LINKED
IO Informatics
May 2016

WE GIVE MEANING TO YOUR DATA

VOLUME 1, EDITION 1

Welcome to LINKED!

Sylvia Vallee, Director - Marketing and Account Management

On behalf of IO Informatics, I would like to extend a warm welcome to our Customers, Partners and Colleagues in the Healthcare and Life Science community and introduce you to LINKED.

This is the inaugural edition of our newsletter. Linked has been created in order to update our readership on the latest news in "big data" harmonization, enrichments to IOI's Sentient Suite of software, our latest successes with customers, and a heads-up on recent IOI appearances in the press. We also include upcoming conferences where members of the IOI team will be making presentations and demos of our technology.

Additionally, each Linked edition will include interviews with IOI users, partners and staff that focus on the latest issues of interest to Healthcare and Life Science organizations. In this edition we feature the first of a two part series of interviews with our Scientific Advisory Board.

Finally, check out the "Recent and Upcoming Press" section at the end of this newsletter to hear about recent contributions to groundbreaking research in the Parkinson's Disease space.

One again, we thank all of you for your continuing support of our technology and services. If you have any comments or questions, please feel free to contact us at:

SVallee@io-informatics.com.

All the best,

Sylvia and the entire IO Informatics team

Our Industry – Thoughts & Insights

Dr. Erich Gombocz - Chair, Scientific Advisory Board, IO Informatics, Inc.

Dear Friends of IO Informatics,

We all learn throughout our entire lives, and when we put our heads together to constructively address how we can make things work better in our immediate environment, we are most successful. Nobody knows all the answers, but by discussing and sharing pitfalls and successes we strive to achieve best practices to address challenges together - that's what IO Informatics' Science Advisory Board was meant to do and has always done exceptionally over many years. As IO Informatics is very grateful to the numerous contributions our Science Advisory Board has made through their guidance and insights, I believe it may interest you to read about their thoughts on pressing issues in the life sciences and the medical community at large, and how to approach best solutions through experiences from their very own projects.

It is for this reason, that we conducted brief interviews with each of our SAB Members last year to share their insights with you and publish them in our regular Newsletter editions.

Being Chair of the SAB at IO Informatics for many years, it is with great pleasure for me to introduce you to their answers in our interviews and hope, you will enjoy them!

Erich

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Here is the first set of two interviews of our SAB members. The second set of interviews will appear in a next edition of Linked.

Bruce McManus, MD, PhD, FRSC, FCAHS
Professor, UBC Department of Pathology and Laboratory Medicine. Director of the James Hogg Research Centre, the Heart + Lung Institute, and the NCE CECR Centre of Excellence for Prevention of Organ Failure (PROOF Centre).

What do you see as the primary cause(s) of the drought in new treatments/cures reaching the market?

The comparative drought in new therapeutic or preventive "pharma" solutions for health care really arises from many confluent factors. Among such, our expectations are much higher than

in past eras. The level of precision and accuracy expected in targeting certain mechanisms of risk or disease has escalated. The ability to provide efficacy and safety is now scrutinized much more than in the past. It has been acceptable for FDA-approved therapeutics to only benefit 50% of patients treated – and to have adverse effects in a sizeable proportion of those treated. With the emergence of an ethos of more precision, more discriminative targeting, and reduced toxicity, the bar has been raised substantially. Many companies are struggling with this new paradigm of value creation that is patient-centered. It does not mean that we cannot achieve better performance, but the stakes are high, the costs bloat, and the timeframe for success is not improving. Another consideration that confounds the progress towards cures is the magnitude of risk to be assumed, and the difficulty in dealing fiscally with high failure rates in therapeutic pipelines….risk aversion leads to impaired innovation! On another front, one must consider the enormity of costs that underpin progress in the arenas of small molecule therapeutics and biologics.

Healthcare budgets are under great stress around the world, and the ability to pay for the innovations in treatments and potential cures that do emerge is finite. Finally, we live in a scientific and health care world, on one hand, flooded with data or information; while on the other hand, we don't have the data we need when we need it. With the vast data resources on the World Wide Web alone, we can and should make better use of them to guide therapeutic development at all stages. Codifying and distilling the essential information for each step of innovation still is cumbersome and plodding in health sciences. We need to do better on the fronts of interoperability, ontological alignment and harnessing data resources through the power of analytics and visualization, including unbiased semantic representation of facts and concepts.

What do you think needs to be done to remove the drought? How is this problem fixed? Who helps fix it? (Government incentives? More Government spending at early stages? Quicker FDA approval? Greater collaborations between academic, industry and patient advocacy groups?)

Droughts need rain!

In this setting we need to rain energy and resources onto the "plains of ideas". To do so, we need more collaborative risk and reward sharing. More public – private partnerships are one strategy. We must, of course, keep the fundamental science wellspring healthy. Some observers would say that we have forsaken basic biological science in our great rush to apply, apply, and apply! The cycles of knowledge generation, aggregation, distillation, application and evaluation need to be tight, recursive, adaptable, and relentless. This requires convergence of purpose by all stakeholders, we more selflessness and less protectiveness about rewards. These are days to emphasize the power of "stone soup". We need full-on patient involvement, charities, foundations, companies, healthcare organizations, universities and governments. This is where people need to lead together without focusing on "owning".

What major projects has your organization been working on in the past year?"

The Centre of Excellence for Prevention of Organ Failure (PROOF Centre) is a biomarker-derived, blood-test solution engine, both for the clinical laboratory and in support of pharma-biotech drug development efforts. While we are focused on biomarker solutions for the life-

cycle of patients with various specific ailments that lead to heart, lung or kidney failure, and we have partnerships that truly public-private in nature in particular contexts for those patients and their wellbeing, we have found that our computationally enabled trans-omic, analytics core is applicable to needs in the realm of spinal cord injury, muscular dystrophy and diabetes therapeutics. We are working hard to get signatures that have replicated and validated into the clinical laboratory such that utilities can be assessed in terms of patient outcomes, costs, and caregiver capabilities to deliver the best care. PROOF Centre is also working with others in the framework of the Personalized Medicine Initiative here in British Columbia in order engage all relevant parties, including patients in conversations and actions that move the dial in modern, more patient-specific health care. Such not only involves the rigorous application of various omic tools, but also structural and functional phenotyping modalities like high resolution imaging, as well as detailed environmental and behavioral characterization.

What major projects will your organization be focusing on in the new year?

In the coming year, we are continuing the large projects mentioned above. We will also press to get our translational clinical laboratory fully operational as a keystone for better health care in our own jurisdiction and as a facility of value to companies committed to biomarker-guided therapeutic development. This is a big direction for us!

Do you feel that Linked-technology (Semantic Web) is seen as a major tool for tackling HCLS Big Data and is finally becoming accepted more and more by the R&D community?

Appreciation for the power of semantics in enabling extraction of the value resident to health sciences and biological data repositories around the world is still in its infancy. More and more emphasis on drawing data sets together and then placing one's own data into a bigger context is occurring. In fact, many would say that this vast publicly-exposed data resource must be minded in order to justify further all of the resources that have been expended on creating such intellectual wealth. Although the inspiration seems to have arisen from the "big data" band-wagon, it is simply true that we do not make enough out of any data set of high quality that is created. Being community-minded in this regard is a pivot point for more speedy progress in using semantic tools to bring new and unexpected insights, some of which will open the box of serendipity that leads to better, more affordable and sustainable health care.

Any other input you would like to provide?

Alignment, alignment, alignment among parties with different skills, knowledge and data, and with the patient squarely front-and-centre, is the most important cultural thread we must cultivate more vigorously in order to reap the rewards of both preventive and interventive care we now know is possible.

Charles N. Mead, MD, MS
Director of Healthcare IT, Octo Consulting Group and CoChair, W3C Healthcare Life Sciences (HCLS) Working Group

What do you see as the primary cause(s) of the drought in new treatments/cures reaching the market?

Not being involved in clinical care, I am somewhat reluctant to respond to this question. However, I sense that the 15+ gap between "research findings" and "clinical point-of-care implementations" that was so dramatically documented more than a decade ago by several very well researched and documented studies hasn't really changed much. The reasons then were most likely the same as the reasons now, i.e. the combination of daily clinical care being – by and large – a fairly conservative context in which you "go for what you know and what works" combined with the ever-increasing amount of specialized knowledge that, if anything, makes the process of change even more difficult since change – by definition – means integration of new data which, in turn, means time to review and judge that data.

Certainly "evidence-based medicine" is the "right" way to deliver maximally effective clinical care. The question then becomes "How does the right evidence show up at the right time for the right patient in the right context at the right time?" The answer to that question is multi-dimensional and involves input from a number of perspectives including both technology-based (availability of data at the point of care plus integrated use of appropriate technologies into the clinical care flow) and non-technology-based (e.g. sociologic, cognitive, etc.) factors. There is no question that the "next generation" of clinicians is more comfortable with technology and its potential benefits than their predecessors. In turn, however, part of the challenge will be how we integrate useful technology into meaningful care without losing the single most important factor in care: the human-to-human element.

What do you think needs to be done to remove the drought? How is this problem fixed? Who helps fix it? (Government incentives? More Government spending at early stages? Quicker FDA approval? Greater collaborations between academic, industry and patient advocacy groups?)

All of the above.

However, sadly it seems to me that the biggest change that is required is probably not one that will easy – or even possible – to make within the context of the US healthcare market and that is the requirement to view healthcare not as a money-making business but rather as a humanity-sustaining necessity. All of the government funding, FDA fast-tracking, etc. thrown at a system that is ultimately not a healthcare system, but rather a utilization-based profit generator will not, IMHO, change the basic dynamics to the degree to which they need to be changed.

As long as clinicians are more concerned with charge codes than clinical outcomes – and this is why certain innovative financial reimbursement programs attempt to close the gap by linking the two – we will fall short of the real goal of delivering the best care to the most possible people, a goal that is NOT without financial responsibilities and accountabilities, but DOES embrace a value system beyond just the bottom line.

What major projects has your organization been working on in the past year?"

I am currently working with a provider of medication information to physicians, pharmacies, and hospitals. Their goal is to provide the best information possible independent of how that information is used. Because they work exclusively in the European healthcare market, their perspectives vary in some very fundamental ways from those of the US healthcare market. In particular, although reimbursement for a given prescription certainly plays a role in the linked information sets that are available from their information repository, such information is provided in the larger context of evidence-based indications, contraindications, and side-effects so that a point-of-care clinician can weigh the balance between cost and quality of a given treatment option.

What major projects will your organization be focusing on in the new year?

Development of an integrated semantic architecture that enables them to produce "use-case-specific semantic profiles" that are developed from finely granulated graphs that represent a significant step beyond their current text/phrase-based – and therefore use-case-hardwired – technology infrastructure.

Do you feel that Linked-technology (Semantic Web) is seen as a major tool for tackling HCLS Big Data and is finally becoming accepted more and more by the R&D community?

I think this question is somewhat misplaced and should instead be directed at the clinical care community. The substantial time gap between "research discovery" and "clinical care reality" has not substantially decreased in the past decade. Semantic technologies can provide genuine impact at the point of care. That is not to say that their increasing adoption in the R&D community is not important. Certainly it is. But there should also be a simultaneous commitment to deployment/uptake in the clinical care community…and such an uptake will require an added dimension of understanding beyond that required for adoption in the R&D community, for integration into point-of-care operationalization involves understanding issues such as multi-tasking, cognitive processing, and value proposition tradeoffs as they relate to the integrated use of meaningful technologies at the point-of-care.

Any other input you would like to provide?

None at this time except that the value proposition of semantic technologies in addressing the overarching challenges of integrating the cost and quality of care cannot be overemphasized.

In the end, computable semantics are one of the critical linchpins necessary if we are to ever achieve the almost mythical goal of "personalized medicine." Anything that can be done to accelerate the power of the message of the usefulness of semantic technologies is money well spent for all the involved stakeholders: vendors, providers, and – most important of all – patients.

Mark A. Musen, MD, PhD
Professor of Medicine (Biomedical Informatics), Division Head (BMIR) and Co-Director (Biomedical Informatics Training Program)

What do you see as the primary cause(s) of the drought in new treatments/cures reaching the market?

The development of new pharmaceuticals is getting increasingly expensive, which makes drug companies increasingly cautious about pursuing new discoveries. Although drug companies have a major problem knowing what projects they should be pursuing most aggressively, they often have a more difficult problem in knowing which projects *to kill*. The sooner they can abandon a fruitless pursuit, the less loss they will encounter. Of course, knowing what is going to be fruitless and what is going to lead to the next blockbuster drug is not always easy! Making such determinations often requires bringing together data from any different sources in many different formats—something that IO technology has been designed to address from the beginning.

What do you think needs to be done to remove the drought? How is this problem fixed? Who helps fix it? (Government incentives? More Government spending at early stages? Quicker FDA approval? Greater collaborations between academic, industry and patient advocacy groups?)

Although pharmaceutical companies always argue for faster FDA approval and less regulation, I'm not convinced that is where the bottleneck really is, and I believe that careful regulation serves an essential role. I think the fundamental problem still is for pharmaceutical companies to be able to identify as early as possible which candidate drugs are likely to be blockbusters and which candidate drugs are likely to be duds. I am very excited about the activities that the Pistoia Alliance and other organizations are taking on to help pharmaceutical companies share pre-competitive strategies that can help everyone in the early stages of drug discovery. Not surprisingly, many of these strategies involve working to make sense out of as much data as possible, often taking advantage of semantic technology to do so.

What major projects has your organization been working on in the past year?"

We're finishing our work helping the WHO to develop the next iteration of the International Classification of Diseases (ICD-11) using our Protégé ontology editing system. We have

investigated new methods to help the WHO to define building blocks from which they can piece together much of the complicated terminology required in ICD-11. We've been doing some interesting work to see whether crowdsourcing platforms such as Amazon Mechanical Turk can be used to perform quality assurance on scientific ontologies such as SNOMED CT. And we continue to add new features to the technology that we make available through the National Center for Biomedical Ontology.

What major projects will your organization be focusing on in the new year?

The big news is that we will be creating a new Center for Excellence under the NIH Big Data to Knowledge initiative. My team is developing the Center for Expanded Data Annotation and Retrieval (CEDAR; http://metadatacenter.org). Our goal is to use semantic technology to make it easier for biomedical scientists to create the metadata that are required to describe their experiments. We want to simplify the tasks of data discovery and data integration, and to increase the quality of scientific metadata so that experiments are easier to reproduce and verify and are more amenable to secondary analyses by other scientists.

Do you feel that Linked-technology (Semantic Web) is seen as a major tool for tackling HCLS Big Data and is finally becoming accepted more and more by the R&D community?

I think that linked data is getting more recognition by the scientific community, and we all cheer each year as depictions of the famous linked-data cloud show more connections and more resources linked in. We still have the need to be able to point to new scientific discovers that can be attributed to the new associations that emerge when data are linked together, however. Our credibility depends on deriving those kinds of novel associations in a manner that is attributed directly to the data. The moment someone can claim that linked data have led us to a previously unknown connection between a disease and a possible treatment, or between a disease and a possible etiology, the entire biomedical community surely will take notice.

Any other input you would like to provide?

I enjoy serving on the IO Informatics Scientific Advisory Board because I believe strongly in the mission of the company. The people are also great to work with, too!

Recent and Upcoming IOI Press

***Upcoming Press* – look for our upcoming (late May) press release!**

IO INFORMATICS DEEP DATA HARMONIZATION, RETRIEVAL AND INFORMATICS SUPPORTS GROUNDBREAKING PARKINSON'S DISEASE RESEARCH Nature Genetics publishes "Multisystem Lewy Body Disease and the other parkinsonian disorders." J. William Langston et al.

January 13, 2016

THE NICHOLAS CONOR INSTITUTE APPOINTS BILL HAYDEN TO ITS INDUSTRY ADVISORY BOARD Life Science/Healthcare Industry Veteran to Help Increase Collaborations with Industry, Government and Academia for childhood cancer

November 9, 2015

PARKINSON'S INSTITUTE AND CLINICAL CENTER PARTNERS WITH IO INFORMATICS TO ADVANCE PARKINSON'S DISEASE RESEARCH Integrated access to over 25 years of Parkinson's disease high quality data and related public data provides a major step forward for precision medicine research and collaboration

October 21, 2015

IO INFORMATICS, INC. PRESENTS AT tranSMART ANNUAL MEETING Semantic methods improving immediate and long-term value for tranSMART

October 19, 2015

IO INFORMATICS, INC. JOINS THE tranSMART FOUNDATION Bob Stanley, CEO, Elected to Board of Directors

October 14, 2015

IO INFORMATICS & ASTRAZENECA SIEVE - "Safety Information Evaluation and Visual Exploration" - COLLABORATION PRESENTED AT THE ISWC IN BETHLEHEM, PA

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About IO Informatics

From IOI's inception, our goal has been to accelerate healthcare, life science and precision medicine innovation by improving access to meaningful data resources. "Big Data" is not enough! Data must be meaningfully linked to generate insight and actionable knowledge. IOI meets this goal for our customers by providing the most agile enterprise scale solutions to the toughest data harmonization, integration, search and reasoning challenges associated with the growth of big data.

By harnessing and incorporating the latest advances in linked Big Data and computer-based reasoning, IOI's software and services are able to more efficiently integrate, deeply search and reason across data related to an area of interest. This improves our customers' ability to generate actionable knowledge, resulting in a higher return on historical and new data and technology investments. The Company provides software and services in life sciences, biotechnology, pharmaceutical, and medical environments. IO is headquartered in Berkeley, California with offices in the United States, Canada and Europe. IOI works with life science and healthcare customers in industry, academia, and government and not-for-profit foundations.

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