# TRANSCRIPT OF THE LIVE SYMPOSIUM INTERDISCIPLINARY APPROACHES TO MEDICAL NANOTECHNOLOGY: DEFINING THE ISSUES*

TABLE OF CONTENTS


I. WELCOME AND OPENING COMMENTS ........ 386
II. NANOTECHNOLOGY: SCIENCE, MEDICAL APPLICATIONS & IUPUI RESOURCES ........ 388
III. THOUGHTS ON COMMERCIALIZING NANOTECHNOLOGY ........ 393
IV. MEDICAL NANOTECHNOLOGY: THE ETHICAL CONCERNS ........ 399
V. LEGAL ISSUES IN NANOTECHNOLOGY: NEW SIZES – NEW ISSUES 404


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* The *Indiana Health Law Review* and the Health Law Society at the Indiana University school of Law – Indianapolis thank the following speakers for participating in the symposium and providing their unique and informative perspectives on nanotechnology, as well as for allowing the *Indiana Health Law Review* to publish this transcript.



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The *Indiana Health Law Review* would also like to give special thanks to Ms. Amy Lewis Gilbert, President of the Health Law Society and Ms. Carsandra L. Knight, Coordinator for the Center for Law & Health, who worked tirelessly to make the symposium a truly memorable event.

VI. POSSIBLE INTELLECTUAL PROPERTY LAW ISSUES IN NANOTECHNOLOGY .................................................................... 410

## EDITOR'S NOTE

The following is a transcript of a live symposium entitled Interdisciplinary Approaches to Medical Nanotechnology: Defining the Issues. The symposium took place on April 15, 2009 in the Wynn Courtroom of the Indiana University School of Law – Indianapolis. The symposium was presented by the IUPUI Consortium for Health, Policy, Law and Bioethics, Indiana University School of Law – Indianapolis, the *Indiana Health Law Review*, and the Indiana University School of Law – Indianapolis Health Law Society. The symposium was designed to address introductory issues of nanotechnology across a broad range of disciplines by incorporating presentations from several different professionals into one event. Each presenter focused on an issue of nanotechnology within his or her expertise. Following the presentations, a brief moderated panel discussion was held to allow audience members to ask questions of the presenters. Due to technical difficulties, the transcript was unable to include the panel discussion.

To preserve the dialectic flavor of the transcript, the portion of the transcript presented here has been edited in form but not in content. During the editing process, a distinct effort was made to retain both the original tone of the panelists' remarks and the verbal mannerisms of the individual panelists. The power point slides from each presenter are available at www.indylaw.indiana.edu/news/browse.cfm.

## I. WELCOME AND OPENING COMMENTS

PROFESSOR KINNEY: Welcome and thank you for coming this afternoon. At any rate, what we have in store this afternoon is a program sponsored by the Hall Center for Law and Health and its Health Law Society and Indiana Health Law Review, our law school, of course, and the Consortium for a Health Policy, Law and Bioethics, IUPUI Signature Center.

Before I go onto the merits I would like to advertise our consortium, bring it your attention. And this is -- there are brochures outside. What we are up to with the consortium for Health Policy, Law and Bioethics, IUPUI, a consortium of three policy, three research centers in three different schools, is to provide opportunities for interdisciplinary environment that it enhances research, education like we are about today, and of course, service and that's what we are about today, as well.

So I urge you to please take one of our brochures and become familiar with the consortium. We have a website; we are anxious to include all who are interested in our activities. I would also like to recognize before we open, Monica M.C. Allain of the Birck Nanotechnology Center at Purdue, thank you very much for coming.

And I would be remiss, there many others in the audience and I definitely should recognize including our visiting professors Ralph Hall who will be on the panel today. But I would like to specially recognize Amy Lewis Gilbert who is the President of the Health Law Society and has put together this conference as part of an advanced clinical experience in health law where we have advanced clinical experience in any ranges of law, but we have some very exciting programs development activities under the advanced clinical experience, and I trust this will be the same.

Indeed our advanced clinical experience has occurred seven years ago, and now is a national conference that we have every year for which we have to get hotel space for outside speakers and guests who come from around the country. At any rate, without any further due I would like to introduce the speakers now before each of them speaks and kind of give you a heads up, as to why we invited them to speak. And then as they come forward, we'll just move along through the program and at the end we'll have a panel where there is an opportunity for the speakers to comment on the presentations of the other speakers, and also for you to ask questions, and we urge to be vocal and asking questions.

Our first speaker is Dr. Kody Varahramyan, who is our Vice Chancellor for Research at IUPUI. He has really brought a real breath of fresh air, and a lot of energy to the research enterprise of this campus. That's one of the reasons we invited him, but the other reason we invited him is he probably one of the few speakers that we have today who actually know something about nanotechnology and that he is an electrical engineer. You'll be hearing from several lawyers and business types, and sometimes our knowledge is derivative, but it is nice to hear from a scientist at the start.

We have then Kyle Salyers following up from the Director of Business Development Clarian Health Ventures, and he is very knowledgeable about how we get these great ideas from the laboratory to where they can actually benefits some folks. And I suppose that's where the lawyers come in. We'll follow up with Dr. David Orentlicher who not only is a lawyer, but also an ethicist, and a politician. Again, very well educated, and highly accomplished. And when I say well educated on the part of all these speakers, we are taking Harvard, Brandeis, Indiana University, it's a very distinguish group, duke, if I might add my own alma mater, but at anyway.

So David will talk to us about the ethical challenges that are involved, and he brings a little sense of political reality to the subject as he served in the Indiana House of Representatives from 2002–2008, and then we will be followed by Emily Morris our new Associate Professor of Law. Emily is a tremendous asset to our Health Law program and to our program generally at the law school. She comes with knowledge of intellectual property, issues in the pharmaceutical and medical device world, and I think you are going to enjoy what she has to say.

We'll conclude with Ralph Hall who is our distinguish visiting professor here at the law school this spring, hopefully next summer, the next fall, and beyond but in addition to spending time here is also a Counsel of Baker & Daniels here in town, and he is probably one of the most knowledgeable people, knowledgeable lawyers I know about science. And not only he is a knowledgeable practicing lawyer, but he has a tremendous sense of the academic enterprise and what we are about in law schools. So we have a very distinguished panel today.

We will start with Kody Varahramyan, if you will come forward, and I think we are in for a really good afternoon. Thank you.

## II. NANOTECHNOLOGY: SCIENCE, MEDICAL APPLICATIONS & IUPUI RESOURCES

VICE CHANCELLOR VARAHRAMYAN: Well, Good Afternoon! I am Kody Varahramyan. I am very happy to be here. My presentation is on nanotechnology and I am going to cover the science, medical applications, and some of the IUPUI resources here. I should also say that this maybe an ambitious goal covering this really three distinct topics from science to medical applications to the resources that we have on campus to cover that within 20 minutes. But I'll do the best I can.

Maybe the first slide would be appropriate to provide a definition for nanotechnology. And quite frankly, if you look up there to see if there is one definition that most people adopt or use. The answer is, No. So this definition is a combination of some other definitions and little bit mount thinking and some other staff members we have that we came up with this one here.

So nanotechnology is the creation of functional, materials, devices, and systems to understanding and control of matter or dimensions in the nanometer scale length where newer functionalities and properties of method are observed and harnessed for a broad range of applications. So this is meant to be as brief as possible of a definition that we could come up to capture the field of nanotechnology.

The next slide, actually, provides a very brief history of nanotechnology, and actually a key point of this slide is that the term nanotechnology was coined in mid 70s. But just because we started then increasingly calling this field nanotechnology, and then there where some key inventions like in the 80s, like this Scanning Tunneling Microscope and all of that; that really started launching the field.

However, the point that also needs to be made is that actually nanotechnology in one form or another has existed for thousands of years. And in fact, if you go back to about say, 2,000 years ago the Greeks and Romans were already using sulfide nanocrystals to dye their hairs.

Then about 1,000 years later, or about 1,000 years ago in the Middle Ages, gold nanoparticles of different sizes were used to get different kind of colors for stained glasses, stained glass windows. So the field of nanotechnology from some points of view has been around for thousands of years. But, of course, in the last few decades you may say that we really have got into the science of it, and then technology of it, and now increasingly we are getting into the commercialization aspect of it.

All right, now those of you who may not have an idea, what is nanoscale? Well, this slide is meant to assist us with that. On the left side we see the Earth, which we should have some idea about, that is an object that is very large. Well, how large, is exactly of the order of 1.27x7 meters.

All right, in the middle, we see a soccer ball, and that's about 0.22 meter. I mean 1 meter is about a distance this long. So a soccer ball is about this much wide in diameter. On the right side, we see this nanoparticle known as a form of carbon structure fullerene, and the size of it is 0.7x9 meters, or 0.7 nanometers. So one meter is about this long, and one billionth of a meter, if I take one meter and divide up into one billion parts, the one billionth part is one nanometer.

Now the other point of this slide is that if you think of the Earth and the soccer ball, the Earth is about 10 million times larger or the soccer ball is 10 million times smaller than Earth, but if you go from the soccer ball to the fullerene, which is a nanoparticle, actually the difference is one billion times smaller. So think about it, the Earth with respect to the soccer ball is 10 million times larger or the soccer ball is smaller. But from the soccer ball to the nanotechnology size, dimensions of objects, we are talking about one billion times in difference.

One other way you can think about it is, if you take one of your hairs out and think of the diameter of your hair. All right, we can have of the order of 100 million of those nanoparticles place on the diameter of your head, about 100 million.

All right, well, but what is the big deal about this business of a nanoscale?

Well, there are a number of tremendous advantages. One of them is that, if you can make devices that are ever smaller and smaller and smaller, then you can't take bunch of them that do different operations that integrate them in a very small size area.

Now the system of this kind that we are the most familiar with is the microchip, which is the brain of our computers. Actually these days is no longer accurate to call it microchip, it's really a nanochip. Why? Because inside that chip, the individual devices are already in the nanoscale range-size, and a modern nanochip has of the order of one billion individual tiny little electrical devices on it.

All right, now it is because of that capability of reducing the size and having one billion tiny little devices doing operations on the chip, which is the brain of our computers that; that is why we can have a PC sitting on our desk with such strong capabilities. So that's one of the great advantages of reducing the size of devices into smaller and smaller dimensions.

Another way to look at it is that if we have not done this, if we wanted to build a computer of the power of our PC, of what a PC on our desktop does by using the 1950s technology, which means that the individual devices would be made of vacuum tubes. Would you know what will be the size of that PC?

All right, the size of that PC would be of the order of the size of this building and actually you would need maybe 30, 40, or 50 people actually to go around and continuously replacing the unreliable vacuum tubes. And by the way, you would also probably require at least half of the power consumption of this campus just to power that computer.

So again these are all the arguments to why it's goodness to be able to miniaturize something. So this is not just a novelty or something nice to.

Alright, but there are some other interesting things that happen, is that when you make something smaller and smaller and smaller, actually you are also increasing the surface area of that object with respect to its volume, and there are some advantages about that maybe I will give you an example in a moment. The other interesting effect is that you can take a typical material in bulk size and has set them proper design characteristics.

Now you take the same exact material and make it into the very small nanoscale size. On one behold, you will find that generally physical, chemical, optical, mechanical characteristics of material has dramatically changed. Maybe in its bulk size the material is not chemically reactive, maybe optically behaves certainly, but the moment you reduce it in size, those characteristics change.

So going back to the gold nanoparticles that our friends in the middle ages used to get different colors coming out of them, actually the different sizes of those gold nanoparticles would give you different wavelength of light. So that was the whole point.

So effectively nano-size materials from a scientific point of view, we can make them to behave if you know what we are doing in them to acquire the properties that we desire them to acquire.

And as well as applications of nanotechnology -- already, there are increasing areas where nanotechnology is being applied from information technology area, I already talked to you about the nanochip to medicine, I have few slides about that in a moment, to the energy area and as well as consumables.

Now not everything about nanotechnology is wonderful and beautiful. Like anything else in life, there are also some issues. For example, when you make these nanoparticles, if you don't know how you are processing them, how you are making them, it can be dangerous, maybe not all nanoparticles, but some of them, if they are inhaled for example by the people who are processing them. It can be also harmful in some cases to the environment. So all of these as we are speaking, they are also people including at universities that they are studying all of these effects and they are becoming more and more important. So we have to, for completeness, we have to keep that in mind.

Now, I guess, I just want to highlight that we can have different kinds of what we called nanoscale materials. Some of them can simply be nanoparticles where, for example, if you think of gold, if we have chunks of gold in the nanometer scale range, we called those gold nanoparticles.

We can also -- I guess, the slide there, almost in the middle there is actually showing you that we can have the technology to take individual atoms and put them on a particular substrate in any way that one wants to do, and by doing that on an economic scale effectively, you are changing the properties and characteristics of that material.

All right, this slide shows other kinds of nanoscale materials. And actually the picture on the right, like the lower one, is showing you what they called nanowires. Now nanowires there, you can think of them like the hair on your head except that this hair is made of all sorts of different kinds of materials. The materials can have electrical properties, mechanical, chemical, and optical and so forth.

Now this is an example where if you have nanowires stacked up next to each other like this, is an example where you have maximally increased surface area with respect to the volume where this material is. So if you used this material, for example, as the absorbing surface in a solar cell to absorb the lights of the sun and produce electricity. That means that the more surface area you have, the more electricity you can produce.

So this means that in a very small area you've maximized your surface area. And effectively, you can have something that maybe the size of a penny, but the surface areas maybe the size of a football field. In other words, if you just as though if you walked over all the surfaces available there and put them together on a flat surface, it could be the size of the football field.

So these are all important considerations about nanomaterials, but nanoscale materials can also be of biological type and bionanomaterials could either be simply be biological materials that or on the nanoscale range like the proteins, enzymes, DNA, RNA, peptides or they could also be synthetic materials that are used in biomedical type of applications. Okay, I have five minutes.

Well, there are different approaches for the fabrication of -- in other words to take nanomaterials and make them into certain kind of devices and systems, and again because of my time limitation, I better move on. These are some examples of actually completed systems where you have nanodevices combine with devices on the micro and major and microscale.

For example, you can have nanochips and some other systems of that kind. Fuel cells, for example, are examples where the materials inside the fuel cell to increase its efficiency are increasingly made of nanomaterials.

Lab-on-a-chip and drug delivery systems. Again, these are systems that some of which can also be implantable and they have great functionality because of having bunch of small size devices combined on the system there.

Now Nanomedicine is effectively the field where nanotechnology materials, devices, and systems are applied in medicine. These are applications where you can develop cures, for say, cancer, and diseases, and I guess again because of my time limitation, I will move on. I have a video here. (Video Playing)

Well, the next slides are really more or less the repetition of what you saw in the video as far as some of the examples where nanotechnology can be applied in the health care area like for treatment against cancer, targeted drug delivery applications where the drugs are delivered exactly where you want them to go rather than flooding the whole body, like if you do chemotherapy with very poisonous drugs, but you can send them exactly where they are suppose to go and release the amount of drugs only at the right time and at the right place. Other examples where we can have nano-based system for detection and diagnosis of, again disease.

I will just been spent, maybe, a minute or two in this final part. Since last summer, you may say, that we now have a new initiative on the IUPUI campus where effectively, previous to last summer there were bunch of people here and there in different units on campus doing nanotechnology oriented work and this Integrated Nanosystems Development Institute or INDI is meant to be like an umbrella organization that brings together these entities and coordinates their work and their efforts.

We also have already a number of existing centers on the IUPUI campus, like the Center for Regenerative Biology and Medicine, the Lugar Center for Renewable Energy, and all the other centers listed there, that for some of the work they do like the Lugar Center, one of their big projects is to make fuel cells, and to make better fuel cells, you need nanomaterials. And effectively, it's like INDI is meant to be a collaborative entity to assist all of the centers in a very collaborative and cooperative manner.

I will just move on and this slide effectively highlights a number of projects that we have on the INDI. A number of projects are oriented towards biomedical applications of nanotechnology, energy applications, and information technology applications. We already have a reasonable set of resources that are available for processing measurement and as well as computational work. But at the same time now through this sort of coordinated effort, we are also looking at what are some of the areas where maybe there is need for enhancement of resources and how to go about effectively securing them.

So having said that, I believe that's my last slide and I thank you for your attention.

## III. THOUGHTS ON COMMERCIALIZING NANOTECHNOLOGY

MR. SALYERS: Good afternoon, my name is Kyle Salyers. I am the Managing Director of Business Development at Clarian Health Ventures. First, I will start with my disclaimer and that is I know nothing about nanotechnology, but what I hope I can speak to a bit is may be some more generic observations about the process of commercializing the technology, and I hope I can provide a bit of may be integrated perspective, in that my background has been informed by both involvement from a public policy and economic development perspective as it relates to commercializing various kinds of technology involvement from an academic perspective both at IU, Purdue, and Rose-Hulman.

From a product development perspective, most notably at Rose-Hulman Ventures and as an investor, principally a medical investor, now at Clarian Health Ventures. So I hope to add those perspectives to the discussion and as well as some observations maybe from an operational perspective being a Director on two medical device companies.

Clarian Health Ventures: two quick commercial slides, I won't spend a lot of time on this, but we were formed about two years ago and as an independent for-profit investment subsidiary of Clarian Health partners. So our mission is to invest in early-stage medical technology companies, technologies which are both born within the IU and Clarian system, as well as technologies that come to us from the external marketplace and do not only present a good economic value proposition, but are highly synergistic with clinical Centers of Excellence within Clarian and Medical Research Centers of Excellence within the medical school.

We have four investment professionals and have made five investments to date, two of those are in diagnostics, and three of those are in the medical device field.

So our investment thesis, as a firm, really has four principles.

First, is to generate a market rate of return.

To do that based on the second principle which is being consistent with Clarian Health Partners mission.

We feel then, in service of that, the third and fourth principle relate to what we feel is our distinct advantage in the marketplace. So what's our unfair advantage as an investor and we feel that, that really is two-fold. First, is hopefully, we are in a position to make more informed judgments on technologies upfront because of our access to expertise, clinical expertise, and after having made an investment, we feel we are uniquely positioned to add value to the company based on our proximity to clinical assets. That's kind of our basic investment model.

I Googled this afternoon commercialization, and I was going to put a definition up and I thought well let's see what Google has to say? So there were 3.4 million hits if you put Google at least as of 10 o'clock this morning, which those numbers probably have grown even since then.

So this is kind of my own very simplistic views and what I think about commercialization; again, a generic perspective and that is an acknowledgment first that it does start with a core innovation, then reducing that innovation to practice, then protecting, repeating, and testing that practice, funding that application and then continued development of the practice itself leading hopefully to the dissemination of that practice. I am using practice really for proxy of may be a technology, but proxy for some repeatable set of processes that we are able to now put into place, and then ultimately from an investor's perspective, optimal commercialization were to take place when we are able to monetize those benefits for an investor.

This is not meant as a joke. I know you can't read it. It's my one and only slide that's nanotechnology specific which is why you can't read it. So you can't ask me any questions that you have. Well, maybe you can read it, I don't know. But I thought it was -- it was, kind of, interesting because as I read this, I had a couple of takeaways and I will read this if you can -- excerpts of it.

This is from IndustryWeek, entitled "*Nanotechnology Commercialization Efforts Continue*", "*As potential nanotech sales grow, so too does scrutiny. The nascent nanotechnology industry is facing many of the same challenges experienced by any young technology: lots of hope, lots of hype, and lots of scrutiny. Even the appropriate definition for nanotechnology remains a matter of some debate,*" which is, by the way, I contend like the ultimate definition of success. When everything becomes the defined under your category, no one really knows the definition, but they lump it in a broad cat and do a broad cat.

So a March report on nanotechnology which was spearheaded by Representative Saxton, out of New Jersey, a ranking member of the Joint Economic Committee, of The United States Congress, speaks to these rapid technological advances by saying, "*Advances in just the last five years have proceeded much faster than even the best experts had predicted. Looking forward, science is likely to continue outrunning expectations,*" the report states.

So the next paragraph then goes on to talk about some of the public policy considerations and it acknowledges the fact that undoubtedly regulatory processes and potentially political oversight would need to be much more robust in this area.

The next set of sentences highlights a couple of statistics and these are 2006 statistics, statistics being what they are; I don't know that the numbers are may be as important as the specific metrics that they are tracking, which is what I will speak to in the next slide, but what these particular statistics cite is that in 2006, $50 billion of nanotechnology-enabled products were sold worldwide, $12.4 billion was invested in nanotech R&D. Corporate spending of that R&D amount was $5.3 billion, $6.4 was from government institutions; these are worldwide numbers. Then venture capital investments, flowing towards nanotechnology, was expected to reach $650 million in that same year and then it closes with a quote here saying that "*Nanotechnology leaders are showing both the optimism and uncertainty of pioneers.*"

So my takeaway from this from a measurement standpoint was, okay, how might we asses the market for -- in this case, nanotechnology commercialization, again, I would probably generalize this in terms of the health of a market for commercialization of most technologies and there are a couple of measures here which I think we certainly pay attention to as venture capital participants and related to technology, but I think has some applicability in multiple areas and that's the following.

These are six government funding flows, corporate investment in R&D, intellectual property output, private risk capital flows, the size of the market for end products, and then this broad kind of catchall category of constraints and that's not to suggest it's negative or positive, but rather just an acknowledgment that as we begin to get momentum on the first five, we begin to get in some public policy and regulatory types of considerations that we need to be mindful of.

So having said all that is context; what I did here was is in these next couple of slides is just maybe to have a little bit of fun with this and say, okay, what's some commercialization Top 10?

I mean as I look back at not only some of the public policy considerations that I have been involved with but the 50 some companies we invested in at Rose-Hulman and then the most recent ones we have done, the five at Clarian Health Ventures, what were some Top 10 observations relative to the commercialization process and the first speaks to the continuum of funding.

If I were to -- I should have made this change, I don't know that it's so much funding as it is resources, a continuum of resources to match the appropriate developmental stage of a project and what I mean here is just a systems level view of governmental resources, and down the foundation resources, market return oriented resources, and have that systemic view of matching what we call the *color of money* or the *color of resource*.

Point two is just a distinguishment between where research begins to evolve into development. So I kind of talk about it in terms of the pursuit of knowledge to the probability of application and where that tipping point occurs in the commercialization process. Usually, indicative of many more engineers sitting around the table looking for the true application and the Design-Test-Build process.

Number three is just an observation that takes all kinds. It takes partners from all sectors of multiple disciplines.

Point four is a more tactical observation, don't forget the freedom to operate; oftentimes we found the propensity to jump very quickly to the protectability of intellectual property sometimes bypassing the first step of, "Hey! Can I even do this and am I in a freedom to operate position?"

Investor's demand a return commensurate with risk; it's often about fit versus good or bad. So the risk-free rate on the 30-year treasuring now is what 3.6%, 3.7%. As you move up, different elements of risk, as an investor you are asking yourself from a finance perspective, of course. So what additional element of return can I realize based on that additional element of risk? So if you have a venture capitalist or a private investor say, "Gee! I need 30% rate of return." You are like, "Oh my God! This person is -- just how greedy he is?" Well, it's predicated on the risk free rate, right? I can get almost 4%, if taking on no risk, I need to -- based on the dispersion of those returns and in fact if maybe one out of ten will succeed, I need to shoot for 30% for it to even itself out.

Talk to end users, in my field, my best friends and what we do, other nurses. They will tell you, right? They are in the field, it will work, it won't work, and they understand the workflows. So just an observation in the commercialization process early on, talk to the end users.

Clearly distinguish the technology license versus a company build strategy, there are a lot implications, I think, higher education and others who have intellectual property or blessed with intellectual property in their institution, how do we push that out, do we build companies, or do we license the technology?

Point A speaks to the importance of -- and this, at times, can be a difficult transition. It speaks the importance of the initial innovation relative to the commercialization, and the success diminishes over time and this isn't just to say not that the founding technology is not important but it's only to acknowledge that fact that over time along critical path of development, multi-disciplinary inputs are going to be required.

So it's about bringing in the management team, it's about bringing in the capital, it's about bringing in lots of other multi-disciplinary skill sets to compliment that core technology, and so sometimes from a founder's perspective, that can be a very difficult reality to come to grips with and then as you are adding incremental technology improvements which are more oriented towards application those two become very important.

Point nine; beware of the progression into new risk factors. So if we think about the commercialization process right, it's almost binary in terms of the technology, it works or it doesn't work. So you prove over time that with reasonable probability this thing can work, healthcare in particular; work towards commercialization; we begin to thinking about regulatory risk, what does the FDA think about this? Being to get into reimbursement risk, will somebody pay for this, then you get into these market issues and you get in these management execution and then lastly a list of the liquidity risk as an investor assuming grand commercialization success of this product or this technology, can I get out of the investment, will this company ultimately become liquid in some way?

Point ten, being -- an undergraduate degree from DePaul University, a liberal arts institution, I love number ten. I believe this firmly that technology commercialization is the ultimate multidisciplinary skill set.

I know I have got about 60 seconds and I have about three slides left. I will work through them very quickly. The last three slides are examples of templates that we use within Clarian Health Ventures to help come to judgments.

This first one is pretty common. Most of you have probably seen different iterations of this. First brush of technology or early stage business we are looking at, we are looking at these three factors. We are assessing the technology, the IP, the product, the market, the management, the deal structure and exit scenarios and associated probabilities with them.

The second, again this is an unfilled matrix, but this is always an interesting one to look at from the medical technology perspective; looking at it through the lens of a provider such as Clarian. Typically we populate this matrix with what's called predicate, either predicate surgery or predicate technology and then proposed technology or proposed innovation and you lay it across this matrix.

So we say clinical indication is to say - so what is the clinical indication that this new technology is targeting, what intervention is then taken, what is done to address those indications, where is it done, which is a setting of cares, inpatient, outpatient, then payment, what are the economics of this?

So this is a way when we are evaluating the potential impact within a provider setting of a new technology, it could be a nanotechnology, what does this matrix tell us? Not the only way we make the decision, it's one process we use to inform our decision-making process.

Then the last, this is another matrix we use which relates to risk management. I alluded to this early on. We both try to balance our portfolio of investments against this, but in any one particular technology or one specific company, we are also constantly reevaluating where are we from a technology risk standpoint, how apt or how able are we to protect this technology, how reliable is the technology, how dependent is the business model on the technology? Again is it binary or not? If this thing doesn't work, are we done or do we have a plan B?

Regulatory risk, what's the FDA process, what's our regulatory path, how much time and how much money will be required to move through to market, reimbursement, can we get paid for this market, management, execution, liquidity, and so forth?

So, again, I just want to provide a three -- we use many, but these are three of the tools that we use as we are evaluating the potential commercialization success of a medical technology. So with that, thank you very much.

## IV. MEDICAL NANOTECHNOLOGY: THE ETHICAL CONCERNS

DR. ORENTLICHER: Very good, it's good to be here. Thanks for including me. I will now talk about the ethical concerns and since Kody did a great job, going through the science, I can skip my first slide. As you said, this is not new; he gave some good examples of nano-particles, lots of other natural examples, they are indicated here and we've generated nano-particles for decades now or centuries even, with some of the things we do. So you are getting exposed to nano-particles all the time.

But now we're going to just increase that by some of these new scientific and medical developments. Kody mentioned some of the important medical uses, collection of more data. That was a nice video tape that talked about how we can do more efficient and nuance job of detecting abnormalities of blood chemistry and genetic makeup, cancer cell detection, more focused delivery of drugs in that video tape.

If you go to the website of the National Cancer Institute, you can track this. They are really doing a great job of keeping us up-to-date. But here's this website and you see there's Nanotech News, nano-particles delivered gene therapy killing tumors, nano-particles open door to cancer prevention. If you go to that link, they talk about a T-derivative of natural substance that they think has cancer preventive properties, but if you just drink it or deliver it in the normal way, it degrades very quickly and doesn't hang around long enough to knock off any nascent cancer cells. But with nano-particle delivery, you can get doses that are effective, at least, in these early studies. So that's very exciting and nano.cancer.gov if you want to follow that.

And then there are some things that I would be interested when we get to the panel to hear what Kody's thoughts are. When you read people are speculating, what's the potential for nano-particles, and I guess, there is a lot of exaggeration here and I'll talk about that problem. But some writers talk about the ability to develop these nano-scavengers that will come in and remove our infectious agents more effectively than antibiotics and toxins and repair or replace damaged cells. And since that's what causes to age the rehab cells that become deteriorate overtime, may be we can forestall age. I'm skeptic but may be there's something to that. Nano devices to improve the precision of surgery, then you hear people talking about the ability to enhance our normal attributes, to give us radar like visions, supernormal hearing and so on.

The ethical concerns; well, one of the concerns is, as I've suggested with this previous slide, is new technologies are often overhyped and I'll now give you a quote from a 2004 article in the Annals of the New York Academy of Sciences. Over the next 15 years, we will see an acceleration of innovation, change and disruptions on a scale no civilization has ever seen before. Nano scientists disruptively astounding for the potential it may hold to alter much of what we know. And this is just, as I said, it's a pretty respectable journal; the Annals of the New York Academy of Sciences.

So will it be overhyped? And it's not surprising if you read this kind of stuff. I mean if you're a developer of a new technology, you want to persuade venture capitalist like Kyle here to invest Clarian's money. So you want to make it sound exciting, and we, ethicists, are guilty that too really maybe we made (inaudible) with the human genome project, where we spend trillions of dollars to decode the genome and a few percent was set aside for ethicists and legal scholars. That was kind of a gravy change for the field for a number of years. I think ethicists are hoping nano-technology will turn up the same way. So it's kind of a drumming up of the ethics problems.

But the problem is if we overhype a new technology, and they tend be, will we divert funding from better uses? It's great to treat cancer but there are a lot of preventive things we could do, like turning people from smoking that we might get more for our bank for our buck.

A major concern is, is in the -- and I'll just give you some other examples of overhyping. There was an article published some while ago, one of their early proponents of nano-technology who claimed that someday we will be able to build the respirocyte, a little nano-particle that's 236 times -- I don't know how it came out 236 times, by the way. 236 times more efficient than red blood cells in delivering oxygen. So you send these little respirocytes into our blood stream with little nano-computers and they will tell us, our physician our current state and our physician can tell our little respirocyte exactly how much oxygen to deliver, and if we're going out to run a marathon, they will up the oxygen and if we are sitting on a computer, we get over a little bit less.

One thing that's been pretty much repudiated by scholars, but they were some of the early writers who talked about these nanobots, the nano-robots, that would take on life of their own, kind of a 2001, 3001, where they come into our body and then some way reproduce some out of control and takeover and overrun humanity. Well, that isn't too much talk about that anymore, but that's the kind of thing very science-fictiony in the writing.

The other thing is in the overhype, failure to account for potential risk for the serious scholars and Kody acknowledged that there are important risk that we have to take into account when you reduce these. As you said, they're not just little particles; when you reduce the size, they take on different properties. One of the concerns as one of the positive things about nano-particles is they are lighter, they're more durable so you get very strong, light particles when you reduce the size and they are durable but their durability means they'll be more persistent in environment. So our landfills are now filling up with plastic and now they fill up with nano-particles.

The other concern that environmentalists point out, because they are so small, you need very sensitive, very expensive equipment to detect them. So you may not -- not everybody has that. So, we may not be aware of the environmental hazards because it's hard to measure their presence.

There are concerns of the smaller size that will make it more likely to be inhaled and cause respiratory problems. People talk about, can they just -- normally, things don't get into through your skin unless you have a cut but nano-particles are small enough, may be that if you flex your wrist, that may be some nano-particles can sneak in there. That greater surface area has a lot of important biological benefits, lower doses as Kody said but may they can also hide in the flammatory responses.

And one of the concerns that you are see as people write in the area is because of the possibility of overhyping and the risk of overlooking, unknown risk or even known risk is that the public will be scared and you'll read a lot about the concern in the field that we not repeat what happened with genetically modified foods.

If you live in France or in other parts of Western Europe, genetically modified foods have been driven out of the market, not necessarily for good reasons; often there are benefits to have a genetically modified food but they got labeled as Frankenfoods, and even legislators in our state in country want to have labels that if your cow has various hormones, then you got to label the milk and make sure you don't get involved with any genetically modifies foods. Even though, for the most part, the risk had been exaggerated. So one of the concerns is that we lose public support for some very important advances.

Risk to privacy; our common concern. If we develop these nano-chips that could be implanted or run through the body that can find even more comprehensive in Nuance Data and then we can download it into a computer, the good thing is, physicians know more about your needs and can treat you better but the risk to privacy are even greater if people can hack into the computer or into your chip and find out all this information.

So we have to make sure that we have the safeguards to protect people.

Then here is another thing that I suspect is more on the science-fiction side but you read about, people tell me about these neuro-implants that can improve cognitive ability and allow us to communicate with each other just through our little nano-chips in our brain and people would be monitoring. I suspect that is not going to happen but if it ever did happen, we'd have to be worried about privacy there.

The over-identification of illness concern; if we have these ability to start, picking up these cell changes and blood chemistry or have subtle changes in our DNA or find cancer cells sooner because we've got these nano-detectors that are smaller and can pick up these abnormalities sooner, will we start being over-identifying illness? My guess is that a lot of people have cancer cells that pop up and then the body disables them before they reproduce enough but now that if we can pick up, identify these little cancer cells early and sooner, when we will make the cancer diagnoses, how many will it take; one cell, fifty cells, a thousand cells. If we start picking up these abnormalities sooner and identify people at risk or even, as I say, starting to label them with disease, will we provoke unwarranted anxiety in patients or will we lead to over-treatment of risk factors?

We have that debate already with prostate cancer; how much should we be doing measuring prostate-specific antigen androgen and men who are sixty-five and how much should we be treating prostrate cancer and men who are sixty-five or seventy. There are probably a lot of men who are getting treated and getting tested who shouldn't be.

So, the concern is that with nano-technology, we would magnify all those concerns. The other concern is, sort of, the enhancement versus treatment and again, this gets into and how much I am interested how much of this is likely, but you read some readers the whence I gave you the guy, that overhyped quote I get in his article. In that same article, he talks about all these remarkable possibilities for nano-medicine. Hence memory that will be able to recall everything and he has also talked about also disabling traumatic memories, so they don't dog you for the rest of your life. I think Kenny Perry is probably looking for one of those options. He was terrific at the Masters this past weekend.

Infrared night vision, long-ranged vision, wide spectrum here, who knows how all that is. But if we can do any of these things, then a lot of scholars start getting worried about the difference between enhancement, a lot of people are worried about enhancing normal attributes as opposed to treating disease, and we go through this debate now with steroids for athletes, Prozac to make us feel better and lots of other drugs that are out there. Now, there is a lot of ambivalence about human improvement; I give you a couple of examples where we commence self-improvement.

Here is Jarred and his before and after pants and you may recognize the government of California, Arnold Schwarzenegger and his pre-political days, and we all, we admire people who become accomplished musicians and innovative scholars. On the other hand, we are not always very enthusiastic about efforts of self-improvement; Barry Bonds and his steroid use. Michael Jackson; I am not sure this has ended up self-improvement, but that was the goal, involving his plastic surgeries and things.

So this tension, even without getting into all of the speculative aspects of nano-technology, anytime we have sort of brave, new world, new exciting technology whether it is genetic engineering or nano-medicine, people get very concerned. There is a lot of ambivalence and it's illustrated in literature, people get worried about, trying to improve the human condition. As I say, even if it's pretty even, given what is plausible and already happened with nanotechnology; Doctor Jekyll / Mr. Hyde, Frankenstein, genetic engineering, people get worried if we try to -- on one hand, we want to improve the natural state; on the other hand, tampering with nature, people start to worry, we are going to mess things up.

Genetic engineering, there are lots of movies about the potential horrors of genetic engineering. When we talk about artificial methods of reproduction, people get nervous; the cloning debate. Anytime we talk about changing the way life has dealt with, people get worried. This is going to be a problem when we deal with nano-technology. People very-- why this ambivalence; people aren't comfortable with change that we went through that with surrogate parenting, surrogate motherhood. If you remember, go back to the Baby M days, people got really worried about; how can you've kissed this way. Now, nobody even notices that surrogacy happens fairly regularly. Cloning is the more recent example of whether we can deal with new ways of having kids.

Part of it is the history of abuse. We know that in the past, we have misused technology. So people worry that in the future, we will misuse this, especially, again, we are trying to use these new technologies to improve the human condition and the history of eugenics movement and abuse in Indiana, in our country, and in Nazi Germany. And then people talk about concern for personal identity; if we can have these technological interventions that can help us see and hear and think and move more effectively and then are we doing it ourselves, how much of it is personal achievement, how much of it is the technology. So when Bobby Bonds, with his steroid, pumped up muscles, hit 70 home runs, is it the steroid or is it Bobby Bonds that hit the home runs.

So people get worried about that and if we become more and more wired neurologically, if that is ever possible, where we allow uniqueness dissipate, is that so also bad anyway? That is the other thing if why are we so worried about all of this.

This ties in why we worry about it. Well, the undermining event for it, if we can turn to nanotechnology, will we suffer diminish, try to succeed, no pain no gain. If you can pop a pill and your muscles bulk up or you can stay up for your exam or you can do all these other things, people get worried about that. Is that bad? Right, do we need to kind of suffer through life and work harder? The other way to look at it is this about just not exposing the myth of success based on effort, sort of, want to believe that people succeed through hard work. Sometimes they do but then sometimes you can be the grand -- the son of a president and get elected to the presidency, maybe 12 years later.

Now the important concern and this one I think is real, the most real, is the widening of socio-economic disparities. Anytime we have a new technology, it costs money. I don't know what the budget is for these new nanodrug delivery systems is, but I am guessing they are expensive. And those of us, who have good IU insurance, will be able to afford them and get that treatment, but the uninsured won't. Will we then widen the benefits, the differences, socio-economic differences that already exists and that are problematic in our society? That's already with existing treatments people have trouble but the more we get fancier, more expensive, new treatments, the more the wealthier have and other people don't have.

So, I look forward to your comments and questions and thanks again for including me today.

## V. LEGAL ISSUES IN NANOTECHNOLOGY: NEW SIZES – NEW ISSUES

PROFESSOR HALL: I have pleasure to be here. Let me tell you what we are going to try here. What I want to do is to try to link this, and I have a theme. The theme is that the activities you are talking about with the individual speakers, require answers, but they require cross-disciplinary answers, and that as we think about these things, the need for the very specialties; science, ethic, law, medicine, etcetera, to work together is absolutely critical.

I am going to briefly talk about this interface. I am going to talk primarily about two major challenges; one is the whole problem of definition, and then I am going to go through three examples to try to put some flesh on these otherwise theoretical bones of where all of you science types, have really made my life difficult. My world was really pretty nice, nice and simple, we understood it, and you have messed up everything.

What we are really trying to do here, is to avoid the Gelsinger situation. This is in the gene therapy area, an unfortunate event early on with a patient death, 18-year-old clinical trial subject. It has set back gene therapy by a decade or more, because of the reaction to that. What we need to do, and what the effort is to take this ethical, legal, social implications of nanotechnology, link them with the science, medical, technical world, so that we both minimize the risks, but also maximize the benefits. And remember while we are doing this, the public expects us to do this. I am not sure this is optional, the public makes us -- and I think they are right, mandates that we do this.

There is a tremendous intersection; you have seen some of that. I am not going to go through the details here, but I want you to think about the tremendous number of areas, international trade. We have seen in other areas, for example, genetically modified, or foods that international trade becomes an issue here, homeland security. When you think about product uses, you have export users, you have consumers.

I also want to mention the NNI, the National Nanotech Initiative, created in the 2000-2001 timeframe, a government cross-agency, operation to promote responsible development and use of nanotechnology. What I want you to think about is the broad range of the organizations within the government that are already linked into this. It cuts across everything. I do mostly FDA work but a lot of these is non-FDA, but they are linked, and remember there are other aspects of regulatory oversight models that are not in this, Federal Trade Commission, FTC.

Probably the most public problem with nano in Europe, if anybody remembers the product Nano Magic, it was a bathroom grout that the company made as Nano Magic, and it ended up sending several dozen people to the hospital. It didn't have anything to do with nano. There wasn't a nano particle in it, it was a solvent. That's FTC issues here in the US, for investors, what you say in your very financing statements.

The question; you have heard a couple of speakers say, well, nanotechnology or nanoparticles more accurately have been around for a long time. They have actually been here for about 10,000,000,000 years. Is this technology even new from our world? Can we regulate this using our existing systems? Do we need some special testing, some special oversight models, whatever it happens to be? And this is an open question, as to whether our existing systems are adequate? As you think about it, what we are trying to do here is this balance of innovation, and promoting the benefits with management and mitigation of risk.

The other question here which remains, is that we have to decide where these decisions are going to be made, either it is going to be at the global level, at national level, state, local? That's all unclear right now, and that can impact us very directly. Berkeley, California has passed regulations on nanotechnology research. So you see an example of local activity. You have international standards setting groups that are also involved here. So we have this open question of where is the regulation going to take place, where should it take place?

In the spirit of full disclosure, I was a History Major, I took science in high school. I got mostly A's, and declared victory over the sciences and moved on. So when I talk about this stuff, understand the perspective. You have heard a number of people talk about the impact of surface area, the greater exposure of atoms as you get smaller size, etcetera, and the characteristics change with size. Asbestos is an example. At some sizes, it's very dangerous, others it's very safe, but understand from the regulatory world that I live in, environmental FDA/USDA.

We have had a mass mindset. We regulate based upon mass, usually in my, the drug world, milligrams-per-kilogram, all of you scientists are making us rethink that entire paradigm, and it may no longer be our traditional measure. If you look at environmental standards, pollution standards, its particles-per-million, drug dosing or adverse events is a mass-based calculation and that can be very problematic. We also are potentially, emphasize potentially, creating issues that we haven't in my world thought through, and that is at this particle size our traditional views of the blood-brain barrier, the potential barrier, all changed.

I did not do the math here, alright, just on that. If you take a cube, 6,000 nanometers in each dimension, and 6,000 nanometers about the length of a red blood cell, just to give you, we give it a mass of one, our total surface area is 216 nanomicron, now I forget the unit, see I told you I am no good at science. If I take that same mass, and I divided into cubes that are 93 nanometers, look what happens, 216*13,000. Yet historically my world had looked at these two things as identical. That's our challenge. And we have to understand what those differences are, and how relevant they are.

In my world, we live by words. If we say we need some regulatory oversight model, that means we have to be able to define it, and right now, we don't have a consensus on what nanotechnology, or nanoparticle, or Nanomedicine, or any of those terms really mean, and that lack of definition is a major problem, because we can't regulate it until I get to define it, and by the way, you don't want me defining it by myself. The FDA has a nanotechnology task-force, created several years ago, they have come up with several reports, they have had public meetings, and they have explicitly refused to define nanotechnology or any of the other terms. I consider that very problematic.

There are some scientific descriptions of -- I am using the term nanotechnology, to accomplish all of these, but they are general, they are nonspecific, and they don't meet the need for a legal definition. I'll give you some examples. From NNI, here is their definition of nanotechnology; dimensions between approximately 1 and 100 nanometers. What do lawyers say when they see the word, approximately? It's like blood in the water to a shark. And it also includes things like imaging and measuring.

Well, the European Commission has a description of nanotechnology, which is not identical, and even on the most simplistic level, the size, 1:100, 1:100, friends of earth is on record of saying nano is really at 300 nanometers not 100. We just encompass the whole new world, because we don't know is it 100, is it 300, is it 200? And by the way, what's the magic of 100 compared to 101 or 99? And until the scientists can tell me where that line is, we are going to struggle here. Take that same cube, if you graph out, I again did not do the math. The cube size with the surface area, you can see if you are up at this part of the curve, these lines don't mean a lot. I might be 4000, 4001 who cares. But once you get down here, it makes a tremendous difference. This is the area where we are applying it in this 100 nanometer approximation, and this curve is what causes people like me to lose sleep, because if we are going to regulate nanotechnology in some form or another, we have to answer this question, of being simplistic.

Let's assume we have a definition that says a 100 nanometers. I will give you three scenarios cleverly A, B, C. In A, 90% of the particles are under 100 nanometers. In B, it is 50-50 and, in C, it is 10% or under 90% or over. Which one of these meets my definition? And if you tell me it's got to be more than 50%, under a 100 nanometers, what am I going to do? My products have an average size of 101, right? Very simplistic example but you understand how this is so important to my world.

We also have to remember, we already have products out there that are nanoproducts. Here are some examples of them. Till date, no one who has identified and established to a high level of probability, any unique safety issues.

Now, I am not saying they don't exist, I am saying they haven't been identified. This gives some people a sense of comfort, other people get nervous about this. Are these even new? This is from FDA. This is their works, not mine. Many approved products, currently on the market with components manufactured the nanoscale. Most drugs act at their site at the atomic level, the nano level. FDA says, we think everything is fine with our regulatory structures. There are number of stakeholders that disagree with that.

So if this isn't new or at least had existed before, why the fuss? Well, part of it is, this perceived difference, and perception becomes reality. This is the hype that David talked about, and others have talked about. The other, we've just been lucky, or we don't understand the risks we should be looking at. Do you have different bioaccumulations of particles based upon size? Do we have actually different risks? Is this just technophobia?

And all of these is going into the debate right now on the Ethical, Legal, Social areas. So let's look at three quick examples of where the Science Legal Regulatory Ethical areas intercede in ways that I do not know the answers to. I will start off there.

The first one comes from the FDA world. Drugs and devices are assigned their categories, essentially that drugs act chemically, and devices act physically or mechanically. Remember that this differentiation started to come into place in the mid 1930s, when Congress passed the 1938 Act. If you think of who was in Congress at the time, this means they took their high school science around World War I. Science has changed a bit since then.

So at the nano-level, the distinction between physics and chemistry disappears. I was having a discussion with a professor of chemical engineering about a particular nanoparticle, and I said, does this work chemically or physically? And she said, that's the dumbest question I have heard in the long time, because there is no difference. My response was, I don't care, Congress says there is a difference, and therefore we must determine what that difference is. This has very important practical effects, because they are entirely different regulatory pathways, entirely different toxicology requirements, pharmacokinetics studies, whatever it happens to be.

For Kyle's view, if it is a "drug", it's three-quarters of the billion plus in 10 years to market. If it's a device at the high risks, it's 50 million in 5 years. Slight difference there. That also affects when patients get the benefit.

Simplistic example of a classic receptor model, right. You've got the receptors and the neurotransmitter, this maybe a SSRI, SSIR, excuse me. And I keep using the trumps to define, it binds to the receptor. We want to slow down this or somehow block this from happening.

Conceptual, there are two ways we can do it. We can get a nanoparticle that attaches itself to the messenger, so that that particle no longer physically fits into the receptor. In my device then, because I am working physically, or I can have my nanoparticle attach itself to the receptor site, so it is filled. Is that chemical?

We are doing the same thing. One, we are going to say it's chemical. One, we are going to say is a device. One of the examples, Kody gave was of a product that would attach itself to the tumor cell, you'd then use Infrared energy to heat it up and cause thermal, right? Is that chemical or is that physical?

Now what is heat? Heat increases molecular activity, right? And with the particles attaching itself to the cell, is that chemical? This distinction between chemistry and physics works at the macro level. If we are talking about tongue depressors, you know, and those kinds of things, but when we get to the nanoscale, this merges. And this is a significant issue. This is an example of the type of question we have to answer before the researches, the business people, the consumer knows how this goes.

Another example, Toxic Substances Control Act. Toxic Substances Control Act or TSCA created in the 1970s requires prior notification if you are going to be marketing or distributing a new chemical substance. There maybe testing requirements, etcetera, and the act defines a chemical substance as any organic or inorganic substance of a particular molecular identity, with pick on carbon.

Carbon has been around for how many years? 10 billion, give or take, a billion here or there, right? Is carbon new? And carbon nanoparticles have existed since the dawn of time, right?

So what about a carbon nanotube? There is data, you can debate how good it is, that carbon nanotubes of a particular size may act like asbestos. Should we regulate this under TSCA? Well, we have the same molecular identity, correct? Carbon is carbon is carbon. What's changed here is size and shape. Does TSCA apply here or not?

Well, the agency has indicated in a fairly recent, Federal Register notice, that they view carbon nanotubes as a new chemical substance subject to TSCA. The statutory basis for that is questionable, shall we say? The system was created when we didn't think about or didn't know about peculiarities of size and shape.

The last example, silver. All those -- please I do think of silver as inert, right? We have silver jewelry, silver coins, etc, etc. If the nanoscale is biologically very active, so "regular silver might term, is inert, nanosilver is biologically very active, and in fact, we've nanosilver products already out there." This is a partial list of them. You can buy bandages with nanosilver, you can buy washing machine that has filtration system with nanosilver to help get your clothes deodorized and fight germs. So we have these nanosilver products out there. There is data that says nanosilver can pose an environmental risk in aquatic settings.

What do you do here? In part, let's think about the cluster of statutory structures and regulatory agencies that are involved. See the cross-functional nature here. Remember that FDA has a categorical assumption for environmental impact statements for most of these products, going back 25 or 30 years.

So what is our risk here? How do we assess it? Does a regulatory system fit with the new understanding and the new products? So what are the key issues that we deal with here? What are the new safety issues if any? Our lack of a legal definition, this one bothers me a great deal as you must be able to tell. Because if I can't define it, I can't regulate it. I can't make you do anything, I can't regulate your advertising, for example.

We continue to use old systems for these new technologies, and we have this increasing cross-functional interface between the regulatory systems and the science. We have advertising issues, fair trade issues, the IP issues, that Emily mentioned, etcetera.

So how do we reap the benefits while mitigating the risks, requires this cross-disciplinary work that helps identify the issue, because I certainly don't know most of them, but then requires this linkage in order for us to address it. So that I think ends where we are at this point in time.

## VI. POSSIBLE INTELLECTUAL PROPERTY LAW ISSUES IN NANOTECHNOLOGY

PROFESSOR MORRIS: I would like Kyle don't want to hide behind the podium because it would engulf me. So, I am going to try to stand at the side here. But what I want to talk about today are some of the intellectual property issues that may arise with some nanotechnology, especially nanotechnology in biotechnology and medicine.

So, just a quick overview of the various areas of intellectual property that might be relevant. First of all, relatively few nanotech inventions are actually out on the market now. That's obviously growing and accelerating but very few are really, have been commercialized. Nevertheless, we see huge increases in some of the IP issues that come up and a lot of the IP scholars are now commenting on nanotechnology.

Perhaps, most obviously relevant is the field of Patent Law and we already see thousands of patents that are relevant to nanotechnology and they may not necessarily create new or unique issues but maybe will change some of the issues for some of the players that are in the industry, particularly in medicine.

Our Trade Secrecy, obviously, is going to be relevant and may actually be the motive-choice for protecting nanotechnology because nanotechnology is difficult to reverse engineer depending on how quickly it evolves, it may not be worth patenting your nanotechnology and for the most part, we don't like this because it doesn't give us the disclosure of the nanotechnology that we would like to have.

Our trademark, believe it or not, trademark can be relevant to nanotechnology. And it's partially this view of nanotechnology is kind of the cutting edge. It's very sexy, right. We have the iPod nano, plus we have this trend of, what they call, the urge to shrink. The smaller it is, the sexier it is, the better it sells.

And then finally Copyright. Not obvious what the copyright issues might be, if any, at this point but perhaps there will be some further down the road and then depending on what happens with the various nanotechnology markets, we may decide that like databases and a variety of other intellectual property assets, that we want to have some sort of sweet generous protection of various types of nanotechnology.

So, starting off with patents. As, I think, Kyle mentioned there are some 6800 patents already in nanotechnology as of March of this year, as of last month. The patent applications are accelerating. So, every year, we are going to see that number double and triple and in particular, patents are very important to Biotech and Pharma, to the Pharmaceutical industry. So, possibly nanotechnology will be of great importance and particularly patents on nanotechs will be important to the biotechnology and Pharmaceutical industries and we have already seen a lot of that in Dr. Varahramyan's presentation.

And of course, there is lots of investment in nanotechnology, a potentially great financial and social return. So, a lot of people are trying to figure out how to internalize those returns and protect their intellectual property assets. Probably, I am guessing the biggest changes we are going to see in Patent Law are the changes in the players.

First of all, as Dr. Varahramyan and few others have noted, universities are increasingly patent owners, particularly in nanotechnology. I have seen estimates where as many as 20% of all nanotechnology patents now come from universities, whereas in other technologies, it's closer to 1% or less. Why is that? Is that unique to nanotechnology or is it due to some other third factor? Well, might be that nanotechnology is still relatively nascent technology and therefore, we are going to see a lot of the patents coming from pure research, which usually takes place in the universities, that hasn't become applied research yet and hasn't moved out into commercial sector.

It may be the Bayh- Dole Act. Bayh- Dole Act was pretty recent and now we are seeing the effects of the Bayh- Dole Act in which inventors that enjoy government funding are now allowed to patent their inventions and so maybe nanotech is the first new technology in which we are really starting to see this taking effect. Because universities are kind of a relatively new player in the patent market, or in terms of licensing patents, it may change the dynamic of how patents are used.

We will talk more about that in a minute. There is some belief that nanotechnology is very cross-disciplinary and that for those reasons, a patent in one industry maybe entirely applicable in another industry. So, you are going to see a lot more negotiation, not only within industries but between industries and perhaps, some effects from that, some more monopoly-like effects, not only within one industry but between industries again.

Is this necessarily new to nanotechnology or to biotechnology and Medicine or have we seen this before? Well, we have seen this before. We have seen this with nuclear medicine and other areas of technology that have been applied in biotechnology and Medicine. So, perhaps this isn't such a new thing that the industries aren't going to be able to deal with.

Because it's cross-disciplinary, we might see more inventors listed on patent applications and what kind of difficulties does that create? Or what kind of benefits does that create? Because co-inventors on a patent are joint owners of that patent. They can each separately license the patent to others. So, maybe we will see greater licensing of nanotechnology patents.

Plus there is the difficulty in valuing nanotechnology patents, in part because we don't have a great deal of commercialization yet. Kind of along the lines of what Kyle was saying earlier and it's largely government and academic funding at this point, not so much commercial funding and that's perhaps because of the difficulties as Kyle said monetizing the benefits of nanotechnology and particularly Nanotechnology IP.

So, maybe the start-ups will have a more difficult time attracting funding, in particular venture capital or maybe as the market becomes more familiar, more comfortable with nanotechnology. People will get over those fears and start to be more comfortable investing in nanotechnology. But as Kyle said, it's kind of the uncertainty of pioneers.

Another danger that a lot of people worry about is what can be loosely referred to as over patenting and the idea is that maybe we will have overlapping patents or patents on things that never should have been patented in the first place. Perhaps because nanotechnology is relatively new or at least our understanding of it is relatively new. So, it is taking a lot for the USPTO to catch up in its expertise. And the USPTO actually has made concerted efforts to try to address this problem, in part by creating this whole cross-referencing system in which the nanotechnology in various areas can be cross-referenced against the nanotechnology in other areas and also training their examiners, so that their examiners are more familiar with various issues in nanotechnology.

There is some concern that, and this one is again from Mark Lemley at Stanford, that a lot of the early patents on biotechnology or nanotechnology were too broad, that people didn't understand how the nanotechnology was going to be used in the future and therefore, granted these very broad patent rights that can now be leveraged and can actually be used to block further developments in nanotechnology.

There is also the idea that maybe some of these things just really shouldn't be patented in the first place. As Dr. Varahramyan mentioned, nanotechnology has been around for centuries, right. People have been using nanotechnology, whether they knew it or not and that a lot of these things already existed in nature, that they are perhaps the phenomena of nature and we saw this a lot with the genetics patents and genetics, of course, are just a sub-type of nanotechnology.

There is some idea that like genetics, some of these things perhaps should not be patented because really they are research tools and that doesn't mean that your microscope can't be patented but perhaps some nanotech particle that you have been working on can't be patented because really it doesn't have a function in and of itself except for further research. And then again, this idea of patent overbreadth and especially with the pioneering patents, the early patents of biotechnology. They have been too broad, not fully enabled and not fully describing what it was that was going to be encompassed within the scope of the patent.

Then finally, in patent now we have a very limited experimentally used defense and given that, nanotechnology is still kind of in its infancy and a lot of people want to continue experimenting and developing nanotechnology, they might have difficulty giving out these pre-existing patents, they have to be licensed in order to study a lot of these things.

However, unlike computer software, which really is, I think, a lot of scholars have seen, an ill-fit with Patent Law and Copyright Law nanotechnology fits pretty fairly within the parameters of what we think of is Patent Law. It's not necessarily something we can't deal with; we just need to learn more about it perhaps and then we will know exactly how to deal with it under Patent Law.

There is also the possibility now that we have these pioneering inventions in nanotechnology, pioneering patents, that will have the certain explosion of further nanotechnology inventions that basically apply the pioneering inventions and that they might actually be obvious in light of these pioneering inventions and therefore, shouldn't be patented in the first place. And thereby creating patent thickets and blocking patents, again which create a lot of transaction cost and a lot of problems.

And perhaps also too many patents and too small patents which create a risk of the tragedy of anti-commons which we saw or at least, we are worried about with regard to genetics. Although, it turns out that a lot of people who do research in genetics have been collaborating and sharing information and so it hasn't been as big a problem as we though it might be.

There is some debate of over what are equivalents of nanotechnology. Because we don't understand nanotechnology completely, we are not sure what actually are equivalent technologies or older technologies that might have used some sort of macro or micro level technology can now replace certain parts of their functioning with nanotechnology and is that just an equivalent use.

In Patent law, we have seen what many believe to be the death of what we call the Doctrine of Equivalents and the certain death of the Reverse Doctrine of Equivalents but maybe with nanotechnology we will see a resurgence in the use of the Doctrine of Equivalents as people get more familiar with the technology.

Then finally, there is a difficulty in detecting infringement, in part because the particles are so small, so how do you know when someone is actually infringing your nanotech patent and there is this idea that as Dr. Orentlicher mentioned nanotech particles are very small, very light, but very durable. So you run the risk of what we call passive transfer. That someone may pick up on your nanotech particle, your nanotech patent, without even knowing it and how are you supposed police that if they don't even know that they are carrying around your nanotech particle.

And then there is some question to also whether or not this is even a problem because we could have individualized medicine or other types of individualized uses of nanotechnology that aren't as much at risk for infringement. And so far we really haven't seen many cases in courts, a lot of this is just conjecture, so the effects have yet to be seen in the courts.

So, how do we solve the potential problem for over patenting? Well, maybe, it will solve itself. Because a lot of this is government funded, we might see some government interventions, and compulsory licensing, cross-licensing or some sort of Hatch-Waxman like legislation that enables people to use patented technology more easily, more quickly than they would otherwise.

Again because the universities are such a big player, they may affect the way this alleged over patenting actually works out. With universities, we have this academic tradition of collaboration, sharing of information, publication. So, we might have some barring disclosures, such that patents can't be granted at all, or even defensive publication, where our university researchers may say, I don't want anybody patenting this, I don't want anybody having exclusive rights to it. Therefore, I am going to publish my information about it so that no one can patent it.

Then third, we could have third party. Standards Setting Organizations that we see in other industries that may help coordinate the nanotechnology, but also help cross-license it and share it and make sure people are collaborating with one another.

As I was thinking about this, I was sitting at my office, kind of free associating about how nanotechnology relates to patent world in particular. And I started to think about the pharmaceutical industry. Historically, the pharmaceutical industry has been very depended on patents, in part because drugs are considered just kind of monolithic or unitary invention and therefore you don't have to coordinate all these other patents in order to produce your pharmaceutical agent. But nanotechnology may change that, in part by bringing these new drug delivery systems that Dr. Orentlicher talked about and Dr. Varahramyan talked about and that in order to take advantage of these new drug delivery systems, you essentially have to combine them with your drug, with you pharmaceutical agent, that can't be separate the way, an intravenous needle and the drug that you actually inject through the needle could be separate. These actually but have to be bundled together and sold together and therefore, you may see the pharmaceutical industry having to license patents for probably the first time in it's life.

So, just a quick, I think, others have shown you pictures of this, but just a quick review of some of the differences in drug delivery that we may see in the pharmaceutical industry, these are nanoshells attacking a cancer cell and these little green things here are antibodies. This colorful thing here is what's called a liposome where you have basically fatty acids on the outside and then some sort of aqueous solution on the inside in which you can hide drugs, right, not from the airport, but in terms of the cancer cell that you are targeting.

And then these are micelles, this fussy guy here is a micelle which is basically a liposome turned inside out. So that the fatty acids are on the inside, then these are kind of hydrophilic extensions. Again, useful ways of introducing drugs into cells.

So, we may see more cross-licensing, more defensive patenting or maybe less aggressive enforcement of patents in the pharmaceutical industry. We could maybe see a chance to evergreen pharmaceutical patents simply by adding these drug delivery systems onto the drugs and then trying to re-patent them perhaps. And then this is kind of my conspiracy theory conjecture here, you might even see attempts by the pharmaceutical industry to stifle nanotechnology because it threatens their existing business, I don't know, I mean people make a lot of this kind of conjectures about the oil industry, you can take your guess as in the pharmaceutical industry.

Alright, trade secrecy and I will go through this quickly. Trade secrecy obviously attracted for nanotechnology in part because reverse engineering is difficult, but security is also difficult, again because of passive transfer and other things like that. In part because universities are such a big player in nanotechnology, we may see more collaboration, more publication and therefore, more difficulty in keeping nanotechnology a trade secret, and do we want trade secrecy in nanotechnology at all?

Well, generally trade secrecy is considered bad because you are not sharing the information in disclosure. Again, this field is kind of in its infancy, it's a cross-disciplinary field so trade secrecy might be difficult anyway and would certainly be harmful to further development of the field. Then again, in particular with biotechnology and medicine where there is a strong public interest obviously in open access to nanotechnology. And so, we need to look for ways to encourage patenting or better yet open licensing allowing this new nanotechnology.

Alright, I promise you, I will cover trademarks, nobody has thought the trademarks would apply to nanotechnology but they in fact do. To some extent nano is a very popular marketing device. Again, it's the urge to shrink, it's very sexy. And there has been a race to register trademarks that have a nano in their name somewhere. And the question is, as we actually have things that are of the nano size. Does the word nano become arbitrary? Right, the iPod nano is not nanometers in size, or does it become descriptive, when we actually talk about real nano particles.

And may be there is some question about truth and advertising and this is where you might see some of the moral concerns or social concerns about nanotechnology combing back to bite people. If you put nano in your name, people might be more likely to buy it or they might be less likely to buy it. We have seen a lot of this back actually in terms of organic foods, genetically modified foods, the frankenfood as Dr. Orentlicher mentioned.

Alright, so is the word nano a boon or burn? Well we will see that in trademarks. Especially in biotechnology and medicine because branding and trademarks are becoming increasingly frequent in those fields. And then finally copyright and I swear this is my last slide. It's difficult again to foresee how copyright might apply the nanotechnology, but you can use your imaginations and actually for those law students that are out in the audience, I challenge you to think of how to leverage Copyright Law in nanotechnology, your law firms will love you because you figured out new claims that you can make against other people under Copyright Law and not just Patent Law and Trade Secrecy.

Possibly with regard to software for nanotechnology we might have some copyright issues. We might have issues with regard to nanotechnological mask work, something similar to the Semiconductor Chip Protection Act. Which is more or less obsolete now because it's so difficult to reverse engineer semiconductor chips.

And then there are some possibility and this isn't related obviously to biotech and medicine that people will start using nanotechnology to protect their copyrighted works, kind of in lines of Digital Rights Management, but instead of having it on your machine on your computer or you VCR player, you will actually have it on the DVD itself, possibly. Thank you very much.