genome research results.

Polly asked if the collaborative would be best served by using incremental baby steps to make pilot programs launch to demonstrate the partnership, and wondered if there was too high a level of resistance to creating a collaborative bio bank? Amy pointed out that the true goal is to organize and collect patient samples and their consents, and that any organization that can put that together will be an important partner in any collaborative.

That said, if the Connecticut collaborative builds on existing databases and creates statewide bio bank, Connecticut could rapidly move its group into the sequencing and counseling levels which would presently demonstrate how unique the Connecticut program is if the state government can commit to at least seed funding, that would be a very strong signal and could make the program competitive across the nation. Lisa added that telemedicine via broadband services is already beginning to emerge in this area, and as genetic issues are identified in each patient, the group is already recognize the counseling will be immediately required on behalf of the entire treatment team. Amy added that statewide teams will be necessary on all levels of the process, from sampling to analytics, and that broadband services would be required to network them into productive teams in order to achieve the highest efficiencies and productivity possible.

Marat again reminded the group that one of the problems with this entire field is that if sampling reveals a potential for a disease about which nothing can be done (Alzheimer’s disease), versus diabetes in which lifestyle choices and medications can have substantial effects, the spectrum has a major effect on the project. It must, in short be addressed as part of the calculations. **Mark M. agreed and voiced the need to identify steps necessary for organizing the group into a cohort focused on well-established goals he noted that the group has been successful in identifying issues and ideas for developing infrastructure for economic development and jobs creation, but what remains today is “what vessel do we need to create in order to accomplish and meet our goals?”** He wondered aloud whether or not the group needed to go

“back to the government” for further advice or should an independent body be formed immediately in order to proceed? Tom P. added that it was critical to immediately **address the framework of the organization** so that all parties will know where and how they fit in the collaboration. He stated that in his opinion the odds of a success for successfully receiving a NIH grant were low, but that the effort to obtain an NIH grant alone will provide the group with a target to develop an organizational structure essential for the creation and ultimate implementation of pilot projects or other ideas on a far greater fast-track basis than if we continue to circle around as a group merely batting ideas around.

Polly pointed out that we have in fact already developed many ideas that have the potential for leading us directly in that path: asset inventory, development of a bio bank, identifying collaborators, gathering patients and consents, then attempting to obtain a grant, which can lead in turn to human genomic sequencing and analytics for profit. She agreed that the question today is “who does what within the collaborative structure that has developed? And Polly believes that the CHDC has an ongoing role in coordinating and facilitating that effort, along with advancing any potential legislative initiatives that may be necessary.

Mike Critelli stressed that “competitiveness” is a key ingredient to a successful collaboration and ultimate partnership for business success. He speculated that “personalized medicine” seems a stretch today, but ultimately will be “table stakes” for collaboration with the organizational and individual knowledge base of the partners already involved. He looks to pharmaceutical genomic products and services of the future, perhaps including the human biome noninvasive treatments for a vast array of diseases and conditions that remain extremely expensive, and difficult in terms of treatment and recovery at this time. While there may be ethical questions related to non-health treatments that would have to be considered prior to any attempt to enter a business plan centered on such treatments, it is important at this stage of the collaboration to look to all potential avenues for partnership and business development. For instance, manipulation of genes to reduce the potential for “shortness” in human beings related to sports activities would obviously be a bad goal, but this avenue merely illustrates the range and spectrum of thinking that should be featured in our discussions in order to fully recognize the potential opportunities. The point is that the collaborative group needs to expand its vision to encompass all

potential uses of whole genome sequencing, including uses of a non-medical nature.

It seems quite clear that eventually all the billions of letters in the human genome will be discovered and fully explored, and it would seem likely that pharmaceutical opportunities will follow the research that develops this full understanding of the human genome. Investment pour into possible business opportunities as the knowledge base increases, and remedial drugs and other treatments of all types will inevitably ensue.

Sen. Hartley remarked that she will remain in the state Senate and most probably on the commerce committee in the impending legislative session. She also pointed out that Joe McGee and the commission on economic competitiveness will also remain active and interested in these topics generated by the CHDC. She agreed with the group that **developing a knowledge base that generates products with a high potential return on investment should remain the central focus of this group**. She added that Connecticut Innovations has been an active member of the group for a while now and it is bit to be hoped that the state in collaboration with CI be able to launch a number of potentially successful business opportunities. Also at the top of the goals for the CHDC is to distinguish the state and its healthcare data organizations as national leaders, each of which individually and more importantly as a collective group will be led by industry in pursuit of developing pilot projects with business development and jobs creation potential. She added that the state has just created a new position of the “chief policy officer” and that it will be important for this group to present public policy goals ideas to that person (Vicki Veltri) in order to attract state involvement in potential opportunities.

**Gwynne Jenkins, chief of staff at the NIH join the conversation by telephone from Washington DC.** She pointed out that the NIH has a central policy of growing accessibility to human genomic research and treatment across the United States. The NIH is apparently interested in “creating a mash up” between various cohort lawyers across the United States, in a way modeled on the English bio bank. The initial goals are to construct research groups to create new protocol development strategies among the various cohorts, in order to create a “best of breed.” Issue at present for NIH is whether or not stitching together various cohorts into a giant group is preferable then simply creating a multimillion samples

database in order to create a research data set available to many players, guarded by strong consent processes, which may allow for more seamless organization and opportunities for all the players involved. Of equal interest to the NIH is the question of whether to start fresh or string together existing databases? At bottom, NIH is interested in “cross talk” among all the cowards with which it is working.

Tom P. chimed in by noting that there is an “essential dissonance on difficulties in grouping cohorts.” His experience is that there is an inevitable awkwardness generated by the exchange of data among pilot group partners. The challenge of enrolling patients into new programs, in other words “fresh recruits with new samples,” requires strong teamwork, with well-defined workflows and procedures, all guided by express goals.

It is apparent that the Mayo Clinic is NIH’s favored bio bank already, and it the process and protocols to be implemented by NIH players must be completely transparent and public. It was agreed that NIH is most likely not going to be involved in Connecticut’s effort to put together a collaborative, but it could possibly help with advice and funding.

The group recognized that NIH wants to disrupt the current science employed by most cohorts collecting human genome samples in the country.

**NIH wants to promote far greater diversity among the samples, not just focusing on race differentials, but sex, sexual orientation, and other non-health issues that would broaden the sampling profile.**

Essentially, NIH is promoting the study of Americans by a wide diversity of groupings, and it is therefore attempting to find the best ways to promote and encourage a wide diversity of samples. NIH apparently wants transactional relationships among patients and demands “real skin in the game” from a diverse group of collaborators seeking to generate a database of equally diverse patients.

**NIH is therefore focused on developing new methods of outreach in order to focus on underserved communities, including communities that will form an integral and essential part of the governance of the collaborating partners.** This potential collaboration will create far more “voices heard” which at present real remains an aspirational goal, being one which is practically turning out to be difficult to actually implement. A singular problem with this implementation is the proverbial “silos” in which the attempt to stitched together existing cohorts doesn’t work because each

of the individual organizations are set in their ways. The hope is that by expanding the diversity of the cohorts and the database profile, new entities will follow the NIH model and do it better. It is clear that there is a need for a database foundation to be built right and maximize the engagement of all patients and partners in order to generate longitudinal transactions for the long-term of both research and treatment.

It is obvious that NIH cannot do “whole genomic sequencing” for one million patients since the cost would be prohibitive. That begs the question, what can NIH actually accomplish? At this point the strategy is to use a 80/20 statistical analysis program and build from that structure and its results. The NIH does not anticipate bio sampling to begin for at least two years from now and it is unclear therefore at what point into what scale and scope genomic counselors will be required. Therefore, NIH cannot ascribe a score for awarding grants for training of such counselors. Amy Justice pointed out that NIH grants are reviewed by peer committees, the individuals of which will know that counselors are an essential aspect of the teams that will be required as human genomic research proceeds, and that such project officers will most probably generously regard program such as UConn has developed.

Discussion ensued as to the fact that Marat has pointed out that due to political changes in Washington that the NIH may become short on grant funding in the near future, so this could be among the last opportunities for research cohorts to gain financial support for diversity in new database samplings. Joe McGee added that the **CHDC’s report is due in mid-January to the Gen. assembly and so some coordination between the differing time tracks for the report (1/16/17) and the application (Feb 2017) to the NIH must be calibrated.** Joe asserted that Connecticut Innovations could be helpful in the development of the application to help demonstrate the support of the state of Connecticut and to refine the focus on business development and jobs creation.

Mark Micelli pointed out that the application must reflect a new restructuring reality that the CHDC must confront: **we need to recruit diverse groups to the collaboration and to the ultimate structure of the partnership.** This should include the NAACP and Hispanic groups, just for instance, with meaningful engagement on the part of these diversity groups, an element that is not easy to implement. It was noted that persons of color in the

United States are often suspicious with regard to the use of their human genomic information, and that there “buy-in” is often difficult to obtain, no matter how different important it is to broaden sample diversity among such databases. Amy mentioned that one role for the CHDC could involve discussions with various community entities in order to help grow the diversity of the patient sampling enrollment. Such a group could focus on the feedback from patients regarding what it is they anticipate obtaining from sampling, in order to generate proper consents to address their concerns. She added that wellness programs exist and could be expanded to include human genomic sampling churches and other community anchor institutions.

Polly Painter asked where the providers and insurers are on this question, and Amy replied that at least in the case of the veterans administration, provider see the benefits, but that patient buy-in remains difficult to obtain.

Joe agreed that all of the moving parts of attempting to apply for an NIH grant, under strict and rapid timelines and requiring a broad range of people of diversity within the structures of government, we both time-consuming and difficult to manage. John Hartley added that advocates of all kinds will be needed in order to transform the CHDC into a platform of action involving industry to the largest extent. She did not believe that a large executive or legislative branch of state government role will be required, merely as a facilitator.

Marat noted that he does not believe that funding from state government at this time is essential, but that a strong letter of support should be included with the application to the NIH, perhaps from the Office of the Governor. Lisa added that while the support of the executive and general assembly government branches may not be necessary, it will be highly necessary for consumer groups representing patients to become directly involved in this project for it to be successful.

**Lisa noted that there may be value in having state legislation enacted that would address the question of patient concerns regarding a contribution of genomic material being held against them for insurance actuarial calculations.** If a sample result could be held by an insurance company to be a negative for insurability, that would obviously be a severe detriment to the recruitment of patients for sampling purposes. There was discussion among John Hartley and the other

participants as to whether or not legislation on the state level would be effective, but it was agreed that the question should be answered in time for the impending 2017 legislative session.

Marat added that it is essential at this moment to gather the players that will be necessary for the grant application, then create and file what he hopes will be a successful application with NIH, and then regroup with the same and perhaps additional players for the next phase. Micelli agreed, and pointed out that each of the individual organizations that should be at the table, will need a valid and substantial reason to be there.

Marat pointed out that ancestry tests have been successful because they are fun and they initiate a personal interest in engaging in sampling tests. He noted that researchers and providers need to be sensitive regarding racial questions in that regard. It was agreed that at the next meeting of the group discussion should be had regarding the need for actual collaboration on a demonstration project, and the role that each partner will play in such a project.

Joe added that there is an ethical question with regard to offering a in inexpensive initial sampling test to potential patient participants, when the plan is for such patients to be required to pay more substantial charges for subs subsequent information. While such a financial organizational procedure makes sense because it would essentially pay for itself quickly, great ill will could be generated if potential health hazards are revealed in the cost for continued investigation or treatment fell entirely on the shoulders of the participating patients. The question is therefore raised whether researchers or insurers would be capable or willing to pay for such subsequent research. At bottom, of course, this group is most concerned with how the participants can in fact generate revenues and income on the ideas that have been stimulated by the discussions of the CHDC?

**Tom Peters raise the vital question regarding storage and broadband access as issues that will grow in importance as the collaborative moves forward toward the development of a large health database.**

He pointed to comments made by Bill Vallee of the group as to the extreme costs that are presently imposed on broadband users in the state as a potentially important impediment to the database production. Vallee has explained that residential, business, and including large research facilities such as Jackson Labs, UConn, and Yale, have found broadband access to be

a market hurdle toward expanding collaboration. There could be opportunities for legislation and perhaps modest financial inputs from the state government, since the incumbent market of broadband Internet access providers itself is proving difficult to overcome with advanced services at reasonable prices.

There was discussion regarding the work of Polly Painter in developing the "Mission of the Connecticut Center for Precision Medicine," specifically focusing on the definition and use of "precision medicine," versus "personalized medicine," or "precision health." It was agreed, however, that such a bullet sheet as Polly has created would be very useful for recruiting new partners, including laypeople with little understanding of the human genome research procedures and objectives.

It was agreed that the group would meet in mid-December and that further work should include:

- language and definitions to be revised on Polly's mission statement should be pursued individually;
- that legislative language with regard to the actuarial use of genomic results might be helpful;
- community health services should be investigated as potential outreach organizations;
- development of names of diversity groups that could help with the organization of the CHDC, as well as outreach to potential diversity patients; new development of the "value proposition" for partners of the collaboration to use in stimulating interest and support in their organizations; and
- Marat agreed that EL would sponsor a January "kick off" with regard to the development of the application due by September 2017 to the NIH for a grant to further the interests of the CHDC.