

Regulatory and Liability Considerations

Moderator: Prof. Michael Baram

Panelists:

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Michael Baram:

You can tell from remarks by prior speakers that regulatory approvals and liability prevention are of critical importance to progress in biomaterials. Gene therapy trials and the tragic outcomes of some of those trials have raised the specter of government suspension of clinical studies, termination of funding, and potential liability for personal injury under malpractice or products liability doctrines. Regulatory requirements and the terms of research grants and contracts have to be very carefully addressed by organizations testing, developing, making, selling and using biomaterials, biotechnology, and medical devices. However, many regulatory requirements are incomplete, ambiguous and confusing because the agencies have not fully formulated coherent regulatory policies and coordinated procedures. Nevertheless, today we are going to do our best to learn what needs to be done to satisfy regulators and, later, to determine how to best address the threat posed by liability as exemplified by recent Dow silicon breast implant litigation [\[1\]](#) and *DuPont* “TMJ Implants” litigation. [\[2\]](#)

Thus, it is my pleasure now to turn this event over to our panel. We begin with Ellen Flannery, a partner with the Washington, D.C. law firm of Covington and Burling, who specializes in drug and device regulation, products liability and Medicare law. Ellen has written several journal articles and taught food and drug law at Boston University School of Law and University of Virginia Law School. She now chairs the ABA’s Coordinating Group on Bioethics and the Law, and graduated with honors from Mount Holyoke, and Boston University School of Law where Ellen served as Editor-in-Chief of the Boston University *Law Review*.

Ellen Flannery, Esq.:

When I started at Covington & Burling in 1979, I volunteered to do medical device work. There was no big rush of lawyers wanting to do medical device work because there was not much to do. The devices were fairly simple and the area was deemed to be not nearly as exciting as pharmaceutical law or even food law. But in the past twenty years, I have found that I am now in the midst of a very exciting practice in medical devices. There have been so many changes – in not only biomaterials but also computer software, expert systems, artificial intelligence systems that can read Pap smears, and so many other kinds of products. I am really pleased that I decided to become a part of that practice. Now my colleagues are really quite jealous, I think.

I have been asked to cover some of the Food and Drug Administration (“FDA”) approval requirements with you today. I have been asked to do in fifteen minutes what I usually spend either a semester doing or at least three hours doing in other kinds of courses, so this survey is going to be condensed. You will also notice as I go through the requirements that it would not be sufficient to talk about just medical device regulatory requirements. There are now many combination products, and it is important for people in this area to have some understanding of those other regulatory requirements.

With regard to the FDA approval requirements, no matter what kind of product you have that is regulated by the FDA, there will have to be some sort of testing. The type of testing will depend upon the level of regulatory scrutiny for premarket approval that the FDA will apply to your product. Usually, for medical devices, there will be some sort of laboratory testing and bench testing. Both *in vitro* tests and animal studies will need to be done. In animal studies, for example, the FDA regulates good laboratory practices (“GLP”). It is important to note that there

are FDA guidelines for various kinds of testing. Some of these are called “guidance documents” and some are called “points to consider documents.” There are also international guidelines that are becoming increasingly more important. The FDA is trying to harmonize its regulatory requirements with those of other nations, particularly European nations.

There are a number of international guidelines, one of which covers biocompatibility testing. When you have human contact materials you have to pay attention to biocompatibility testing. One of the participants this morning mentioned an FDA approved list of biomaterials. [3] The FDA was trying to come up with a list of biomaterials that, when put into a medical device, the manufacturers would not have to reprove, through animal testing or other means, the safety of that product material for human contact. The FDA has been slow in developing that list, in part because some of the information is proprietary to companies who have done that testing already. Those companies do not want disclosure of the material they use or their testing data.

After you get through some of those testing levels, you then must perform clinical testing. Someone else today mentioned that medical device regulation traditionally was deemed to be a shorter and easier route to market than regulation as a pharmaceutical product or a biological product. [4] To some extent that is true, but to some extent it is not. The FDA has user fees that pharmaceutical manufacturers pay to have their marketing applications reviewed. For pharmaceutical and biological products, once you get beyond the animal testing and clinical testing, the FDA approval process itself goes faster than the approval process for a medical device.

While it is not always apparent, especially for combination products, you should try to determine the FDA’s classification of your product early on. This is important because you have to decide which route to clinical testing you are going to take. To do human testing, there needs to be institutional review board (“IRB”) approval [5] and informed consent. Usually FDA approval of either an investigational new drug exemption, called an “IND” (for drugs or biologics), or an investigational device exemption, called an “IDE” (for medical devices) is needed. [6] Thus, you have to decide which path you are going to be taking before you are ready to begin clinical studies.

If you have a medical device, there is a variation on the IDE requirement. When a medical device is deemed to be a “non-significant risk” device, then you can proceed with clinical studies under what is called an abbreviated IDE. You get IRB approval and informed consent, but you do not need FDA approval of an IDE. Thus, you do not have to go through an FDA approval process to begin the clinical studies. This exemption is very significant. For example, in just the past two months, I have gone into the FDA with three different medical device clients. The FDA had held up their request to go forward with clinical studies, between six months to a year, with concerns about the protocol, the power of the studies, and various other issues. If you have a non-significant risk device (an “NSR” device), it is important to know that so that the FDA will not delay your clinical studies within the IDE approval process.

With regard to devices, the FDA also authorizes feasibility studies. If there is a brand new device that the FDA does not have much experience with, the agency often will want a small pilot study, fewer than ten patients, for example, so that they can figure out the risks and the problems before allowing a larger study. For example, I had one client preparing to announce that it was going to get approval of its IDE, but the FDA said, “we’re only going to give you a feasibility study, with ten patients, and one clinical site.” You can imagine what that did to the investors and to the people working on the product.

Once the clinical testing is finished, you then need to submit your marketing application for approval. For medical devices, the easiest way to get into the market is through what is called a 510(k) notification, submitted under Section 510(k) of the Federal Food, Drug, and Cosmetic Act (“FDCA”). [7] You need to show that your device is substantially equivalent to a device already on the market. To be substantially equivalent, the device has to have either the same intended use as another device and use the same technology, or the same intended use and a different technology but only if that different technology does not raise new questions of safety and effectiveness.

Now, the key to 510(k) notification is the “same intended use” language, and while you may think you have the same intended use, you may not. For example, one product may be used for gynecological purposes, but if you try to label another product for the treatment of abnormal uterine bleeding, that is going to be a new intended use, and FDA can find your product not substantially equivalent. When there are differences in technology, for example if you tried to move from one type of energy source to a different kind of energy source, like to a laser source, then

you can have a new product that could not go through the 510(k) process. The 510(k) process is for class I or class II devices, class I and II devices being the least risky. The FDA recently has been granting 510(k) exemptions for most of the class I devices, but some were what is called “held back,” and still need 510(k)’s.

For class III devices, which include implants or life sustaining products, to get pre-market approval (“PMA”) you must prove the safety and effectiveness of the product and its clinical utility. [8] Thus, it would not be enough to say a device can detect uterine contractions. You must say the device can detect uterine contractions and therefore has some use in pre-term labor, such as preventing premature births or preventing some sort of problem with the fetus. That clinical utility requirement has been a very controversial application of the “effectiveness” standard by the FDA.

Sometimes, the FDA will also designate a device a “restricted device” under Section 520(e) of the FDCA. [9] Then, in addition to approval under either a 510(k) notification or a PMA, the FDA will restrict the device under 520 (e) by restricting its sale, distribution, or use. The FDA will impose specific requirements for a product, like use of the device only in certain kinds of medical settings, or requiring training before the device can be used. The specifically imposed requirements under a “restricted device” designation become significant for some product liability and preemption issues, which I will mention a little later.

A pharmaceutical product (drug) must go through a new drug application (“NDA”) process to prove the product’s safety and effectiveness for its intended use. Biological products are regulated under the Public Health Service Act and need a biologics license application (“BLA”). [10] The BLA process used to be a two-part process of an establishment license application (“ELA”) and a product license application (“PLA”), but these have been combined into one, which is the BLA. In a BLA application, you need to show the safety, purity, and potency of the product.

I mention all these approval requirements because there are now a number of combination products. For example, there can be a situation where a device is combined with a drug product or with a licensed biological product. The combination raises the question of whether the FDA will regulate a combination product as a drug, device, biologic, or some combination thereof. You could end up with two different processes for regulatory approval. An example of a combination would be a medical device or a tissue graft that incorporates an anti-microbial agent. Or, you might have an intravenous filter that incorporates a clot-busting agent, so that the filter may be working physically, but there is a drug component that will have some sort of chemical action. If the primary intended purpose is to serve the device purpose, for example a hip implant that is primarily to serve a device purpose, but the product may have an accompanying anti-microbial agent, then it is likely that the FDA will regulate the combination as a device so long as the anti-microbial drug is already approved. However, if you try to incorporate an unapproved drug or biologic into a device, the drug or biologic must first be approved by the FDA, and you will have two sets of regulatory requirements to meet. You would have to prove the safety and the effectiveness of both the drug and the device.

Another set of rules applies to tissue products under FDA regulations at 21 C.F.R. Part 1270. [11] If your product is indeed a tissue product, that is probably the best news, because you do not need premarket approval to market a true tissue product. There are regulatory requirements that are aimed at donor suitability and preventing the transmission of infectious diseases. However, for various kinds of tissues, such as fascia, so long as it was not substantially processed it would not be a medical device product and it would not need a BLA as a biological product.

The expedited review of premarket applications is important because you want to get many of these biotech products in the marketplace as quickly as possible. There are various expedited review procedures. For devices, there is an FDA guidance document from 1998 that allows for expedited review of devices to treat life-threatening or irreversibly debilitating illnesses, if, in addition to having that purpose, the product is a breakthrough technology, or there is no approved alternative, or it has a significant advantage over existing alternatives. [12] There is also a fast track development and review process for drugs and biologics that are intended to treat a serious or life-threatening condition. [13] This can also be of assistance, and usually the FDA will give you some expedited review and assistance during the clinical studies phase, as well as during the marketing application phase.

When dealing with orphan drugs and biological products, there is the Orphan Drug Act, which may allow expedited review, grants, tax incentives, and seven years of market exclusivity for the first product to treat an orphan

indication that gets approved by the FDA. [14] An orphan indication is one where the incidence of a disease or condition is fewer than 200,000 persons in the United States with that condition. On the device side, there is a humanitarian device exemption, which applies to the marketing of products to treat diseases or conditions that occur in fewer than 4,000 people in the United States. [15]

That is a summary of the regulatory landscape. How do you determine, particularly if you have a combination product, how your product will be regulated? First, you could try to figure it out yourself. As a second possibility, the FDA has three Intercenter Agreements, which it published in 1991. [16] There is one between the Center for Devices and the Center for Biologics, a second one between the Center for Devices and the Center for Drugs, and a third one between the Center for Drugs and the Center for Biologics. [17] The FDA entered into these agreements because the agency recognized that there were breakthroughs in biotechnology, for example the use of monoclonal antibodies in cellular-based products for therapeutic purposes. These agreements set forth some general principles as to when the FDA will regulate something as a drug, or as a biologic, or as a device. The FDA also tried to provide some concrete product examples. Take, for example, a product that might consist of an immunoglobulin within a syringe. That will be a biologic product because the regulatory path follows the licensed biological product. The Center for Biologics regulates, as either biologics or devices depending on their mode of action, devices used for collection or processing of cellular biologicals, tissue implants, and bone marrow. There is also a document that the FDA issued in 1998, which lists, for tissue products, which will be regulated by the Center for Biologics and which will be regulated by the Center for Devices. [18]

If you cannot figure it out yourself, or you do not want to take the risk that you start down the wrong path, as a second possibility you can submit a request for designation to the FDA, where you say “this is the product I want to market,” describe the product, and explain what it does. Do not ask the FDA, “What am I?” Tell them “I think I am going to have a product that is a device,” or whatever you want that product to be, and then argue your case for why the product should be that. These requests for designation are submitted under 21 C.F.R. Part 3, and they are often used for combination products. [19] Then you meet with the FDA, and the agency will give you the FDA’s formal position on how your product will be regulated.

The last thing I was asked to address was medical device preemption and the *Medtronic v. Lohr* case. [20] So, let me briefly turn to that. For medical devices, but not for drugs or biological products or foods, Section 521 of the FDCA contains an express preemption provision applicable to medical devices. [21] It says no state “may establish or continue in effect with respect to a device . . . any requirement” – that’s the key word – “which is different from, or in addition to, any requirement applicable under this [Act] to the device . . .” [22]

The question of what a “requirement” is has been a tricky one for the medical device industry. Certainly, a specific statute or a specific regulation enacted by a state would be a specific requirement. The FDA has regulations in 21 C.F.R. Part 808 that address some of these requirements. [23] In *Cipollone v. Liggett*, the Supreme Court said that common law claims brought in product liability actions can also impose a requirement on the manufacturer of a product. [24] Following that case, a number of device manufacturers raised as a defense to product liability lawsuits the FDCA’s preemption clause and claimed they could not be sued by injured plaintiffs in product liability cases because such claims would impose an additional requirement in addition to the FDA regulatory requirements.

In *Medtronic v. Lohr*, the Supreme Court held that indeed a state common law requirement could be a requirement that is preempted under the FDCA. [25] But, if the product is cleared through the 510(k) notification process, where all you do is show the device is substantially equivalent to some other product on the market, that is not a sufficiently specific requirement, and so devices cleared under that process get no preemption of liability claims. The case left open the question of whether approval of a device under the pre-market approval process (the PMA process) might be a specific requirement for preemption of liability claims.

The lower courts have been split on that issue. I will note that a federal district court in Massachusetts, this past October, found no preemption by a PMA in a case involving injectible collagen products. [26] The court said the PMA process, even though it requires proof of safety and effectiveness and FDA approval of labeling, was not a sufficiently specific requirement on the product.

The FDA proposed a rule in 1997 that would have said specifically that a 510(k) notification, PMA, or IDE would not itself preempt state common law requirements. [27] However, there were some procedural irregularities,

including the fact that the FDA released that proposal to the Public Citizen Health Research Group before putting it out for public comment. The FDA also did not tell Congress it was considering this proposed rule while talking to Members about product liability issues in negotiations prior to enactment the FDA Modernization Act (“FDAMA”). [28] So, the FDA withdrew that rule in 1998. [29] But it likely could come back again at some point in the future.

That concludes my overview of the FDA regulatory requirements. I would be happy to take questions later.

Michael Baram:

Thank you, Ellen, for illuminating the universe of regulatory issues. Our next speaker is Ms. Patricia Davis, senior patent counsel for Boston Scientific Corporation. At Boston Scientific, she is responsible for patent prosecution, licensing, and litigation concerning BSC’s intellectual property. She has also been leading her firm’s effort to prevent unregulated use of single use and disposable devices. Before joining BSC, Patty was a patent agent, and then a design engineer for the Digital Equipment Company. She graduated from Northeastern University with an electrical engineering background, like so many of our speakers today who have integrated their scientific and legal backgrounds, and then received her law degree from Suffolk University Law School. She has published on the topic of biomedical device misuse, and virtually every article I have read on the misuse of medical devices over the last year or so has discussed her work and views.

Patricia Davis, Esq.:

Thank you for having me here today. I’m going to talk about the topic of device reuse. As you may know, some devices are reusable and then some devices are single-use. Single-use devices were developed because hospitals and doctors asked for them. Plastics developed to a point where we could develop cheaper devices that were not meant to be reused, but instead could be thrown away. Single-use medical devices prevent disease transmission, and we are moving towards minimally invasive therapy, where instead of some open heart procedure, for example, a surgeon will perform the technique through an incision. That is how and why single-use devices were created: angioplasty catheters, biopsy forceps that are seven feet long, and electrophysiology catheters - these are the kinds of plastic devices that are meant to be thrown away. At least, device manufacturers believe they should be thrown away.

Hospitals have been reprocessing devices for years. Most of these devices are reusable devices, and were approved by the FDA as reusable devices. They were meant to be cleaned and used on another patient. Hospitals have also reprocessed open, but unused, single-use devices. A nurse prepares a surgery center for a surgical procedure so that when the doctor walks in, the devices are already out of their packages and laying on a sterile field. The nurse has to guess as to which devices the doctor is most likely going to use. Sometimes the doctor doesn’t use them all. These devices are not fatigued, but they are contaminated, as the sterile barrier has been breached. A huge number of devices in a hospital are re-sterilized, but re-sterilization is not the issue I’m talking about. I am going to talk about circumstances when those single-use devices are actually used on one patient, reprocessed, and then used on another. My company does not believe this practice should be happening with respect to single use devices.

Why does reprocessing happen? Cost containment is one reason. Hospitals are under an enormous amount of pressure to reduce all of their costs. They should be looking at everything to keep costs down. We are not completely against the reprocessing and reuse of single-use devices. There probably are some single-use devices that should be labeled “reusable.” Those devices can be cleaned, sterilized, and reused in a way that is safe for patients. To ensure that these devices are safe, we want to make sure that the reprocessing is FDA approved. Right now, the FDA is looking the other way.

A whole new industry has cropped up in a business called “third party reprocessing.” Third party reproducers are convincing hospitals that they have the technology to clean and reprocess very complex medical devices. For example, take angioplasty catheters, which are long, thin devices. The lumens, the holes in them, are less than a millimeter in diameter. The lumens cannot be scrubbed to remove the blood that gets in them. Reprocessors, however, want to use them on multiple patients. It is an easy business to start, in part because there are very low regulatory costs. Also, reproducers do not have Research & Development costs because the device was designed by an original equipment manufacturer (“OEM”). They have very little overhead, so reproducers are starting up

everyday. I can actually say everyday because this morning I found out about two new ones; one in Florida and the other in Connecticut. There are reprocessing devices are all over the country, including here in Boston.

With respect to the OEM's bottom line, reprocessing has actually made a very small economic impact at this point because in most cases, hospitals do not reprocess open and used devices. But the practice is growing and the number of reprocessing companies is growing. For startup biomedical device companies, I was told by some people here from startup companies that reprocessing can be very problematic because it may take years to get FDA approval and finally enter the market. However, all existing financial models are blown when a reprocessor appears and allows a hospital to reuse a device several times over. This was not what manufacturers told their venture capitalists would happen. These are some of the economic issues.

There are many issues in this area. There are patient-safety, disease, and functional failure problems; there are ethical issues with informed consent. There are regulatory issues, liability issues, patent infringement issues, and potential reimbursement issues. Some people have raised the issue of whether they are defrauding the patient, which remains an open question. We know that hospitals charge the same amount of money no matter which device is used; reprocessed or new. Somewhere there is some extra money, and there remains a question about how that extra money is used. I am going to focus today on the liability and regulatory issues.

With regard to liability, under the tort law doctrine of joint and several liability, if a patient is injured, multiple parties are going to be sued. The reprocessor, the OEM, the doctor, and the hospital are each going to be sued. The patient can stand back and let the defendants fight it out. That is the simplest route for an injured plaintiff. Some reproprocessors are larger than others and they are offering indemnification for hospitals. However, the indemnification agreements we have looked at are worded very well from the reproprocessors standpoint.

BSC has tried to get hospitals to concentrate on the language and seek lawyers' advice, because when you really read the indemnification agreements, they only cover the reprocessor's own negligence. If the reprocessor does not properly carry out its own procedures then it might be held liable. However, if they carry their procedures out the way they told the hospital they would, whether the procedures are sufficient or not, the reprocessor may not be held negligent. The indemnification agreements do not cover the hospital or doctor's negligence. Doctors today are commonly independent, non-employees of the hospital, and as such they are not going to have privity of contract that exists between the reprocessor and the hospital. The indemnification agreements do not cover settlement agreements, but if a patient is hurt, often a hospital is going to want to settle the claim immediately before it goes public, because these claims are publicity nightmares. The agreements also often include the terms "indemnify" or "defend," so if the reproprocessors choose to wait and indemnify the hospital later, they will not cover the hospital's up front attorney's fees or discovery costs, which are expensive. Further, the agreements will also not cover punitive damages. In a case where a patient is injured, this clause gives no economic benefit to the hospital, where punitive damages might be very high. The reprocessor obviously cannot compensate a hospital for injury to its reputation.

A hospital and doctor may be found negligent for failure to use reasonable care. Why is that going to be an issue? First, the FDA has not approved the device for this use. It is not an off-label use. An off-label use occurs when a doctor needs to take a device and use it in a way that is not FDA approved. But the reason doctors are doing off-label uses is for the benefit of the patient. For example, if you have a pediatric patient and you do not have a device that works for that patient, you can take a tube from something else that you know will fit down their throat. That is off-label use. However, you can see that the doctor is doing that purely for the benefit of the patient; this kind of use is allowed by the FDA. When a use is not off-label, there is an increased risk to the patient that it is against the manufacturer's warnings. There is a lack of studies proving that it is safe. Reuse of single-use medical devices, therefore, is not off-label because there is no benefit to the patient. The alternative is to use a new device. The negligence concern about reasonable care for a hospital and a doctor is serious.

I also think that doctors are the most vulnerable to liability because they are termed the "learned intermediaries."

OEMs are required to file with each package and each device instructions for the device's use. In those instructions are warnings, contradictions, and everything the FDA requires to be included. Because we do not talk to the patients directly, the doctor is the learned intermediary. The doctor is required to pass on the necessary warnings, and the doctors choose which ones they are going to pass on. The doctors also may be negligent for failure to obtain informed consent. To our knowledge, hospitals are not obtaining informed consent. They are making the judgment that a reprocessed device is as safe as a new one, and based on that decision they do not get informed consent from the patient. A doctor may also be found negligent for failure to diagnose and treat injuries caused by a reprocessed device. Thus, if a reprocessed device were to fail or cause injury and a doctor did not diagnose and treat the situation quickly enough, hospitals could also be found liable because of that activity. The reprocessor will most likely be treated as a manufacturer, so they will have strict liability concerns and negligent failure to warn problems because they do not include the instructions for use as required by the FDA.

OEMs will, of course, be sued, since they are the deep pockets. The reproducers are companies, but they are little companies. They will raise the defense of known misuse. Under the doctrine of known misuse, if a manufacturer knows its product is going to be misused in a certain way, it must take all reasonable steps to make it as safe for that use as possible. Reprocessors are going to argue, of course, that they took all reasonable steps. They will argue that they have educated doctors about the use of their product, gone to the FDA, and gone to Congress. They will argue that they have done what they can to prevent the reuse of these devices. A lawsuit will determine what is going to happen, but I can tell you that this topic is one of the top three issues that the American Trial Lawyers Association's annual meeting this year will address. I think we will have an answer soon.

The last issue with regard to liability is that the reproducers do not remove the OEM's name from the products. When a device fails and injures a person, the OEMs are the ones that get called and told the device hurt somebody. Even if they are later proven not liable for an injury, nothing can make up for the injury to their reputation and our goodwill. People will remember that it was a Boston Scientific device that ruptured in a patient's heart and killed a patient, and they will forget the fact that someone reprocessed the device. The long term damage to reputation is a concern to BSC.

What is the FDA doing? You just heard about the enormous burdens that people have to go through to get FDA approval for devices, which is what my company does. When I first heard about reprocessing, my first response was that this could not be possible - someone should tell the FDA. Unfortunately, it is very possible. They have been aware of the practice since at least 1996, when their own task force discovered injuries. Their response has been disappointing. Let me quickly discuss what is going on with the FDA.

Right now, the current regulation in place today is inequitable. We have asked the FDA for permission to reprocess our own devices by bringing them back from a hospital, reprocessing it, and sending them back to the hospital. The FDA has responded in the negative, requiring a 510(k) and a PMA to be filed. It depends on the device - you have to file pre-market notification. Our response was that companies in the market are currently in the reprocessing business. The FDA has responded that they are exercising their enforcement discretion, and will not require them to file a 510(k) or PMA. In response, we have asked whether it was acceptable if we bought the reprocessor. Their final response was that if this purchase were to take place, they would still require a 510(k) and a PMA to be filed. This response does not make sense logically, legally, or in terms of patient safety.

We have been fighting with the FDA for more than four years, simply to get them to enforce the current law, mainly the Federal Food, Drug, and Cosmetic Act. [30] That is all we are asking the FDA to do. There were enough manufacturers who were separately working on the same issue through lobbyists that we started seeing each other at regular meetings. We realized that we should combine forces, because you are allowed to work with your competitors to lobby government. We even formed a trade association about a year and a half ago called the Association of Disposable Device Manufacturers ("ADAM"). We have to be very careful at our meetings. We currently lobby the FDA and Congress.

We have sent data to the FDA. Boston Scientific has done many studies, and at least six times has gone into hospitals and removed reprocessed equipment, such as a biopsy forceps. The forceps is normally about seven feet long, and it will go into your throat, your stomach, or in your colon to take a sample to determine if a patient has cancer. We took devices off hospital shelves that had been reprocessed. In exchange for these devices, which had been reprocessed for the hospitals by primary reproducers, mostly registered primary processors, we gave them new

devices. We sent the reprocessed devices to independent sterilization labs for testing and every time, in every single set of tests performed, over forty-five percent of the devices turned out to be non-sterile. In some cases, there were bacteria on the devices that are on the Center for Disease Control's Top Twenty list of diseases to watch out for because they are multi-drug resistant. This is another device, where even without the aid of a microscope the blood and the debris are visible. [31] These devices are used in the gastrointestinal tract, so one could speculate as to what the debris is. [32] This device, for example, is smooth and you can see the debris that is on the electrodes. [33] These are the kinds of devices that are sitting on hospital shelves, awaiting use in patients, and we have sent all this into the FDA as justification for enforcing the law.

Aside from contamination issues, there have been device failures in patients. This is an electrophysiology catheter, and you can see the wire hanging out of it. [34] This catheter failed. This is one of my catheters, and it failed in its second use. When the doctors put it into the patient's heart, it looked normal. The doctors threaded it from a small incision in the groin all the way up into the chamber of the heart. When the doctor attempted to remove the catheter from the heart he felt resistance. You do not have to be a heart surgeon to know what was resisting. The doctor had a hard time getting it out of the patient. We are lucky – the reason that I can show you this and the reason that the doctor shared it with me is because after manipulating it for a while, he was able to get it out of the patient without injury.

The potential for injury was obviously big. Last year, doctors were using a catheter like this manufactured by one of BSC's competitors. That procedure was the *sixth* use of the catheter. It was supposed to be used only once. During the procedure, a piece of the catheter fell off of the electrode and is still in her heart today because the risk of removing it is far greater than the risk of leaving it in. She is monitored now to see if it moves. The FDA actually refers to this debris as the "gunk" factor.

We have been lobbying the FDA, often through citizens' petitions, and have done essentially everything we could to get the FDA's attention. When we did not get the FDA's attention, we went to Congress. We told Congress basically that we do not want new law, but rather for Congress to pressure the FDA through hearings, asking questions, and letters. Especially at appropriations hearings when FDA is asking for money, it is a good time for Congress to ask the FDA if they are addressing all the relevant concerns. We were successful and we got those requests. That effort helped, but Congress was not getting very far. Of course, on Capital Hill legislatures like to legislate, so Congress filed two bills, one on the senate side and the other on the house side. These bills would have removed the FDA's discretion, and would have forced them to enforce the law. They actually put into both bills that hospitals would be required to give patients informed consent.

Those bills are still pending, but last week we had a hearing before the House Commerce Committee: Subcommittee on Oversight and Investigations. David Feigal, who is the Director for the Center for Devices and Radiological Health, [35] testified for five minutes and then answered questions for well over two hours. Many of the representatives wanted to know why the FDA sat on the sidelines, and they were alarmed with the practice. Actually, Sixty Minutes, 20/20, and several other news cameras were there, so there may be press coverage. They said they wanted to talk to an injured patient. I cannot name any injured patients, as there is a doctor-client privilege that we must respect.

What is really fortunate though, is that two days before the hearing, the FDA finally got the message and they launched a draft guidance document that basically gives us what we were looking for. [36] The FDA said that all reproprocessors will have to file pre-market notifications. There is one loophole for exempt devices. You heard that some devices are exempt from pre-market notification. Those are devices that were exempt before the FDA looked at a specific device and granted an exemption. The FDA said that if it is exempt when new, the device is exempt when reprocessed. The biopsy forcep I first put up is an exempt device; however, when it was exempted, it was a single-use disposable device, and the FDA never considered all the risks associated with reuse. Our point is that you should not grant the exemption until you have reviewed that data. In the future, we plan to address the exemption and the time lines. These guidelines dealt with some issues but we continue to have questions like whether there should be informed consent. The message is if you have an issue, you have to keep working to resolve it. It has been four years, but we almost have the solutions we need.

Michael Baram:

Our last speaker today is Gary Marchant, who recently left a partnership at Kirkland & Ellis in Washington, D.C. for academia. One up for academia. Gary is now a Professor of Law at the Arizona State University Law School, and a Smith-Kline-Beecham Fellow in Genetics and Law at the Arizona State Center for the Study of Law, Science, and Technology. Gary, like many of our other panelists today, holds multiple degrees in diverse fields. He has a Ph.D. in Zoology, a Masters in Public Policy from Harvard's Kennedy School, and a J.D. *magna cum laude* from Harvard Law School. As I recollect, he graduated first in his class at that law school. It was my privilege to work with Gary many years ago when he was a student at Harvard, and marveled at his capabilities and capacities. We are now working on a treatise together, and it is our good fortune to have him here today to discuss liability issues.

Gary Marchant:

It is a pleasure to be here today because, as Michael said, when I was going to law school across the river I was really interested in the area of law, science and technology. There was not a single faculty member over at that law school that had any interest in that field at that time. I came over here, met Michael, and did a lot of work with the Boston University Center for Law and Technology, which is really one of the pioneering law school centers in this field of law, science, and technology. The area has just gotten bigger and bigger since I was working with Michael here.

The topic I want to talk about is liability issues for biomaterials suppliers, as opposed to device manufacturers, although I might say a little bit about that at the end if time permits. The basic bottom line is that the law is absolutely clear, quite unlike many areas of the law where you must say on the one side this, and the other side that. The biomaterials supplier will always win in a lawsuit. In fact, some people say that there has never been a single case where a biomaterials supplier has lost. There have been a couple of cases that might be close, but they are very rare.

The doctrine under which the suppliers always win is called the “bulk-supplier”/ “raw material,” or sometimes the “component supplier”/“learned intermediary” doctrine. The learned intermediary doctrine is what Patricia Davis was talking about. It is normally applied in the medical context where the assumption is that the manufacturer of a drug gives the risk information to the doctor, who then transfers it to the patient. A similar learned intermediary doctrine applies in the component supplier context. The rationale is that the manufacturer of the component or the raw material will pass on the material to the manufacturer of the device or the final product, and then that manufacturer of the final product will pass the information on to the consumer or final user. It is unclear whether that rationale always works, though. In fact, there may not even be a legal requirement for the supplier to pass on the information to the final manufacturer. I will get to that point in a moment.

Normally, the suppliers win these cases on summary judgment. This means that the case never goes to a jury to make a decision on the facts, but rather as a matter of law the supplier wins under these doctrines. This trend applies both to what are called design defects, where the material allegedly has some flaw in how it was designed that causes a risk, or in a failure to warn claim where there wasn't adequate information or warning given about those risks. Thus, the bottom line is very clear – the biomaterials supplier always wins. If that were everything to be said on the subject, I could stop now. Perhaps unfortunately for you, I have to go on because there are some more complicated issues that arise despite this clear trend.

An example of one case where a court granted summary judgment for the part supplier is one of the DuPont cases involving the TMJ jaw implant. [37] Basically, this decision says that even if the company that supplies the raw materials can foresee that there will be risks, that is irrelevant because the liability lies with the person who makes the final product. “The alleged foreseeability of the risk of the finished product is irrelevant to determining the liability of the component part manufacturer because imposing such a duty would force the supplier to retain an expert in every finished product manufacturer's line of business and second-guess the finished product manufacturer . . .” [38] Many raw materials might be used in hundreds of different products. The rationale is that requiring those companies to be aware of, and concerned about, every possible use of their raw material would put an unreasonable burden on them. On the other hand, the company that makes the final product does have a regulatory responsibility to ensure that it is approved by the FDA, not to mention a common law duty to ensure the product's safety. The rationale for supplier immunity then is that it would be too burdensome on the supplier, and the final product manufacturer has a responsibility to ensure safety in any event.

You could argue that there are countervailing arguments in favor of imposing liability on the supplier in some cases if they have been culpable, if they fail to test their material, or if they covered up the risks of their materials. For example, what if the supplier was a large corporation and the final product manufacturer is just a small business who does not really have much expertise? Maybe the original biomaterials supplier might be the one with the expertise and should have the duty. The supplier may also be the only one to have the deep pockets to fund people who are injured. Thus, various policy arguments have been made stating that perhaps there should be supplier liability in these type of situations.

The only example I have found of a supplier potentially being held liable (and arguably this is not a supplier liability issue because the company did not sell the material to a manufacturer), involves the sale a 100 ft. roll of polyethylene tubing to a hospital. [39] Only if you count the hospital as a primary manufacturer would this actually be supplier liability. The hospital modified the tubing into a catheter that it injected into the heart of a patient. The patient was injured because the tubing kinked. The company knew that the hospital was going to use the tubing for this purpose when it sold it, and the company did not conduct any tests to determine whether or not the tubing had adequate strength for this use. The company was denied summary judgment, and the court said that whether the company was negligent or failed to adequately test its product was an issue for the jury to decide. That was a 1970 case and the only one I can find where there is even arguably supplier liability, which shows just how unlikely it is that a supplier would ever be held liable. It is not even clear what happened later in that case because there is no record of an actual trial or the jury's decision.

Although the supplier is consistently held to be not liable, the courts cite a whole litany of factors that they use when making that determination. The factors differ from case to case. The factors that courts cite as arguing against any liability for the supplier include:

- the fact that the material met the contract specifications;
- the material is used in a broad range of different applications (this obviously does not apply in every case, but when it does it is cited by the court);
- the supplier had no specialized knowledge of how the purchaser would use the material (again this does not apply in every case, but in many it does);
- the material was altered by the purchaser;
- a supplier disclosed the known risk to purchaser (again doesn't happen every time); and
- the supplier provided a disclaimer on safety and required a waiver from the purchaser (again, this does not happen every time).

When those factors do occur (usually the typical case will involve two, three, or four of them), the court cites these factors as a basis for, essentially, giving immunity to the supplier. The fact that sometimes these conditions are not met is probably why plaintiffs continue to routinely include the supplier in the lawsuit. One might wonder, at some point, why do plaintiffs' attorneys bother including the supplier in the law suit? The reason is that sometimes these conditions are not met, and I suppose the plaintiffs and plaintiffs' counsel think at some point they might actually win one. But that has not happened so far.

There is a document called the Restatement of Law, which is primarily a consensus of where existing law stands. Sometimes it also pushes the law beyond its current consensus. Restatements are done quite rarely. The last Restatement of Torts is about 30-40 years old. [40] Just a couple years ago, a new Third Restatement of Torts was enacted for product liability, and this will probably become the prevailing standard in most jurisdictions. [41] Each state has to independently adopt the new Restatement before it becomes binding in that state, but I think 47 states adopted the Second Restatement and a similar number will eventually probably adopt the Third Restatement. The Third Restatement codifies the strong protection for suppliers of raw materials or component parts.

It essentially says that “a component part supplier” (and they define component part to include raw materials and bulk materials) is not liable for the injury from the final product, even if they know or should have known the risks of that material. [42] That statement is giving suppliers pretty broad immunity, and the only exception is if the component is itself defective. While it is not totally clear what the exception means, clearly if the component does not meet its own specifications it would probably be defective. The drafters of the Restatement gave a few examples to try to illustrate this exception. They said, for example, that someone who produces a pool liner without depth markings on it would be supplying a defective component, because people might dive into the pool and injure themselves, if they did not realize the depth. It is hard to see how that is necessarily always defective. On the other hand, the Restatement’s explanation states that an allergenic foam that is used in dishware would not be a defective component. Thus it seems something that could cause, by itself, health harm would not be defective, but something that could cause, in a sort of indirect route (someone else would dive into a pool and get a physical injury), would be defective. There is obviously some leeway in what exactly is a defective component.

The second exception is if the component supplier substantially participates in integration of the component into the final product. Again, you can see there is leeway in this exception as well. What does it mean to substantially participate? The Restatement gives some guidance and says, basically, if you help your purchaser develop the specifications and recommend particular uses for your materials, those actions would be considered substantial participation. But these actions are things that a company would normally want to do. If you produce a raw material or a biomaterial, or anything, you would want to recommend uses and suggest how it could be used. The Restatement appears to be saying that these suggestions could involve substantial participation and could open the door to liability. Additionally, the Restatement left open the possibility of liability when the supplier has knowledge or expertise that the purchaser lacks. In other words, when the supplier is a big company with expertise and the purchaser is a smaller, less expert company, there could be liability in that situation. The Restatement concedes that there are no known cases like that, but expressly notes that this exception should remain a possibility. Thus, the Restatement leaves the door open for potential liability of a supplier. Again, however, there have yet to be any actual cases where they have been held liable.

The real poster child of supplier liability is what Professor Baram referred to a few minutes ago as the DuPont TMJ implants litigation. These implants replaced a joint between your lower and upper jaw. A small company, Vitek, developed an implant that included some Teflon supplied by DuPont. Apparently Vitek used only about five cents of Teflon per implant, and DuPont made total sales of less than \$1000.

These implants eventually fractured within the jaw after they had been implanted and caused a lot of pain and health problems for people who had them. The patients brought lawsuits against the manufacturer (Vitek) and DuPont. Vitek soon declared bankruptcy and its owner fled to Switzerland. DuPont was left as the sole defendant in these cases.

Over 1600 claims and 650 lawsuits were brought against DuPont, which obviously had the deep pocket in these cases. DuPont lost a couple of cases at the trial level, but in every case, won in the end, either after trial, on summary judgment, or sometimes on appeal. Despite winning every case eventually, they spent about 40 million dollars defending themselves. For \$1000 in sales DuPont ended up with 40 million dollars in legal costs, even though in each case the company was exonerated.

The other famous example of litigation problems is the silicone breast implant litigation. When looking at the role of Dow Chemical as opposed to Dow Corning (the manufacturer of the breast implants), it is important to note that this is not a supplier liability case. Dow Chemical never supplied silicone to Dow Corning, its only role was to conduct some testing of non-breast implant silicone materials provided to it for that purpose by Dow Corning. Nevertheless, the litigation could show a different route to attach liability to someone who has a relationship (like a supplier) with the manufacturer. Dow Corning was fifty percent owned by Dow Chemical and fifty percent by Corning Glass. Both corporations elect one third of the Board of Directors of Dow Corning; however, under traditional corporate law doctrine, Dow Corning’s liability does not extend to Dow Chemical or to Corning unless there is some other duty established.

In *Dow Chemical Co. v. Mahlum*, the Nevada Supreme Court upheld a jury decision that Dow Chemical was liable for injuries allegedly suffered by the plaintiff from her silicone breast implants. [43] Dow Corning was removed from the litigation as a result of its bankruptcy proceeding, so the plaintiff’s case proceeded against Dow Chemical

only. The Nevada Supreme Court held that although Dow Chemical would normally not be liable through its corporate relationship, here Dow Chemical had conducted tests on Dow Corning's silicone products.

The vast majority of the tests conducted by Dow Chemical were not on silicone used in breast implants. Dow Corning produced over 100,000 different silicone compounds with over 4,000 commercial silicone products. Many of those different silicone chemicals have very different health properties. Some were biologically active, and some were not. Dow Chemical performed 180 tests on a variety of different silicone compounds for Dow Corning before Dow Corning got its own toxicology lab in 1968. Twelve of these tests were done on silicone fluid that was used in breast implants. These tests were primarily acute animal studies that were looking for the effects of handling the silicone by workers. They were animal eye studies (putting some in the eye and seeing what happens) and skin studies, as Dow Corning was considering using some of these silicone compounds for burn treatments. These tests were mostly done long before breast implants were first invented in the early sixties.

There was one study that was more of a health study than an industrial hygiene study. It involved injecting silicone, and some inhalation of silicone, into dogs. Dow Chemical found that the silicone spread through the body in 1956. However, they did not perform any studies evaluating breast implants per se or evaluating the safety of silicone used in breast implants in a health-type study that would normally be conducted for a material put in the human body. In addition to the testing, Dow Chemical also had their chief toxicologist, the founder of industrial toxicology named V.K. Roe, serve as a consultant to Dow Corning on testing labs and protocols for subsequent testing.

The court held that this was enough to make Dow Chemical liable for the injuries to the plaintiff under the good samaritan doctrine. Dow Chemical had undertaken to test some of the liquid silicone, and once it undertook that obligation, it was required, according to the court, to do all the testing that was appropriate. Moreover, the court found that Dow Chemical should have published its data and used its influence to halt the marketing of the breast implants. Thus, by taking this initial step in testing the raw materials, Dow Chemical assumed a duty under the good samaritan doctrine to ensure the safety of silicone breast implants, a product is never tested or manufactured.

This concept was further extended in another case, which is the largest breast implant case to have been litigated. [44] It involved an 1800-woman class action in Louisiana, again against both Dow Corning and Dow Chemical originally. Once Dow Corning entered bankruptcy, the class action went ahead solely against Dow Chemical. The first stage of the trial concerned Dow Chemical's culpability, and it did not involve the causation issue or damages. After a trial lasting several months, Dow Chemical was found culpable by the jury.

Dow Chemical tried to argue to the judge that the issue of culpability should have been decided as a matter of law. Dow Chemical argued it had no duty since it did not make the breast implants; it only did some testing. The judge rejected that legal argument and said that in deciding whether or not to impose a duty the two key factors she considered were "morality" and the "type of activity." [45] The moral factor is defined simply whether something seems right or wrong. According to the court, "[i]f plaintiffs' allegations of [morally wrong acts] are proven then justice demands that a duty be imposed." [46] Thus, there is no pre-existing legally defined duty – it is a question of whether what you did is viewed as "right" or "wrong." Second, the "type of activity" inquiry requires that the court look "into the nature of the defendant's enterprise." If it is proven that these breast implants cause the conditions that plaintiff allege, then there "is no social utility" to the product. [47] In summary, this decision is saying that if the product you test causes harm, then it is simply a matter for the jury to decide whether what you did was right or wrong in determining whether you have a legal duty and are liable.

The Louisiana court went on to say it appears the Louisiana Civil Code envisions a universal duty - "we are our brother's keeper." [48] These are very broad words. "We owe a duty not to cause damage to another. And under Louisiana law, when one's act of commission or omission, directly or indirectly, alone or in concert, intentionally or negligently, causes damage, whatever the act, he by whose fault it is occasioned is obligated to repair it. The courts have imposed this duty when the act of one falls below a reasonable or prudent man standard. Whether one falls below that standard is a matter for the trier of fact to determine . . ." [49] The whole issue of duty and liability here is a question that goes to the jury.

Any plaintiff's lawyer will tell you that if they have an injured client and at least some possibility that the product caused that plaintiff's injury, the one thing they want to do is get the case in front of a jury where they make a passionate or ethical argument that the jury should impose liability. The defendant tries to avoid the jury with some

kind of legal argument, perhaps the lack of a duty. The court said, in this case, Dow Chemical did not have that legal argument. Because Dow Chemical engaged in some activities like testing, its actions are now subject to evaluation by a jury. By this argument, a company that is not a manufacturer of a product, but has some role in the development of the product (e.g., as a supplier), could be subject to evaluation by a jury, and very likely liability.

The DuPont litigation became a poster boy for Congress' recent enactment of the Biomaterials Access Assurance Act of 1998, which provides additional protection to biomaterial suppliers. [50] Biomaterials are defined in the statute as basically anything that goes into an implant that is subsequently put into the human body. The Act provides a general grant of immunity for biomaterials suppliers. The only exceptions are if you are a manufacturer or seller of the implant, rather than the raw materials of the component part, or if you provide materials that are different from the contractor's specifications. The Act also exempted silicone products. Silicone did not get protection from this Act because it was already tied up in controversial, ongoing litigation.

The Biomaterials Access Assurance Act basically codifies the existing substantive law. You are essentially immune from liability if you are a supplier. Congress intended that this Act would give a supplier a procedure where they would not have to pay \$40 million to defend itself in order to get relief from liability. The Act provides a supplier a quick out through an expedited summary judgment-like determination that it is not a seller or manufacturer of the final product and its material does meet its own specifications. If this is the case, the supplier can get out of the case quickly, and no other issue can be raised against it. Additionally, and very importantly, no one can take discovery against the supplier, which is a very expensive part of this litigation. Thus, in summary, the main thing the statute provides is a quick out for biomaterials suppliers provided they have produced materials meeting their own specifications.

One complication exists. After the supplier is excluded and the case goes to trial and a decision is entered against the manufacturer, within ninety days the parties can bring the supplier back into the case when certain conditions exist: if it was clearly negligent, or intentionally did something wrong, and the negligence caused the injury. However, even then other procedural protections, including no discovery, can protect the supplier.

The consequences of this Act are unknown. The Act is very recent, and no definitive cases have interpreted it or even tried to explain what it means yet. It is generally believed that it will have a very positive impact on biomaterials suppliers, though, by giving them protection. However, a lot of the deep pockets, the big companies that do make some of these raw materials, such as Dow and DuPont, have said they are still going to avoid the market at this time. They will wait to see how the Act is actually applied in the real world before agreeing to supply biomaterials for many products.

As mentioned earlier, the Act does not apply to silicone suppliers. Also, the Act may not protect a supplier from the good samaritan duty put forth in the Dow Chemical cases, where once a supplier does testing or something similar, the supplier assumes a duty to carry it through fully and could be liable through that route. I do not think that liability as a result of those actions would be protected through this Act. Additionally, the Act does not protect the people who manufacture the device and use the raw materials.

Thus, in conclusion, from this case law, statutory requirements, and the Third Restatement, several recommendations make sense for suppliers. Some of these suggestions may have some unfortunate side effects or consequences. First, a supplier should be certain that its material meets all of its own specifications, and to make sure its specifications are written in a way that that it can meet them and show that objectively. It will also be beneficial if the supplier can show that its material is used in several different applications, and not just one.

In addition, a biomaterials supplier will be safer if it does not communicate with the manufacturer in the design of the final product and does not recommend uses or specifications. Unfortunately, a manufacturer of biomaterials would want to have that interaction with people who are going to use its materials, and indeed it would like to suggest ways a biomaterial could be used and assist with its use. But basically the law provides a deterrent to doing that. A supplier can be held to be substantially participating if it goes ahead and works with the manufacturer in those types of activities.

A supplier should provide a disclaimer, and obtain a waiver and indemnification. This could be harmful to device manufacturers, as I think one of the speakers this morning mentioned, if they have to sign this waiver and

indemnification agreement to Dow Chemical or DuPont, promising to spend the millions of dollars protecting them if something should go wrong and lawsuits get filed. That can be very prohibitive for small companies that are device manufacturers.

Again, minimize business or other relationship with the manufacturer, beyond the supply contract. Disclose known risks. Yet, because of the Dow Chemical liability and other examples, there seems to be an incentive to stay ignorant of the risks of your material. If you don't test, you don't know the risk and you are protected from assuming any duty. If you do start to learn about the risks and start to study those risks, however, you may have a duty to do more testing, disclose the risk, or even possibly not going forward with your product. This incentive would have the unfortunate result of producing less testing and knowledge about the risks of your product. There might be a little bit of incentive going the other way, but this counterproductive incentive system is unfortunately where the law leaves us right now.

In closing, there is one final story I would like to mention about the Dow Chemical case. I was talking to one defense lawyer, who was representing Dow Chemical in those cases. He said that after one of the long cases where they had several months of jury trial on whether Dow Chemical was sufficiently related to Dow Corning, they interviewed the jury after they found Dow Chemical liable. They asked one of the jurors: "Did you understand the difference between Dow Chemical and Dow Corning?" The juror reportedly said: "No. They're all the same: Dow Corning, Dow Chemical, Dow Jones, they are all the same." Of course, Dow Jones has nothing to do with breast implants. Thank you.

Michael Baram:

We will now have a question and answer session on regulatory and liability issues for about 15-20 minutes.

Karen Connor (British Consulate):

Karen Connor. I'm with the British Consulate and I do business development for medical devices in the United Kingdom. Could you share with me, knowing what you know, what other companies knew that reprocessing, either commercial reprocessors or hospitals was going on. How did you protect yourselves while it was going on and before the FDA woke up. Or, how did you preempt problems?

Patricia Davis:

Well, I am glad you asked that because it is going on today; it is not over. The FDA's guidance documents are draft. They are not finalized and we are at least a year and a half away from any reprocessed device being approved. So, the most we can do is put 'single use only' on the devices, as well as in the instructions for use. There are warnings in the instructions for use that reuse of them can cause disease transmission, a functional failure can cause injury, illness, or death. We also are on a major educational campaign for doctors, hospitals, and nurses to show them why this is very unsafe. We perform testing and share the testing data not only with FDA but with all our hospitals, to let them know 'please do not do this.' It is very difficult because you can look at some of these devices and they seem very sturdy, very durable, and they have to be. The FDA requires that we have a safety margin. So, yes it is proved that it can be used once, but an electrophysiology procedure may last four hours – it may last twelve hours. When the device was used twelve hours, almost the maximum, you have to make sure the device can make it that long, but, obviously we have created a safety margin. The reprocessors are all playing off that safety margin. To tell you the truth, that is the most we can do, because otherwise we would have to stop selling them.

I do not have a way to make them self-destruct. We have looked at that. There is a new surgical probe that is coming out by my company that has a lot of electrodes and electronics. With electronics today, everything has a mini-computer. When you plug it into the console, the probe will say: 'I've been reused once,' and shut itself down. That is one thing we can do. However, that is hard because some of these devices are used in animal trials, where we are not worried about passing diseases between two different dogs. You are worried about whether it

works. There is very little we can do, though – especially with plastic devices, like angioplasty catheters. There is nothing I can do to that device to make it self-destruct, because what if self-destructed when it was in the first patient? In a lot of our product liability suits right now we are trying to figure out whether they were reused. However, it is even very difficult to find out if your device was reused, because most of the time they have already thrown it out. They have usually thrown out the packaging and things like that.

Karen Connor:

Buried the patient...

Patricia Davis:

Right. Unfortunately, we have exhausted all the avenues. The United Kingdom is more on the side of the U.S., which means that they believe it really should not be happening. Their laws are not that clear. France, on the other hand, has completely prohibited this. France has a major problem with hepatitis. The statistic I heard is that one in four persons in France has hepatitis. They are not sure where the hepatitis is coming from, but they are starting to look at absolutely any way that a person can transmit it. Because it is a blood transmission, they are the only country right now that outright prohibits reuse of these devices.

Karen Connor:

Thank you very much.

Michael Baram:

We have heard an overwhelming amount of useful information from this panel on regulatory and liability issues. To make it even more useful, what advice do our panelists have for persons who are interested in starting small startup companies in biomaterials? Should they feel protected from liability by the Biomaterials Access Assurance Act? How can they effectively lobby the FDA for the kind of regulatory treatment they think appropriate? Many in our audience are interested in, or have established biotech startup companies, and would like further guidance on how the law discussed by our speakers should influence their research and progress towards the development of commercial products.

Gary Marchant:

With the liability issue, I think there is a lot of protection for small startup companies. With the Biomaterials Access Assurance Act, you do have this protection against liability. I do not think you are going to be a big target for litigation. You are not a deep pocket if you are a startup company. Usually the litigation resources go towards the deep pocket. It does not make sense for a plaintiff, or plaintiff's counsel, to make a business decision and invest a lot of money going after company without millions of dollars to justify the effort. You sort of have that protection when you are small. It is when you get bigger that you are going to become a target.

Patricia Davis:

Boston Scientific is obviously a large medical device manufacturer. But we do a lot of business with small startups. They come to us at different stages and we are finding that they are coming at earlier stages, because it is so expensive. You do not see very many medical device companies that raise money through IPO's anymore. Mostly they get acquired, or they do a distribution deal, or another sort of other deal with a large company like BSC. I think what has happened is that the regulatory, legal, and distribution burden has forced them to seek earlier help from the larger companies. A lot of the new technology that has developed or is developed by BSC or our competitors is from small startups. I think that the factors that you are bringing up is just forcing them to come to us for help earlier. A lot of times they will come to us maybe after animal testing, which is still very expensive. They will approach us earlier than human clinicals because they need the help performing them. Also, I think most startups are smart enough to get a regulatory expert on board early.

Ellen Flannery:

I think this issue can tend to push the biomaterials suppliers and the manufacturers of the devices apart. It puts a bigger regulatory burden on the manufacturer of the devices, because, as Gary was saying, the advice to the biomaterials supplier is: 'Don't do any testing. Don't give them any data. Don't get involved with the manufacturer.' Then the manufacturer has to do the extra testing, figure out what materials they are working with, sign indemnifications and waivers, and sometimes I think that really can inhibit the market introduction of new materials, because people do not want to go through the hassle. They will stay with the same materials. There is a big issue about blood-bags and whether the PVC was leaching, and people were saying 'ban the PVC - we'll get new blood-bags.' Others were saying it is not all that easy. You cannot do that right away. You have to get FDA approval. The product we know may be better than the product we do not know. We know all the risks here and we can control them. It is a very complicated regulatory issue.

Michael Baram:

Taking the prerogative of the chair, I just want to present a realistic hypothetical case. Assume I have just developed a promising new biomaterial, and several medical device companies are interested in working with me to transform my advance into a product for commerce. But I have been told to keep them at arms length in an informational sense in order to avoid products liability outcomes. Can we more clearly define what I can or should tell them about my product without increasing my liability potential, given their pressure for more information and even collaboration on product testing and development? What kind of communication and working relationship is most appropriate from my perspective and goal of avoiding liability and associated transaction costs? I know this is a matter of first instance since the Biomaterials Access Assurance Act has not been tested, but I am asking if we can we try to define a bright line? Must I inform the manufacturer about any inherently hazardous or potentially risky features of my biomaterial?

Gary Marchant:

It is even questionable whether that is absolutely clear. Under the Biomaterials Access Assurance Act there is no obligation that you disclose. That is not part of the conditions for protection. It is simply that you meet the specifications. Under the common law and the Restatement, the substantial participation standard is what applies. There is some law on that, and they distinguish between technical guidance, where you as a supplier can sometimes go into the manufacturer's process and say that another way might be better or you can solve a problem this way. This could be viewed as technical assistance, and does not count as substantial participation. On the other hand, if you give them the specifications for your material rather than letting the purchaser specify them, that is seen as a substantial participation. Also, if you would recommend particular uses beyond what the purchaser comes to you with, that is substantial participation. So there is some distinguishing. However, under the Biomaterial Access Assurance Act, that substantial participation, if you meet the criteria of the statute, is no longer a source of liability. Liability occurs only if your material does not meet its specifications. I agree with Ellen's point that there is a barrier, erected by both regulatory and liability concerns, between the manufacturer's needs and the biomaterials suppliers' advice. Hopefully this new Act will try and diminish that because the substantial participation exemption no longer applies, providing you meet the criteria of the Act.

Patricia Davis:

If I could just make a point. It also depends on what companies are talking to each other about. Yes, DuPont has pulled a lot of material off the market, some of them BSC was relying on, and we have had to find new suppliers. When we are dealing with a company like DuPont, they are big enough so that they can sell to other people, and they are not worried about losing our business. If you are a new start-up and you have just come up with a new material, the reality of liability and regulation exists, but unless you can convince me to make new regulatory filings or convince me of all its great new properties, BSC is not going to use it. In reality, unfortunately, you may be opening yourself up to liability just to get somebody to buy your product. While it is unfortunate, I do not think there is going to be this huge chasm because there can not be.

Mike Drews: Vascular Sciences:

As a medical entrepreneur myself and a former designer, I find your comments about the Biomaterials Act somewhat reassuring in the sense that maybe it is limiting some of the liability. On the other hand, I think it is a little scary, for a couple of reasons. First, when you really limit the relationship that I can build between myself, as a designer/manufacturer, and a material supplier, I think it is naïve and possibly even negligent not to encourage a relationship between those two parties. I rely on the information that material supplier provides to us all of the time. Also many of the material suppliers have already done the biocompatibility testing and tripartite testing, Why should we have to reinvent that if it has already been done?

Second, I am concerned about new, very novel biomaterials, the true biomaterials, the ones that are not even being used clinically yet. What is the Act going to do to the relationship between the design folks and the suppliers? What is that going to do in terms of stagnating the development of true new biomaterials, for example, polymer-based materials and carbohydrate-based materials, when you can not have a collaboration between those two bodies?

Gary Marchant:

The restrictions on the collaboration come from the common law and Restatement. The Statute essentially gets rid of that factor, so hopefully this will allow there to be more of a collaborative relationship without exposing yourself to liability because you do have to get a new market established, and you have to go talk to people who are going to buy it. One of the motivations behind the Statute is not only the protection against litigation but also to eliminate the disincentive to have collaboration between purchasers and suppliers. The question remains about how the courts will ultimately interpret the Act.

We have this huge body of case law that does suggest that substantial participation can be a factor towards liability, although often it does not result in actual liability because it is simply a factor cited, but we have an established body of case law and a new statute comes along that says that substantial participation is no longer a factor. Will courts bring substantial participation back in when interpreting the statute? That is the question that DuPont and Dow are waiting for an answer to, because they can afford to wait. Smaller companies may not be able to afford the luxury of being able to sit on the sidelines. Thus the big question remains: will the common law factors be brought in when interpreting and applying the statute?

Mike Drews: Vascular Sciences:

As a quick follow-up to that, I'm not an attorney. I do not know the answer to this, but right now it seems like this Act is primarily geared towards the traditional biomaterial manufacturers, people that make urethanes and silicones. What about some of the tissue-engineering materials that people are developing now where there is not a supplier yet? Quite frankly, with all due respect to Ms. Davis, I think that most of the bigger companies are going to sit on the sidelines and wait to see what happens. It is going to be us little guys in the trenches that are going to be thrown to the wolves so to speak.

Ellen Flannery:

To some extent these materials may be tissues, or they may also be devices or biologics themselves, and thus be under the product regulatory scheme and not at all protected by that Act.

Michael Baram:

Let us thank our truly expert panel for rising to the challenge of informing us about some complex legal and management issues. Our next session, which will deal with related issues of health insurance coverage, follows after a short break.

- [1] *Dow Chemical Co. v. Mahlum*, 970 P.2d 98 (Nev. 1998).
- [2] *In re Temporomandibular Joint (TMJ) Implants Prods. Liab. Litig.*, 97 F.3d 1050 (8th Cir. 1996). For a general discussion of the TMJ Implants Litigation, see Brett W. Roubal, Casenote, 31 CREIGHTON L. REV. 617 (1998).
- [3] See Joyce Wong et al., *Advances in Biomaterials & Devices, & Their Financing*, 6 B.U. J. SCI. & TECH. L. 2, ¶ 14 (2000).
- [4] See Michael Meurer & Thomas Meyers, *Patent Rights & Licensing*, 6 B.U. J. SCI. & TECH. L. 3, ¶ 5 (2000).
- [5] 21 C.F.R. pt. 56 (1999).
- [6] 21 C.F.R. pts. 312, 812 (1999).
- [7] Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360(k) (1994).
- [8] 21 U.S.C. §§ 360e(c)-(d) (1994).
- [9] 21 U.S.C. § 360j(e) (1994).
- [10] See Public Health Services Act, 42 U.S.C. § 262 (1994).
- [11] 21 C.F.R. § 1270 (1999).
- [12] PMA/510(k) Expedited Review Guidance for Industry and Center for Devices and Radiological Health Staff; Availability, 63 Fed. Reg. 15,427 (1998).
- [13] FDA, GUIDANCE FOR INDUSTRY: FAST TRACK DRUG DEVELOPMENT PROGRAMS (1998).
- [14] Orphan Drug Act, 21 U.S.C. §§ 360aa-360dd (1994).
- [15] 21 U.S.C. § 360j(m) (1994).
- [16] See 21 C.F.R. § 3.5 (1999).
- [17] See *id.*
- [18] Memorandum from Jerome Davis, CBER, to Director, Division of Emergency and Investigational Operations, Tissue Products Regulated by CBER and CDRH (December 17, 1998).
- [19] 21 C.F.R. pt. 3 (1999).
- [20] *Medtronic, Inc. v. Lohr*, 518 U.S. 470 (1996).
- [21] 21 U.S.C. § 360k (1994).
- [22] *Id.* § 360k(a) (emphasis added).
- [23] See 21 C.F.R. pt. 808 (1999).
- [24] *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504 (1992).

[25] 518 U.S. at 475-76.

[26] *Haidak v. Collagen Corp.*, 67 F. Supp. 2d 21, 34 (D. Mass. 1999).

[27] 62 Fed. Reg. 65,384 (1997).

[28] Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296.

[29] 63 Fed. Reg. 39,789 (1998).

[30] Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq.* (1994 & Supp. IV 1999).

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[35] *See Reuse of Medical Devices: Hearings Before the Subcomm. on Oversight and Investigations of the House Comm. on Commerce*, 106th Cong. (2000) (last modified Feb. 28, 2000) <<http://www.fda.gov/ola/2000/suds.html>>.

[36] Center for Devices and Radiological Health, United States Department of Health and Human Services, *Enforcement Priorities for Single-Use Devices Processed by Third Parties and Hospitals* (last modified Apr. 18, 2000) <<http://www.fda.gov/cdrh/reuse/1029.html>>.

[37] *Kealoha v. E.I. DuPont de Nemours & Co.*, 844 F. Supp. 590, 597 (D. Haw. 1994).

[38] *Id.* at 594 (citing *Childress v. Gresen Mfg. Co.*, 888 F.2d 45, 49 (6th Cir. 1989)).

[39] *Putensen v. Clay Adams, Inc.*, 12 Cal. App. 3d 1062, 1069-70 (Cal. Ct. App. 1970).

[40] RESTATEMENT (SECOND) OF TORTS (1965).

[41] RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY (1998).

[42] *See id.* § 5 & cmt. a.

[43] 970 P.2d 98, 115-21 (Nev. 1998)

[44] *Spitzfaden v. Dow Corning Corp.*, 708 So. 2d 777 (La. Ct. App. 1998).

[45] *Spitzfaden*, Reason for Judgment, June 11, 1997.

[46] *Id.*

[47] *Id.*

[48] *Id.*

[49] *Id.*

[50] Biomaterials Access Assurance Act of 1998, 21 U.S.C. § 1601 (Supp. IV 1998).