Intellectual Property and National Health Systems:
Case Studies of BRCA Testing in Canada
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DR. GOLD: Can you hear me?

DR. EVANS: Yes, great.

DR. GOLD: Great.

DR. EVANS: A disembodied voice.

We have your slides up, Richard, on BRCA testing in Canada, or we're going to momentarily. You can go ahead and start.

DR. GOLD: Well, thank you and thanks to Shobita. I haven't met you before, but I would like to some day since we're working on similar things.

I think my talk is complementary to her talk in a couple of respects. Not only are we dealing with the same subject and taking an international view, but we use different methodologies to do our studies and so there are different things that each one reveals. I think the true story -- in any historical story, you never really get at the truth. So by using different ways to interrogate what happened, we get a fuller picture. Then it's up to, I think, the committee and to other observers to decide what really happened or at least, maybe more importantly, what can be learned.

Let me, just before I get into the overview, just say the way we went about studying this. We started this a few years ago using the public literature. I should say at the start that I've been involved personally with some aspects of this; that is, I was an advisor to the Ontario government who was one of the main actors in Canada. And I also was an expert for the person who did the initial drafting of the OECD guidelines on the legislative genetic *. Obviously, it was the expert committee as a whole that did the actual drafting but I had the pen initially and then handed it over to Christina to take it through the internal process. So I've been involved. That's one aspect.

But what I noticed in going through this is we don't have a full picture. The literature is missing a few important voices, and that includes the voices of the policymakers but also Myriad. And to a large extent, as I'll get into, that's been the fault of Myriad. But we decided to try to resolve that and what we did is we brought together physically some of the main actors, especially in Canada but not exclusively. We brought, other than the Canadians involved, the different governments and so on, someone from the research department in France who was giving advice to the Institute Curie, as well as Bob Cook-Deegan's group down in Durham at Duke. We brought them together to try and get a discussion going about how they perceived what happened.

So what I'm going to take you through is what we heard from them. It's going to be, obviously, up to each and every person to decide whether what we were told is what really happened or it was justified after, et cetera. We had a very frank discussion, so I think people believed what they were saying, but obviously, in any methodology you have to be aware of the risks and one of the risks is that what people reported isn't exactly what happened.

So let me go through and I'll talk about the time line. Since Shobita did it to a certain extent, I'll try to do that quickly, but I'm going to highlight a few different elements and I'll especially concentrate on what happened in Canada.

I want to talk about the business model. This tended to be a very major issue in what happened. And then what were the problems? Why did this gene patent and the way it was being used become a lightning rod? That was really the question that we were trying to answer rather than what should have been the solution.

And it comes down to really three things that we identified: a lack of communication not only by Myriad, although Myriad was very poor on communication, but also by the governments involved, and internal discussions. Lack of trust was a very major issue here on both sides. And institutional failure more, I would argue, on the governmental side than anywhere else. And then I want to end with what I think are some of the implications and conclusions.

So once again, Shobita took us through some this. There was a consortium in '89 that was founded. In 1990, Marie Claire King localized the gene. Importantly, 1991 is when Myriad Genetics was spun off from the University of Utah by Marc Skolnick to get more flexibility. He got financing from Eli Lilly in '93 and there was an initial public offering in '94, which corresponded roughly to when Myriad applied for the first patent on BRCA1. There were other patents subsequently filed, as Shobita said. The Cancer Research Campaign filed a patent then on BRCA2 in 1995, followed by one by Myriad in '96. And then Myriad starts to go into business in the U.S. in 1996, and I think Shobita took us through a little bit of that history. And they introduced a large scale rearrangements panel in 2002, and that's been one of the controversies. I'm not going to get into it terribly, but I'm happy to talk about it. But other technologies were better at doing large-scale rearrangements, and it wasn't until 2002 that Myriad offered a test capable of doing that.

So let me take you to Canada which is really the focus of what I want to do. So in about 2000 -- I don't have the exact date in front of me here -- Myriad entered into an agreement with a private company called MDS Laboratories. MDS had been in the business mostly of providing diagnostic laboratory services to the various governments. So their largest client was the Ontario government and after that, it would be the governments in various other provinces. They had started to get more into biotechnology at this time. They were trying to find new technologies to bring to market.

I guess I should give you a little bit of the Canadian history. What they saw was severe government cutbacks during the 1990s so that we could balance our budget, and a lot of that was felt in provincial government health budgets. That is, the federal government had been funding provincial governments to provide health care and a large portion of the cutbacks occurred in health care, given that it's such a significant part of the Canadian budget.

So the provincial governments had to start cutting back, and what they did is they started cutting back on services. So they either delisted some, but it was easier to just simply not add new services to the menu of services covered by public health care insurance. They more or less allowed private sector providers to provide some services that fell outside what they covered, not explicitly stated or agreed upon, but implicitly that's how MDS at least saw it. So they saw their niche at finding high quality new technologies that were not broadly available through the public system and offering them. That's where they thought they would go into it.

So they came across Myriad. And I'm not entirely sure whether it was MDS that met Myriad or vice versa. Anyway, MDS signed the agreement in around 2000.

So they started to talk with governments about providing these services, and they went to the government procurement departments within their health ministries. So in Ontario, they would

have gone to that department to talk about licensing this. That unit said, well, we're used to buying kits, but this is not a kit. This is a service, and so this is unusual. And they kicked it over basically to their policy unit.

Their policy unit had lots of other things on their plates, but they had been thinking about genetic technology for some time and they were wondering, well, what are the impacts of these new genetic technologies as they come on line. This was the era where we saw all kinds of new diagnostic testing services. Eventually gene therapy, pharmacogenetics were going to come on line very soon, and so they saw this as a wave of new technologies, and they didn't really have a policy framework to deal with it. So the policy unit didn't know what the answer was.

So basically it had been kicked over to them, but they didn't have an answer. So just communication stopped with Myriad, Myriad waiting for a response, and the government is not responding. We're getting no answer. We don't know what's happening.

So in late May early June 2001, they had their lawyers issue cease and desist letters to four provinces, including Ontario, basically telling them we have a patent on this. You're funding hospitals that are providing laboratory services that violate our patent. Please stop or you must stop.

In August 2001, the government of Ontario, in a letter from the then-Minister of Health for Ontario, now the federal Minister of Health, Tony Clement, sent in a letter saying basically, well, our opinion is we are infringing on no valid patents. It was very vaguely stated and could either be argued that they were saying the patent is invalid or because they're only funding hospitals, they're not infringing. So that was left vague.

In response, the presidents of Myriad Laboratories and of MDS, this particular unit of MDS, asked for a meeting with the Minister of Health, and that was accorded in November 2001.

At that meeting, they presented the minister with a stack of letters, including one from your ambassador and from Senator Hatch from Utah basically saying Canada is in violation of its trade agreements, and there might be a reference to the U.S. Trade Representative because Ontario was failing to pay Myriad.

Well, this is not something that gets into the press -- the whole issue had gotten to the press around the summer of 2001. The Minister of Health said we have to have it independent and we don't necessarily think this is valid. So once all this came to the fore, that was seen as exceedingly hostile.

There were also about 100 letters from different scientists that were presented to the minister at that time.

So this was seen as a very hostile action, to threaten Canada with trade sanctions, and the government at that point said, from what we can tell -- this is me guessing, but I don't think the guess is wild -- we really can't be seen to be giving into this. The public health care system has been under some stress because of lack of funding. The principle of a public health care system, organized and controlled by the public, is paramount. If we're giving in to a U.S. private company, this would look terribly bad. So Myriad made some strategic mistakes in raising the stakes and threatening trade sanctions in my opinion.

The minister then held a policy forum in 2001 at which various people from public life, academia, from government, industry were present, and that led to the creation of a report that Ontario prepared and released at the end of January 2002. It dealt mostly with technology assessment. This was a global view of genetics and the challenges it posed. So the biggest one was coordination of technology assessment across Canada so it's not duplicated, coordination of the provision of services so that not each province duplicates everything. Just an aside, health care is provided on a province-by-province basis. So to the extent that there's coordination, they have to work together. So most of the report was concentrating on coordination. But one out of seven chapters dealt with IP and basically said, look, we need policy levers to be able to negotiate and resist what was viewed as a hostile maneuvering by Myriad.

The way that the Ontario government and others viewed it is Myriad had a one-size-fits-all type of approach to licensing. They were unwilling to budge. It wasn't well integrated into the provincial health care systems. It didn't take into account genetic counseling. It didn't allow for an implementation in phases, that is, Ontario provided another test called protein truncation as one of the things that they took into account with genetic counseling to make a decision about whether full testing should be done on the gene. But because it involved the gene, Myriad didn't like it.

So there was this tension where the government said, well, we can't administer the system the way we want. So we need policy levers both on the research side -- so it called for a research exemption, but it also called for a particular compulsory license that would be very narrowly tailored to the particular circumstances of genetic testing and so on. So it wouldn't scare off all of industry, it would be very targeted. There were some other things too like coordination and so on, tougher criteria applied, better management at the Patent Office, and so on.

All provincial governments agreed and supported the Ontario report, including Quebec, and I say including Quebec because Quebec never agrees to anything. So the fact that Quebec agreed with the rest of the provinces on a health care matter is fairly significant.

And in response to all of this BIO intervened and threatened to pull out BIO 2002 which was being held in Toronto that summer. They eventually backed down. But you can see that there was pressure at the political level, and Myriad was politically connected, especially to Senator Hatch, but they also had Paul Cellucci, the ambassador at the time on board. They had BIO. So they thought they had -- presumably, they were getting the big guns out to say you got to do something here, and they expected Ontario to comply and say, okay, well, we made a mistake.

Well, Ontario then started a policy process between the provinces, and Health Canada participated. And Health Canada is responsible for the federal part of the health care system. But then in terms of the more general needs of technology assessment and who should be doing what -- but they also engaged in direct conversation with the unit in Industry Canada that was responsible for the Patent Act because they saw that what they needed was a policy lever. They didn't necessarily want to invoke a compulsory license, but they wanted to have it in their pocket so it was a real threat.

So Myriad knew, as everybody knew, that the existing compulsory license in Canada is, as I said before, a sledge hammer. It was not a realistic proposition that anybody would invoke it. So it wasn't a real threat.

What the provinces wanted was a real threat, not so that they would actually issue a compulsory license, which would be the improper way to think about compulsory licenses, but industry would

know if they went too far, it could be invoked. So it would engage industry in negotiation. That was the goal. So there was a discussion about that and so on, which did not lead anywhere other than I think frustration on both sides.

By the spring of 2003, though, the emphasis of the policy unit on gene patents waned for the simple reason that SARS hit Toronto. So everybody in the policy unit and elsewhere suddenly switched gears and was looking at SARS in response to it. You had a real health crisis, as opposed to a potential one.

And by October 2003, the government of Ontario changed and the new government didn't have this as a particular priority. Discussions still continued, especially at the federal level between Health Canada, which took the side of the provinces, and the patent policy director within Industry Canada, which didn't want to make a change, not leading anywhere.

Eventually in the fall of 2004, a reference was made to the Canadian Biotech Advisory Committee. Now that's a very Canadian solution to things. When you can't agree between two government units, you send it out to a royal commission or some commission. This committee is of particular interest because it issues various reports on biotechnology. It reports to eight ministers, has lots of academics and industry people involved. It has issued report that are not bad but have never been implemented. And I don't even know if most of them, if any of them, have been responded to officially by the government other than to thank them. So sending this out to CBAC to my mind is a little bit of an act of desperation. I'm sure the people involved maybe agreed with that, maybe didn't. You'd have to ask them.

But CBAC did report in 2006 saying gene patents are fine but there need to be policy levers within the Patent Act and we ought to think about that.

So that's the time line in Canada.

Let me now play it out from how was this seen by the various actors. So I have to start with the U.S. because Myriad is a U.S. company, and one of their biggest faults was thinking that the rest of the world looked like the United States. And I won't make any editorial comment about how common or uncommon this may be. But they basically thought that they were entering into, in coming to Canada and I would argue Europe and elsewhere, an environment that was somewhat similar to the United States. It was clear that they didn't have much respect for public health care systems. Mark Skolnick was on record as saying he thinks public health care systems are bad. So they didn't really seem to have taken it into account.

But we have to start with the U.S. model. You have to remember Myriad was and still is operating in the red. They lose money. This particular unit has about three people doing sales for the entire world, so very short-staffed, mostly people with technical background, only one commercial person really. So the business model was to split the market between the proband testing, which was fairly expensive, about $3,000, and follow-on testing. The idea that Myriad had was for every test that we do, the full proband test, if we identify a mutation, we expect that there will be 10 family members that are likely to be tested for that mutation. And the idea was we'll license out the ability to do that testing. We'll keep the proband.

Now, given that the cost of the single-point mutation testing is about a tenth, this seemed to be roughly a split of income. Myriad had built a big lab in Salt Lake and so wanted enough coming through its facility to be able to recoup its investment. So it thought that this business plan worked.

In fact, it turned out to be about 1 to 2 for a variety of reasons that we need not get into. Most family members did not get the subsequent mutation testing. So instead of a 1 to 10 ratio, it was a 1 to 2.

In terms of what Myriad tells us -- and the story should be thought of in parallel to this because different people have different opinions -- Myriad said they had an incredibly broad view of what research was, and in fact, their view was you don't need to come to us for a license to do research. And research to them included the provision of genetic tests if it was done by the same people who were doing the research. What they didn't want, they said, is to outsource the proband testing or any of the testing. If you did it yourself, from their point of view, it was covered by the research exemption.

And the whole controversy at Pennsylvania is that the one unit that was being accused by Myriad of infringement was outsourcing it both for academics within the other departments in the institution and for others. So the institution's view was that this fell within the research exemption, but Myriad saw them as basically an outsourcer, just providing testing services and were no different than anywhere else. So I'll leave it to you to decide which one was right. But Myriad's view at least was they're doing commercial activity. They're not doing research activity. So they didn't care if data was provided to patients and so on.

In fact, if you look at what Myriad did, whenever they did come up with mutation data, they quickly made it available within the Breast Cancer Information Core Database even before sometimes they were assured they would get a patent. In fact, they contributed more mutations than anyone else. So they wanted this information public. It was in their interest, they said, for other people to contribute because it just made the test better and so on. So they had no problem with people contributing, and they had no intention, they said, of actually going after anybody who did so. What they were concerned about were bigger operations that were basically outsourcing. So, again, difference of opinion and it's up to anybody to decide whether you believe what Myriad is saying or not, but they seem to be earnest at least in what they were saying.

DR. TUCKSON: Richard, you're making your points very well. This is Reed. We may need you to truncate a couple of the last slides just a bit, but your points are getting through quite well. So if you could cut a few a little bit down, we'd appreciate it.

DR. GOLD: Okay. Well, I can go fairly quickly through the next slide.

So the international model was basically to replicate what happened in the United States, find a local licensee, and get them to do it. So they did that. They tried to do that around the world. They have gone to France and other places. Even though their model was exactly what it was in the United States, they said they were flexible towards other models. In fact, in Japan, they allowed the Japanese company to do all the testing. In France, where it's illegal to export, they were prepared to allow it to happen there. Australia, they cross-licensed. So there was some indication that Myriad was flexible in its business plan.

Since Myriad seemed, at least from what they're saying, to be reasonable in some ways, why did this turn out the way it did? Well, the research community never heard from Myriad. Myriad never made it public that they wouldn't prosecute. So because of the previous patent battles that Shobita took us through, there's a lot of ill will. So the research community didn't believe Myriad, and so they thought by contributing to the public database, they'd be exposing themselves to patent infringement.

The public health authorities didn't like this business model because, as I said in my previous presentation, there was no ability to manage the health care system. And generally, Myriad thought its business plan was like selling chairs into Canada, and obviously, there are reasons to think that that's not the case.

So what was the health care administrator's view, going ahead a couple of slides? As I said, they were concerned about their ability to determine who should get testing when, how to integrate genetic counseling, how broad a population. And they wanted simply time. Now, they never told Myriad they wanted time, which is another problem.

So what were the failures? How did this come about?

Well, Myriad certainly never informed the research community of what they wanted.

They misinterpreted what the government was saying. The government wasn't saying we're not going to license it. It's that we need to think about it. They just didn't say so explicitly. But Myriad said, well, six months have gone by. Let's escalate it. Escalating was the exact wrong thing to do. What it did is it left the government with the impression, okay, these guys are intransigent and you can't negotiate with them. So the government felt this happened too quickly.

Also, a subtlety in the European opposition, the person who was helping on the government level said that -- the French government purposely didn't launch the opposition because if the French government launches the opposition, it means they're against gene patents in general and the French government was not. What they were signaling is that there may be a problem with this particular patent, and in general practice in Europe, launching an opposition procedure, despite all the rhetoric that was happening in the press, really is an indication, please negotiate with us because we're going to challenge your license. Let's find a solution. Myriad didn't know that. They weren't well advised or they didn't find out, and so they missed this opportunity that France was offering them. And I'm not saying all the intervenors believed that, but at least some of the main ones in France did.

Underlying all this was a lack of trust that came from the scientific community where there was a lot of lack of trust. Ontario had talked to policymakers elsewhere and all they heard was Myriad always came out with the same offer. They didn't hear options about flexibility. And then when Myriad escalated, they just said, well, that proves the point. So lack of trust there.

There was also some lack of trust between the health department and the industry department in Canada that didn't help.

In terms of institutional difficulties, there was a lack of understanding by Myriad that policymakers and people in industry work at different time speeds, and so they just didn't give enough.

Industry groups quickly shunned Myriad and said that they're the black sheep and you shouldn't blame the rest of us, instead of trying to mediate.

There was no government department that really had both the jurisdiction and the willingness to say let's mediate this. So each one sort of stuck to their turf, were unwilling to move and that didn't help.

In terms of the implications, let me move to that. Obviously, better communications would have solved a big part of this problem. Would it have been avoided? I don't know, but I think it could have been. And what was really missing to get trust was the fact there was no honest broker. There was nobody in Industry Canada who were in charge of the Patent Act or in Health Canada who had jurisdiction to be able to broker this. So that was a problem.

I think also you cannot sell genetic testing services the way you sell chairs. It just doesn't work, especially in a public health care system. And just recently a few weeks ago at an OECD meeting in the Netherlands, the chief medical officer of Pfizer said, look, our business model doesn't work. We have to really rethink it. So I don't think it's just me saying it. I think industry is starting to realize they need to change.

There need to be tools that allow technology assessment and a roll-out of technology in a way that makes sense to the health care system.

So I'll stop there.