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## Discussion Following the Speech of Mr. Brosch and Mr. Johnson and Mr. Theofrastous

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## U.S. SPEAKER

*Theodore C. Theofrastous*<sup>†</sup>

With our technology, hopefully it will survive.

I am Ted Theofrastous with the Cleveland Clinic Foundation. Can I ask, are there any members of the press here? I wonder if there is a PLAIN DEALER person here. I will say in advance that I am not here to make official statements of policy for the Cleveland Clinic Foundation. These are my views, and, in part, the reason I say that, as we discussed the best way to prepare for this, I decided rather than focusing on coverage and reimbursement, which I think are the differences between our systems and are remarkable, I wanted to really focus on the aspect of the business of advancing and providing new health care to patients, which is a very hot topic right now, in part, because there is an emerging debate on conflicts of interest and what is the best way to manage conflicts of interest.<sup>1</sup> I think some of you have probably followed some of this debate in the NEW YORK TIMES.<sup>2</sup> Certainly, the PLAIN DEALER has been covering it as well.<sup>3</sup> Anybody who had any financial relationship to Vioxx, certainly their radar is probably up on this issue.

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<sup>1</sup> See John W. Jones, *Legal & Ethical Duties of Medical Researchers*, PHYSICIAN'S NEWS DIGEST, Sept. 2004, <http://www.physiciansnews.com/law/904jones.html> (discussing financial conflicts of interest in research, derived from financial relationships between the sponsors and investigators).

<sup>2</sup> See generally Reed Abelson, *Possible Conflicts for Doctors Are Seen on Medical Devices*, THE N.Y. TIMES, Sept. 22, 2005, at A1 (stating "hospital officials also argue that the constant introduction of new, and more expensive, models can have less to do with innovation than with the appearance of innovation.").

<sup>3</sup> See generally Sarah Treffinger, *Money and Medicine: Scientists Grapple with Expanding Role of Firms in Research* (Cleveland), THE PLAIN DEALER, Mar. 13, 2005, at G1 (explaining a 1999 case where a patient died participating in a gene therapy study and the incident resulted in agencies such as the U.S. General Accounting Office, the Association of American

And, essentially what I would propose is that our system of bringing new medicine to patients really is driven by, you know, three complementary and aligned sources of influence. One is industry. Obviously, the medical-products industry, and I guess you could generalize and say, as any industry, the focus there, or the driving factor, is going to be to make money, increase shareholder returns, et cetera.

Secondly is obviously medicine, and most, particularly academic medical centers, have, as part of their mission, the discovery, and frankly the delivery of newer and better treatments for the sick. But underlying this – and I don't know that this is as well understood as it might be – is federal policy – which, frankly, is a major difference between our systems– which is focused more on the quality of health care, than on the equality of that health care. You know, certainly the number of uninsured people in the United States really speaks to that issue. But to sort of maybe dramatize the issue – and I will try to give the court reporter a run for his money here – we have a scenario – and this would be just really one of really dozens – I work with a young researcher. He is a cardiologist, and he is also a stem cell researcher. And he has discovered that if you take an adult stem cell – we are not talking about fetal stem cells here – and you use an adenovirus, basically you transfect that cell with an adenovirus, you can cause it to express a gene, and the gene is called “Stromal-cell Derived Factor 1,” SDF 1, which is all a lot of gobbledegook until you realize what it actually does, what SDF 1 does with these cells. These things you can get from bone marrow or other parts of the body, it will actually cause that cell to migrate to your heart and attach itself to damaged heart tissue.<sup>4</sup> If you've suffered from congestive heart failure or you've had a myocardial infarction, you have got heart tissue that is damaged and may not be working properly, these stem cells will go and actually repair that tissue. It is an in-body, self-guided therapy that will go right where it is supposed to go. Now, you look at the alternatives, surgical alternatives, pharmaceutical therapies, there are lots of alternatives, but there is nothing that approaches the effectiveness of this.<sup>5</sup>

So the question is: How do you get that therapy? – and you can't read that little circle, I just now realized, that says, “Safer, more effective medical

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Medical Colleges and the Association of American Universities issuing reports on conflicts of interest).

<sup>4</sup> Cleveland Clinic Study Results, *Stem Cell Technology Shows Promise in Helping Hearts to Repair Themselves Weeks After Heart Attack, Heart Failure*, CLEVELAND CLINIC HEART CENTER, Sept. 9, 2004, available at [http://www.clevelandclinic.org/heartcenter/pub/news/archive/2003/stemcell9\\_09.asp](http://www.clevelandclinic.org/heartcenter/pub/news/archive/2003/stemcell9_09.asp).

<sup>5</sup> See generally Cleveland Clinic Study Results, *Innovative Treatments for Heart Failure*, CLEVELAND CLINIC HEART CENTER, available at <http://www.clevelandclinic.org/heartcenter/pub/heartfailure/ptcare.htm> (last visited Nov. 13, 2005) (discusses heart failure surgical strategies and alternative methods of treatment).

products.” How do you get that to the patient? It is right now sitting in a laboratory, and it has been tested on a few animals, but how do you actually turn that into a medical product; something in a bottle that your physician can take off the shelf and give to you as a treatment?

So walking through the three sorts of aspects of this, what I would like to show is that there are underlying things that we have on sort of the emerging debate between industry and medicine: The federal government is actually trying to drive these new products to market as quickly and as effectively as it can.<sup>6</sup> In that context, each of the sectors has really sort of its hot buttons that it is trying to monitor. One, obviously, on the medical side, in addition to delivering a therapy, is the concern that there will be a compromise on scientific and medical integrity,<sup>7</sup> and I will talk a little bit about each of these as we go forward. On the industry side, you know, this is very risky stuff, and it is also very high-yield opportunities. How do you balance the risk with the ultimate payoff, and how do you get ultimately rewarded for the leap you took with that product? And then on the federal side, there is a very strong counterbalancing emphasis on ensuring that patients are treated safely, and that the system of getting these new products to market is transparent.<sup>8</sup>

So talking, first, about the medical sector, I will run very quickly through a discussion of The Cleveland Clinic Foundation. In many ways, it is typical of a large academic medical center. In some other ways, it is a little bit, frankly, a little more progressive on some of these issues than some of its counterparts in the industry. It is a hospital that is well established – has been around for a long time.<sup>9</sup> It is huge. It generates about \$4 billion a year in patient revenues, and has inputs right now in about \$110 million in outside research funding.<sup>10</sup> Like, I think, any large medical center, it is also one of the

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<sup>6</sup> See Dixie Farley, *Benefit Vs. Risk: How FDA Approves New Drugs*, FDA CONSUMER SPECIAL REPORT ON NEW DRUG DEVELOPMENT IN THE UNITED STATES (2005), available at <http://www.fda.gov/fdac/special/newdrug/benefits.html> (stating “[b]efore any drug gets on the market today, FDA decides--as quickly as a thorough evaluation allows--whether the studies submitted by the drug’s sponsor (usually the manufacturer) show it to be safe and effective for its intended use.”).

<sup>7</sup> *Id.*

<sup>8</sup> U.S. Food and Drug Administration, FDA Mission Statement, <http://www.fda.gov/opacom/morechoices/mission.html> (last visited Nov. 13, 2005) [hereinafter FDA Mission Statement].

<sup>9</sup> The Cleveland Clinic Foundation, Facts and Figures, <http://cms.clevelandclinic.org/documents/clevelandclinicfactsheet.pdf> (last visited Nov. 13, 2005).

<sup>10</sup> See Diane Solov, *Leader Looking for His Replacement; But Loop Not Planning to Leave Job Soon*, THE PLAIN DEALER (Cleveland), Jan. 8, 2004, at A1 (stating 2003 operating revenues as \$3.4 billion); Cleveland Clinic Learner College of Medicine, Case Western Reserve University, <http://www.clevelandclinic.org/cclcm/research.htm> (last visited Nov. 13, 2005) (stating \$110 million in total grant revenue).

largest employers in Ohio.<sup>11</sup> I know it is, at least, the second largest employer in Northern Ohio,<sup>12</sup> and if you followed any of the Northeast Ohio economic debate, which is a very serious debate, I think many would view that between The Cleveland Clinic and Case Western Reserve and University Hospitals, that there is a basis for regrowing this economy, and that comes very much back to this concept that you have all this potential locked up inside the institution. So how do you ultimately get it out?

The mission of The Cleveland Clinic, it is almost like a fortune cookie. There is so much meaning wrapped up in each of those words, but essentially, the way I read this mission is, it is to advance health care, to foster ongoing research and education of the profession, and built into this also is this concept of moving innovation to market, moving new products to market – that is part of this economic stewardship role that is out there as well. But it really is sort of a fundamental concept of the clinic that whatever is on the bench, whatever is proven medically needs to get to the bedside, it is going to promote that. Internally, innovation is nothing new at this or any other hospital. It is just something to think about.

As you watch this debate, where did dialysis come from? Well, dialysis came from a very brave clinician experimenting with some very interesting ideas and having, frankly, a lot more regulatory latitude than one has now, to try to test that device.<sup>13</sup> But as you range into biotech and, frankly, really almost all science-fiction type innovation, each of these, there is a product that would ultimately be available to you as a patient, or at least to your children, as a patients.

Now, I think what many people don't realize is that at The Cleveland Clinic –and as you have at a lot of academic medical centers that aren't related directly to a university – there is a dedicated research function. At The Cleveland Clinic, the Lerner Research Institute, it was a \$100 million facility set up by Al Lerner, or at least his family, which has a very significant presence.<sup>14</sup> It is certainly not anywhere near the largest research institution around, but it has essentially about 140 – I think it says 132 here – laboratories that are working on various new ideas and new innovations,<sup>15</sup> and they

<sup>11</sup> Major Ohio Employers: Employers Ranked by Ohio Employment, <http://www.odod.state.oh.us/research/FILES/B10000002.pdf> (last visited Nov. 13, 2005).

<sup>12</sup> *Id.*

<sup>13</sup> See generally Davita, The History of Dialysis: Life, Death and a "Washing Machine," <http://www.davita.com/articles/dialysis/index.shtml?id=197> (last visited Nov. 13, 2005) (discussing Dr. Willem Kolff's invention of the first dialyzer.).

<sup>14</sup> The Cleveland Clinic, Lerner Research Institute, [http://www.clevelandclinic.org/tour/main.asp?site=Lerner\\_Research\\_Institute](http://www.clevelandclinic.org/tour/main.asp?site=Lerner_Research_Institute) (last visited Nov. 13, 2005).

<sup>15</sup> See Lerner Research Institute, Departments and Centers of Research, <http://www.lerner.ccf.org/research/> (last visited Nov. 13, 2005) (stating that the Lerner Re-

take a long time. The annual expenditures right now on research at the Cleveland Clinic are running about \$136 million.<sup>16</sup> But again, the expectation is that whatever is happening here is ultimately going to end up in the marketplace. I wouldn't talk about the specific functions, but it is essentially a very diverse laboratory function.

Now, the way that plays out inside of the institution is – this is an aerial shot of The Cleveland Clinic, which is pretty much this over to the trees there. That's pretty much all The Cleveland Clinic, which is a big part of midtown Cleveland. Inside The Clinic, there are a number of places where research is going on. What is – and this is not completely unique to Cleveland, but it is a strong point of emphasis – that there is a great deal of interaction between the research centers and the actual clinicians to create joint research centers,<sup>17</sup> so we would have a cell biology department, but we also have tie-ins between cell biology and their counterparts on the clinical side, sometimes having joint appointments and joint chairs.<sup>18</sup>

I should also note that a lot of state dollars – if you are familiar with Ohio, and every state has these – I was in Phoenix a couple weeks watching, or talking with some of the folks behind their system for economic development. There are a lot of public dollars nationally going into the creation of new medical technologies. Under the state's biotechnology and technology transfer program, which essentially is a method of distributing the tobacco settlement in Ohio,<sup>19</sup> large grants, 10 to 22, \$23 million grants have been given throughout the state to create new centers of innovation.<sup>20</sup> So, for instance, this is a rendering of the new Center for Stem Cell and Regenerative Medicine, which actually is nearly complete over on – I think it is on east ninety-sixth.<sup>21</sup> And from that will come, again, additional innovation.

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search Institute has 127 research laboratories).

<sup>16</sup> See Lerner Research Institute, <http://www.lri.ccf.org/> (last visited Nov. 13, 2005) (stating that annual research expenditures exceed \$150 million from Federal agencies, non-Federal societies and associations and endowment funds).

<sup>17</sup> See Lerner Research Institute, <http://www.lri.ccf.org/> (last visited Nov. 13, 2005) (“The Lerner Research Institute is an integrated research community consisting of nine Departments and 11 Centers of Research. LRI investigators work in basic, translational and clinical research.”).

<sup>18</sup> Lerner Research Institute, Dept. of Cell Biology, <http://www.lerner.ccf.org/cellbio/overview.php> (last visited Nov. 13, 2005).

<sup>19</sup> Ohio Office of Budget and Management, Ohio's Plan for Using the Tobacco Settlement Revenue, Mar. 6, 2000, <http://www.obm.ohio.gov/budget/tobacco/sb192.pdf> (last visited Nov. 13, 2005).

<sup>20</sup> See Press Release, The National Academies, The National Academies Evaluate Proposals for Ohio's Third Frontier Project (May 10, 2005), <http://www4.nationalacademies.org/news.nsf/isbn/05102005b?OpenDocument>.

<sup>21</sup> See Case Western Reserve University, *The Center for Stem Cell and Regenerative Medicine* (2004), <http://ora.ra.cwru.edu/stemcellcenter/>.

So flipping over to the federal side and looking at what the policies are there, essentially the federal government right now is spending north of \$30 billion a year in university research, and a lot of that is ending up on the life-scientist side.<sup>22</sup> Actually, I should say that \$32 billion captures some of the state funding that is going on.<sup>23</sup> So where does that funding actually play out? Well, if you look at the process, sort of a continuum of getting from an idea to a product you can actually purchase as a patient – and I will talk a little bit about why that’s not exactly what you do – most of the federal funding is lining up on the basic research end.<sup>24</sup> Essentially, there isn’t another funder for this.<sup>25</sup> If you didn’t have the federal funding there, much of this research would not happen because I can tell you, just as exciting as it is – and we can talk about this, sit down and talk about the expression of this gene to treat heart failure, and you would be very excited. You would want to know, if you were a patient, whether they had actually proven it was anywhere near the level of safety that you would need to try to get it into a clinical trial. And as a commercial player, you, frankly, would be sort of crazy to risk your funding there. So underlying behind this, the largest funder is the National Institutes of Health (NIH), which has been around since the 1890s.<sup>26</sup> Obviously, it was a much smaller organization then, but essentially underlying the mission of the NIH is this concept of fostering fundamental creative discoveries, improving and protecting health, and enhancing national economic wellbeing, while maintaining some sense of overall and academic scientific integrity.<sup>27</sup> There are actually twenty separate institutions within the NIH,<sup>28</sup> but each of them is a source of value and, frankly, sometimes the only, as I say, funding for early medical research. And given the time, I won’t spend a tremendous amount of time looking at teasing out their mission.

I think maybe the most important thing when talking about the NIH federally, is that there is annually a continued, let’s say, at least consistent, if not increased commitment, in support of the mission of the NIH. If you look on the right-hand side here, the NIH is sort of on the bottom end of the federal

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<sup>22</sup> See generally Meeting Report, *COGR Meeting Report 2004*, COUNCIL ON GOVERNMENTAL REL. (Nov. 9, 2004), <http://www.cogr.edu/docs/Oct04MeetingReport.doc>.

<sup>23</sup> See generally National Institutes of Health: Office of Extramural Research, *NIH Extramural Awards By State and Foreign Site* (June 23, 2005), <http://grants.nih.gov/grants/award/state/state.htm>.

<sup>24</sup> See generally National Institutes of Health, *Grants & Funding Opportunities* (Oct. 27, 2005), <http://grants1.nih.gov/grants/> [hereinafter *Grants & Funding Opportunities*].

<sup>25</sup> See generally National Institutes of Health, *The NIH Almanac* (Mar. 14, 2005), <http://www.nih.gov/about/almanac/about.htm>.

<sup>26</sup> *Grants & Funding Opportunities*, *supra*, note 24.

<sup>27</sup> See National Institutes of Health, *About NIH: Mission* (Sept. 16, 2005), <http://www.nih.gov/about/index.html#mission.htm>.

<sup>28</sup> See National Institutes of Health, *NIH Organization* (Sept. 16, 2005), <http://www.nih.gov/about/organization.htm>.

agencies that received increased funding over their previous year's budget, but they do receive previous funding virtually every year.<sup>29</sup> It is running about 2% on average; it is up around 5% right now. The other thing you will see, if you look back to the '70s, the spending has gone up significantly,<sup>30</sup> and again, the thought is that a major portion, about 53% of the \$28.8 billion budget, is going to end up in these laboratories driving innovation.<sup>31</sup>

So again, looking at the backdrop of this issue of conflicts, the nexus between industry and medicine, what's the problem? It is not really the problem, but what's the issue? Well, under the laws surrounding the distribution of federal funds, there was actually a revision of the Patent and Trademark Act in the mid '80s, which was put out by Bob Dole and Birch Bayh, and called the "Bayh-Dole Act," which has built into it this concept of promoting commercialization, again delivery of a product to market, and the public availability of inventions that are made in laboratories.<sup>32</sup> So you could very easily wonder if you are going to have billions of dollars spent, 14, \$15 billion on potentially hair brained ideas, even though that's virtually impossible given the level of rigor that goes into reviewing an NIH grant. What happens to it? Where does it go?

The Bayh-Dole Act says you have to take it to market and, in fact, as part of the deal, if you elect – it is within two years of a discovery – actually, the institution, and ultimately the individual who shows up as an inventor of this new technology has a stake now in the outcome. They actually have ownership of the new invention subject to, you know, nonexclusive rights of the federal government and, in fact, federally funded research.<sup>33</sup> Various programs actually can set you up as already having gone through the procurement process, so even the federal government might be willing to buy your invention. So they buy the invention from you that they paid you to create.<sup>34</sup>

What that means is that now you have a stake in the game. The institution has a stake in the game. The inventor, the researcher has a stake in the game. This is not the case in every circumstance, but it certainly is compounded for the Cleveland Clinic and most large academic medical centers that operate as charities under the U.S. tax law – they have an obligation to make sure that whatever they have by way of an asset, which an invention – which is ulti-

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<sup>29</sup> See generally *NIH Budget Barely Increases in 2006, Lags Inflation for the First Time Since Early '80s*, ADVANCING SCI. AND SERVING SOC'Y., (Mar. 4, 2005), available at <http://www.aaas.org/spp/rd/nih06p.pdf>.

<sup>30</sup> *Id.*

<sup>31</sup> *Id.*

<sup>32</sup> Bayh-Dole Act, 35 U.S.C. 200-212 (2005).

<sup>33</sup> *Id.*

<sup>34</sup> See *Technology Transfer: Agencies' Rights To Federally Sponsored Biomedical Inventions*, U.S. GEN. ACCT. OFF. (July 2003), available at <http://www.gao.gov/new.items/d03536.pdf>.



mately ending up in a patent application – is an asset, has to be exchanged only for some kind of demonstrably fair value.<sup>35</sup> The easiest context would be if a charity had your \$1000 that you had given it, they can't turn around and give that \$1000 to their favorite son just because they like him. You want to know that your charitable proceeds are being used responsibly. In this case, there is going to be this commercialization event. It has to be essentially for real money.

And where that ends up, if you look at the process, again of commercializing a new invention, is, there are any number of outcomes that a medical institution would hope to achieve. But all of them result in some kind of ongoing link, I guess, to the medical product. It is either going to go out through a license, through some formation of a new venture, perhaps a new company, or through a strategical alliance with whoever is going to take that product to market. That means that, as that medical product comes out the other end, you have this residual tieback again to the investigator and to the institution.

If we take a look at the industry perspective on this – and again, I will go quickly so we don't run out of time – obviously, there is an ongoing sort of general corporate debate in some sectors as to whether industry should have any eye on the concept of a greater good, or whether shareholder outcome is exactly why corporations exist. But, with that said, I think it is relatively certain that the medical industry is primarily motivated by trying to make money and get a return on their investigators' capital.<sup>36</sup> The creation of new medical products, which I think is intuitive, obviously creates or represents a vast potential, but it is matched with risk. And an extremely high level of capital that is needed, underlying this, though, is an emerging phenomena, and I won't say it is colliding, but it is lining up very functionally with this new source of technology coming out of institutions, which are the pipelines of large, particularly pharmaceutical, companies, which are drying up. It is not dire; there is not a crisis emerging, but where you might have had decades ago had a number of smaller or midsize pharmaceutical companies that had large R & D capacity and were essentially doing a lot of basic research themselves, through mergers and acquisitions, the consolidation of the industry, and frankly the availability of some of this technology, there is a greater reliance and a greater expectation that new medical products will, in fact, be coming out of these sectors.

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<sup>35</sup> See Press Release, Internal Revenue Service, IRS, Treasury Issue Notice Regarding Improper Deductions for Charitable Contributions of Patents and Other Intellectual Property (Dec. 22, 2003), <http://www.irs.gov/newsroom/article/0,,id=118864,00.html>.

<sup>36</sup> See generally Centers for Medicare & Medicaid Services, *Health Care Industry Market Update* (Oct. 10, 2002), [http://www.cms.hhs.gov/reports/hcimu/hcimu\\_10102002.pdf](http://www.cms.hhs.gov/reports/hcimu/hcimu_10102002.pdf).

In terms of the economic opportunity, the market is growing. This is sort of the small market. This is what I guess you would call “biotech on the esoteric end.” It is expected to be a \$14 billion market by the end of 2009<sup>37</sup> – but acknowledge that the medical device industry is about \$117 billion, which is a slightly more straight forward market, but anyway, these are opportunities that ultimately are the ones you want.

This is the concept of personalized medicine. This is the outcome of the human genome project, and if you think about it, the current state of – particularly in pharmaceutical technology – it is a little crude. And that’s no disrespect to any scientific centers. I am not a scientist, but if you think about it, you are creating a small molecule you ingest. It goes into your body. And it has to be designed in such a way that whatever positive effect it had on a part of your body, is not matched with some negative effect somewhere else in your body. It is flowing through your entire system being metabolized, and you are looking for one sort of uniform, widely acceptable outcome when, in fact, we are all different. Genetically, we are not all the same, and wouldn’t it be better if you could better identify exactly the therapy needed for you, the course of therapy, and the amount of the compound or drug that you are ingesting and, in fact, may be using some other modes of delivery, like the stem-cell technology I was talking about. So this is a great point of emphasis for industry right now, but it is relying upon federal funding to move it forward.<sup>38</sup>

The fence that has to be run over to bring a medical product to market is really significant, and this is where the countervailing federal priority comes in, in that as much as the federal government wants to move the technology quickly to market, it also wants to make sure it is done in a way that is safe and effective.<sup>39</sup> And so the process of developing a pharmaceutical is your worst case. It is a matter of at least ten years. The estimates are \$400 to \$500 million to produce a single drug.<sup>40</sup> Failure rates are huge. One to two percent of products that start at one end actually come out the other end, and then when they do come out the other end, who knows if it is actually going to be everything that you thought it was in the clinical trial? Again, I come back to Vioxx as certainly a disappointment for investors. The long and short of it is

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<sup>37</sup> See generally *US Medical Technology Industry Fact Sheet 2003*, ADVANCED MED. TECH. ASS’N (2005), available at [http://www.advamed.org/publicdocs/fact\\_sheet\\_2003.pdf](http://www.advamed.org/publicdocs/fact_sheet_2003.pdf).

<sup>38</sup> Ernie Hood, *Pharmacogenetics: The Focus on Personalized Medicine*, ENVTL. HEALTH PERSP. (Aug. 2003), available at <http://ehp.niehs.nih.gov/txg/members/2003/111-11/focus/111T11focus.pdf>.

<sup>39</sup> *FDA Mission Statement*, supra note 8.

<sup>40</sup> William S. Comanor, *The Pharmaceutical Research and Development Process, and its Costs* (1999), available at <http://www.accessmedmsf.org/prod/publications.asp?scntid=4920012352125&contenttype=P> ARA&.

that through this process, there is by necessity, as much as that initial technology came out of the institution, there is going to be a need to go back to the institution frankly to get you through.

If you move down the spectrum here to preclinical and the FDA's research, this is actually where industry will start applying its funds, to move the research forward so it is going to develop a relationship with that investigator, whoever the primary investigator was. They are going to want to see a sufficiently strong intellectual property position to move forward. They are going to want to see basically that you, as the institution, have that vested interest that ultimately comes out of federal policy. And, in order to do this, there are other facets of federal law that ultimately sort of tighten up this relationship even further. One thing – this is not a huge point of emphasis but comes up all the time – which is in order to sponsor research, in order to basically apply funding at this point or, as you get further down, most sponsored research is conducted in tax-exempt, bond finance facilities.<sup>41</sup> And if you think about it, if you are going to put together a \$250 million facility, are you going to go and borrow money from the market? And if you are, which you probably would, if you could, you would do a tax exempt bond offering.

The attractiveness as an investment for a well-rated institution is huge, and you can raise a lot of money. So the challenge is that that now has to fall under your sort of overall charitable purpose. Unfortunately, the IRS, which is opaque on virtually every issue, is extremely clear on this issue, that you essentially can't give the technology to the sponsor. You can't contractually say, "Thanks for the million dollars and sponsored research, and by the way, you can have whatever we discover." You have to have a separate negotiation. There has to be a separate *quid pro quo*,<sup>42</sup> and ultimately, again, your vested interest in the outcome, as the institution, is even tighter than it might otherwise have been.

As you get into clinical studies, which is – I will just say it is complicated. It is overviewed extensively by the Food and Drug Administration and takes a long time and is very expensive.<sup>43</sup> Again, what I would point out, the FDA views itself as primarily a consumer protection unit. The reality is here that this is where the government seeks to impose that countervailing principle of safety for humans.<sup>44</sup> I will just sort of go through this. The way it does that is through institutional review boards inside the institution. Every academic

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<sup>41</sup> Iain Cockburn & Rebecca Henderson, *Public-Private Interaction in Pharmaceutical Research*, 93 PROC. OF THE NAT'L ACAD. OF SCI. 12725, 12725 (1996) (discussing the importance of public institutions in pharmaceutical research), available at <http://www.pnas.org/cgi/content/full/93/23/12725>.

<sup>42</sup> Rev. Proc. 97-14, 1997-5 I.R.B. 20.

<sup>43</sup> Food and Drug Administration Home Page, <http://www.fda.gov> (last visited Nov. 11, 2005).

<sup>44</sup> *FDA Mission Statement*, *supra* note 8.

medical center has one. They have to interface with the FDA, and ultimately, if you think about it, how could the FDA monitor every single clinical trial? They rely on the culture and the expertise of the hospital to select patients and to inform the FDA if there are any problems.<sup>45</sup>

There are other legal parameters built into this, and essentially, the closer you get to market, the more law that is involved. HIPPA (Health Insurance Portability and Accountability Act),<sup>46</sup> which is essentially the privacy act for patients, plays into clinical trials. It is something that has to be very carefully monitored. And, what has essentially come out of the debate, and frankly, it is a little bit of a recursive process – this emerging dialogue on conflicts of interest. Essentially, the question is, if the institution has this financial interest in a medical product, or if the investigator, who by necessity is going to be conducting that research, has a financial interest, how do you know that the data is right? How do you know that that interest isn't tainting the evaluation of the product that is going to be delivered to market?

The initial steps that have gone in this direction have been essentially to take more of an IRB (Independent Research Board) approach, the institution review board, and set up separate groups within the hospitals to review the potential conflict.<sup>47</sup> There is a strong presumption against the conflict or against proceeding with research if there is a conflict. But essentially, the onus is on the institution to say that there is some compelling circumstance that requires this person or institution with the conflict to proceed with the trial anyway, and to actually manage that conflict.<sup>48</sup>

Again, this is a sort of growing national debate. The reality is – notwithstanding actually pretty clear guidelines from the American Association of Medical Colleges (AAMC)<sup>49</sup> and some new rulemaking by the Department of Health and Human Services,<sup>50</sup> and actually some very draconian measures recently implemented by the NIH.<sup>51</sup> The general view is that it is not working as well as it could. There is no huge consistency across institutions as to how

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<sup>45</sup> See Guidance for Institutional Review Boards and Clinical Investigation, <http://www.fda.gov/oc/ohrt/irbs/default.htm> (last visited Nov. 11, 2005) [hereinafter Guidance for Institutional Review Boards].

<sup>46</sup> Health Insurance Portability and Accountability Act, Pub. L. No. 104-191, 110 Stat. 1936 (1996).

<sup>47</sup> See Guidance for Institutional Review Boards, *supra* note 45.

<sup>48</sup> See *Id.*

<sup>49</sup> Robert Levine, M.D., Professor of Medicine, Yale University School of Medicine and Chairperson, Institutional Review Board, Yale-New Haven Medical Center, Statement on Institutional Review Boards (June 11, 1998), available at <http://www.aamc.org/advocacy/library/research/testimony/1998/061198.htm>.

<sup>50</sup> Institutional Review Boards; Registration Requirements, 69 Fed. Reg. 128 (June 6, 2004) (to be codified at 21 C.F.R. pt. 56).

<sup>51</sup> Sheet 12 NIH Institutional Review Board Administrative Procedures, <http://www.nihtraining.com/ohsr/site/info/sheet12.html> (last visited Nov. 12, 2005).

it is being handled. I can tell you, having gone through the process of implementing some of this, you kind of make it up as you go along relative to the rules. You want to come up with something that is compliant with the rules, but also works within your own culture. And I guess the point I would make here is, though, if you read the AAMC guidelines, you would think that the real issue is on the clinical side, but the reality is, it is pretty much throughout the entire research process.

I have been told I am out of time, so I guess I will tip my hat to the fact that once you are in commercial sales, there is actually a tremendous amount of regulation relegated to trying to mitigate some of these issues. There is an antikickback statute.<sup>52</sup> There is the Stark Law, which prohibits self-referral,<sup>53</sup> which if you can imagine, if you had a huge interest in a medical product and you are prescribing it to patients at anything other than some fair basis, that's not going to look right, and that the industry itself is providing some level of policing through industry groups like AdvaMed,<sup>54</sup> which are essentially trying to police the interaction between a very active and aggressive sales force, and clinician researchers.<sup>55</sup>

Just to close, though, I will say, notwithstanding the amount of law and the amount of real attention that goes into this, it is still an emerging debate. This is a new story that came out on March 31st. This essentially is an action against the Justice Department, against the entire orthopedics industry looking into their consulting relationships with clinicians.<sup>56</sup> None of us know how this is going to come out. This is yet another variation on a theme.

So to wrap up, I guess what I would say is while the debate continues, I think it is important that those engaged in the debate think about, you know, the necessity of these aligned interests and also acknowledge that underlying the entire issue in my mind is ultimately our own federal policy to fund and promote this research and to engage institutions and researchers in a way that gives them this long-term interest, and ultimately, the solution is going to have to be one that all three sectors of this alliance weigh in on.

(Applause.)

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<sup>52</sup> Medicare and Medicaid Patient Protection Act of 1987, 42 U.S.C. § 1320a-7b (2000).

<sup>53</sup> Limitation on Certain Physician Referrals, 42 U.S.C.A. § 1395nn (2003).

<sup>54</sup> AdvaMed, <http://www.advamed.org> (last visited Nov. 13, 2005).

<sup>55</sup> See *Id.*

<sup>56</sup> Barnaby J. Feder, *Subpoenas Seek Data on Orthopedics Makers' Ties to Surgeons*, N.Y. TIMES, Mar. 31, 2005, at C12.