CRISPR: REGULATORY CHALLENGES AND OPPORTUNITIES

Panel Moderator: *Louise Fresco*
October 17, 2018 – 3:10 p.m.

Introduction

Margaret Catley-Carlson
Council of Advisors, World Food Prize

Thanking Previous Panel

From this panel we had real looks at the importance that research will have as we go on in the future. There's some confidence that the public is now more mature in its expectations of research results, but people thought this could make the acceptability of research results both easier and more difficult because there is a wider range of expectation. There was some good audience response from the idea that this should be hurried up, but the panel thought "not at all." As I said this was a good panel with a lot of fresh and feisty ideas and I think again we would give them another round… They don't win the prize for getting off the stage the quickest.

CRISPR Introduction

So our next panel is on CRISPR, so I would like to ask Louise to get her panel to move up onto the… (As you'll notice, we don't get coffee breaks in this place. There's coffee and water out there, and you go quietly.)

The previous panel talked a little bit about CRISPR. I think if you'd been here four years ago, you would notice that most people looked rather baffled when CRISPR was mentioned. Are they talking about a new character of lettuce, crisper and better? But as the years have gone by, there's much more knowledge. I think this panel will still have to do a little bit of explaining about what CRISPR actually is, but there's a great deal more knowledge than there was a few years ago, and this conference has had a good deal to do with that.

You've got really good people to talk about this this afternoon. And again let me remind you that if you go to the website, you will get the full background of this very impressive group. The moderator is Louise Fresco. She's the president of Wageningen University, one of the best agricultural universities in the world. I want to stay friends with the heads of all of them, so therefore is "one" okay? But she also, just like our last university president, she finds she is running a university presidency so easy that she's written a number of books, fiction and nonfiction. And she's written a wonderful one called *Hamburgers in Paradise.* Now, if the title of that alone doesn't make you go out and buy it, nothing should. It's a really good, well-written, very witty book.

Greg Jaffe has worked on biosafety issues in the United States, Kenya, Uganda, Tanzania, Ghana, Malawi, Ethiopia, Indonesia, the Philippines and Nigeria. So he has a very wide, comparative experience that he can bring to us. Very interesting. Before that he was a trial attorney—Isn't that interesting? Yes.—in the U.S. DOJ, Department of Justice and a senior counsel for the EPA. So that's an interesting combination. (I won't make any jokes about that at all.)

Dr. Dan Voytas is the Chief Science Officer and co-founder of Calyxt, a consumer-centric food and agriculture focused company. He co-invented the TALEN technology, which is one of the premier gene editing platforms.

And Ren Wang. Hi, Ren. I haven't seen you for years. Ren Wang is the special advisor to the chairman of BGI in the world's largest genomic organization. He guides them in the interior cooperation and agriculture initiative, and he is obviously from China and an important advisor to many Chinese authorities.

So, Louise, good luck!

Panel Members

Greg Jaffe	Biotechnology Project Director, Center for Science in the Public Interest (CSPI)
Daniel Voytas	Chief Science Officer, Calyxt & Professor, University of Minnesota
Ren Wang	Special Advisor to the President, Beijing Genomics Institute

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Panel Moderator

Louise Fresco
Member of the World Food Prize Council of Advisors &
President of Wageningen University & Research

Thank you very much, Maggie. Thank you. Ladies and gentlemen, it's a great pleasure to present this panel to you. Given the timeframe and given the importance of the subject, we're mainly going to focus on the substance, and there will be ample time for all of you to ask questions and enter in today.

Just a few words on why we wanted to have this panel, and I actually had to twist Ken's arm a little bit to have this panel and to have it today. The reason is that we don't want to particularly talk about CRISPR-Cas or more broadly new breeding techniques or partition breeding, because I think the importance of that and its potential is very clear to all of you. I guess all of you know more or less we're talking about. So we're not going to go so much into the genetics, but we're going into the question of how we can make sure that internationally we have a regulatory regime, given all the differences that we have now between countries, that actually allows to address the pressing issues of today, the issues of draught, the issues of hunger, the issues of accessibility for small countries, small producers, poor consumers, and so on.

Now, I had already had this panel in mind when on the 25th of July the European Court of Justice gave its verdict on CRSPR-Cas, our new breeding techniques or the mutagenesis or

what-have-you, basically saying that all products derived that way would fall under the GMO regulation. And that, for us in Europe, with full support of the rest of the world, came really as a thunderbolt, because it means entering into a game of enormous regulatory complications; and it really blocks a lot of the progress. So needless to say, we as scientists in Europe are very worried about this, even not just as a scientist but I'm proud to say that our students in Wagenagen and have immobilized their counterparts at the European universities and have said—"Don't limit our current generation of new breeders, new Norman Borlaugs, by regulation when lawyers decide on things that, where the public, let alone the public that is at stake that has a stake in the future, the younger generation have not been heard, something is really wrong.

So that's where we stand now in a world where the American rules and regulations are quite different from the ones in the rest of the world, quite different from the ones in Europe. Our aim today is not to accuse or vilify people but to ask ourselves—What's the best way forward? And I think you will find that our basic bottom line here is optimistic.

So without further ado, I'm going to give the floor to our first introductory speaker, Greg, who gives us a little bit of a painting of the whole landscape. So, Greg, go ahead.

Greg So thank you, Louise, and good afternoon to everybody. I am the token lawyer on the panel, and you can't really talk about regulations without having at least one lawyer on the panel. And I have sort of spent many years of my life following the legal issues around biosafety and around GMOs and then following the issues around gene editing. So in the next couple minutes what I thought is I'd give you some observations about the debate that's been going on about the regulation of gene-edited agricultural products.

And it really comes down to one question that's being asked by many of the different stakeholders and regulators. And the question is—Is a gene-edited product a GMO or not? If it is a GMO, then it's regulated like a GMO; and if not, then it's not regulated. And we can talk about whether that's the right question, but that is the question that's really being asked by a lot of the stakeholders around the world.

And in deciding whether a gene-edited product is a GMO or not, there's sort of three different criteria that people are using to make that distinction. One is whether there's any foreign DNA or a transgene in the final product. So this means that DNA from one species has been introduced into the other species with the gene editing. So that's been one criteria that some people are thinking should be the criteria in making the decision of whether it's regulated or not.

A second one is whether the edit could be found in nature. And the best way to describe that is that the edited crop or animal variety sort of mimics and copies an existing genetic sequence that already exists in that crop or animal's population. So that's the second one.

And the third one that people are using is whether the gene editing could have been produced through conventional breeding such as mutagenesis or irradiation. And this sort of means that the genetic change could have been produced with another method, but it's being done here for gene editing because it's either quicker or more precise or

there's a reason to do it there, but it could happen by one of what we would call traditional methods.

And so that's sort of the three criteria that different countries or different stakeholders are saying should be the way that we decide whether something gets regulated. So far most of the countries around the world have not publicly stated whether they will regulate gene-edited crops and, if so, how they're going to regulate them. So I think what we're talking about here today hasn't been decided by most countries.

But there are a few who have made public pronouncements about it, and what I can describe those best is by saying that they form a spectrum. So on one hand we have countries like the United States, whose initial policy pronouncements suggest that the same laws that have been applied to GMOs will be applied to gene-edited agricultural products. What does this mean in practice? So today there are three different laws that are applied in the United States to GMOs, and some GMOs are regulated and some aren't regulated. And similarly those same three laws will be applied to gene-edited product, and some of them will be regulated and some of them will not be regulated.

So that's one category of countries. We have some countries such as Israel and Argentina, and those countries have made the determination based on that foreign DNA that I mentioned earlier. So they've said—"If the final product doesn't have any foreign DNA, then we're not going to treat it was a GMO. We're not going to regulate it." And that's done on a case-by-case basis, but that's their decision.

And then we have, as Louise said, we have the European Union, but the European Union is not the only one. A New Zealand court also said that they looked at the definition of a GMO in the statue and regulations, and they said that gene editing fell within it. So we have not just the European Union but… So that means that all products that are gene edited will be treated just like a GMO and go through that regulation. You know, I would say that it's unlikely, given the 200+ countries that we have around the world that we're going to have harmonization and everybody's going to come to the same decision. And I think especially in the short term that's clearly not going to be the case. And we can talk on this panel about some of the implications of that.

So moving forward I think the detail, I think the devil is really going to be in the details, and the regulatory that we discussed is going to be nuanced, which we know is difficult. But these differences in the regulatory systems will cause obstacles to broad adoption of gene-edited crops, and I'll just give a couple of examples.

They may cause trade disruptions. They can lead to market segmentation. But they're also more importantly going to confuse consumers about whether these things are safe or not, no matter which regulatory system you have. No regulation, consumers say—"Why isn't it being regulated? Is it safe?" Too much regulation—"Oh, it must not be safe is why it needs all that regulation." So getting that balance right is really going to be important.

So I think our challenge here today on this panel and as we move forward with this is sort of to think outside the box. I'm going to say this—You know, I don't think regulation is a dirty word, and it has its value, and it will ensure safety and also help,

as a side benefit, help secure consumer acceptance. If it's done properly, it can establish the pathway to market, which is good for investment and for trade. But if it's not done properly, it can stifle and prevent the adoption of this technology.

So how do we establish a risk- and science-based regulatory system that's fair and functional? Can we establish that risk-based proportionate regulatory system that makes those distinctions among the different kinds of gene-edited products that might be out here, some of which will mimic like transgenics and some of which will mimic conventional breeding. And how do we get those to market without delays to the products that farmers need and at the same time getting consumer acceptance.

So I think that's our challenge—to get the regulators, the lawyers, all the different stakeholders together and be more creative and figure out what can work. And I'll leave it there.

Louise Thank you, thank you, Greg. As you know, lawyers always have lots of words to explain things, but they also have very complicated things to explain. Thank you. That was a great contribution. Dan.

Dan Yes, so I guess I'm a practitioner of gene editing and have been for some time. So I'm a professor at the University of Minnesota where I've been working on gene editing and developing new technologies and new approaches. As was mentioned, we developed the TALEN technology in collaboration with colleagues just up the road at Iowa State University. My lab at the University now practices CRISPR-Cas, also trying to implement it in plants for plant agriculture.

But early on I realized that clearly this technology has real-world applications that can provide benefit. And so I formed the company called Calyxt, which, the goal was to use gene editing really to produce healthier foods. And that company has been around for eight years now, and we have our first product that's going to market this year. We believe it's probably the first genetic-edited crop to enter the food supply. This is a soybean variety that produces a healthier oil that's free from trans fats, and it has a fatty acid composition more akin to olive oil or canola oil. And so we are harvesting right now 17,000 acres of that product. We're contracting with farmers and crushing the seed and hoping to sell the oil.

And so it's through my experience at the company that I came to appreciate the impact our regulatory policy can have on new technology and bringing it to bear to solve real-world problems. So we went to the USDA in the early days and brought our gene-edited products to them to find out how they would regulate it. And it didn't have a trans gene. It didn't have a pest foreign pest plant pest or sequence within the genome. And really they concluded that it was no different than an outcome that could be created through sort of traditional mutagenesis unregulated processes. So they gave us the go-ahead to plant our products out into the field and see how they perform.

Now that we have a product that's going to market, we're talking to the FDA to make sure that the food that we're developing, the food ingredient that we're developing, will have no harmful consequences. So the existing regulatory policy really carefully scrutinized the products that we're making to ensure that they're safe for consumption and for the environment.

But when I circle back and think about my colleagues' academia, it's there that I'm now starting to see the impact of regulatory policy. After the European court decision, my inbox was flooded with emails expressing dismay by my European colleagues that, you know—Are they going to be able to receive governmental support for their research? The possibilities for industries and companies like the one I created here might no longer be possible in Europe. And so there was a lot of frustration there.

And then also we're not just developing healthier food ingredients for the U.S. market. In my academic lab we've made varieties of cassava that could increase yield and reduce labor in Africa. We have virus-resistant lines of rice that could be deployed in East Asia. One of my graduate students is in the audience. She is the daughter of an Ethiopian farmer who grew teff, and she is working. So this is a staple grain of Eastern Africa, and she wants to use gene-editing to improve teff so that yields can be increased and the people of Ethiopia can realize a larger harvest.

But can we deploy these technologies? Right now those products and the products we created are sitting on the shelf waiting for some regulatory guides to how to get them out into the field, out to the farmers, and to some of these real-world problems. So my big concern about not having harmony, global harmony in regulatory policy is that the technology really is not going to be utilized to its full benefit and full potential to solve issues of food security.

Louise Thank you for this very practical sort of view of things. And I think here in the audience, they are of course particularly concerned with the fact that most if not all African countries have very little regulation. And for them to, all of them, develop that by themselves and have the capacity to also monitor that is going to be a hugely time-consuming issue. So having some kind of format for regulation might be very well something we want to move towards.

But before I take more of the floor, I think, Ren, your experience in China is particularly interesting. So tell us what to expect from China—how does it work? What are you doing on the global stage?

Ren Thank you very much. First of all, let me take this opportunity to say a few words of my appreciation really to Ambassador Ken Quinn and also the Foundation of the World Food Prize for bringing me here. It's really wonderful to be back to this very inspiring event. Now, when Louise asked me to join this panel, I said, well, one accommodation is that I will not speak on behalf of the Chinese Government nor on behalf of FAO, which I served for five years before I returned to China.

So with that, let me say that, okay, the development of let's say products and services of biotechnologies, particularly transgenics, GMOs, and now on our topic of the gene-editing, this is very, very interesting in China. But I have to say that may be disappointing to many of the colleagues who are interested in knowing what's going on in China, the first thing I have to say is that there has been no development, no progress in terms of government approval for the application or commercial application of transgenics, let alone gene editing, let's say, products and services derived from CRISPR technologies.

Now, in China now the people believe, let's say, the research community believes that there is quite a strong tendency that products derived from CRISPR technologies, let's say gene editing, will be categorized same as GMOs, let's say transgenic crops, which is rather disappointing from my point of view. However, I wanted to share maybe three of my observations on the trends of the development of CRISPR, the R&Ds in CRISPR technology in China.

One is that the very, very rapid decline of the cost of genome sequencing in China associated with development of sequencers and even DNA synthesizers. Now as we all recall, probably late 2001 when the president of the United States together with Prime Minister of the UK announced the completion of the first human genome, that was at a cost of 3½ billion dollars after 13 years of research in a partnership of six or seven countries. Right? And that was a really vivid memory. Now, this year the company Illumina in the U.S. together with BGI announced the sequencing of one personal genome, complete human genome, is at a cost of $600, and you can do it in two days. And now the new machine, new sequencers, can complete 60 human genome in two days, and the analysis can be completed in two hours. Now, this is much more than the moral law of IT tech industries. So as you can see, we are now moving to a new era when can think the sequencing cost is almost negligible. Right? And now what do we do. That's one.

And the second observation is actually very much reflecting what we heard from Secretary Dan Glickman of our previous panel. There's an interaction and reference with medical science in the rapid development and even deliberations by the government even in China for therapeutical applications of these genetic tools and products, including genetic screening, sequencing, applicational sequencers. And even through the use of CasPERs now there are rapid developments moving into government applications for approval for Parkinson's disease, for high mercies diseases and also a beta type [inaudible], and all of these are moving rapidly. So that, I think, will have profound impact, actually accelerating the considerations on crops and livestock.

Now, the third observation is a very strong trend, is that as I see it, there's a whole new generation of scientists—young, dynamic, and very capable of using the most modern technologies and research tools in China in collaborations and partnerships with universities and institutions, private companies around the world, working on this gene editing. A whole range of crops are popping up, as well as like creating sort of mini pigs for experimental and even for pet purposes and also medical again, from genetic diseases as well as infectious diseases and cancer. So there's a whole generation of new scientists, is really the place where we see hope.

So all of these three, as I see it, is forming into such a strong kind of a trend that will impact on, let's say the approval, hopefully by the Chinese government on the commercial application in the future of not only CRISPR-Cas products but also transgenics.

Now, let me also quickly mention two concerns that I have also. One is actually an obvious missing or lack of adequate public education about this new technology. Although the science is developing, a new generation of scientists are there making a

lot of scientific publications, but public opinions which will strongly influence the government policies, is still very much weak.

And secondly, probably it is not only in China but many other countries as we see, is the ministries in China in the Chinese government machinery that actually will have a say of policymakers on the approvals don't talk to each other. The Minister of Agriculture and Rural Affairs does not necessarily consult with the State Commission on health, for instance, about the approval and the evaluation of genetic, let's say, therapeutical medicines and tools and technologies. So is the real worry. I'll stop there.

Louise Thank you, Ren. I think some of these issues actually are quite recognizable to many countries, to at least some of your last points. But also in general I think there is a younger generation of scientists that is far less, even in Europe, far less fearful of progress and of science and technology.

Now, maybe just one quick reaction, not talking to everybody on every [inaudible], but, Greg, do you want to react to anything that has been said?

Greg Well, I think what we've all sort of said, I think, which is important is that the regulatory landscape out there is really uncertain. And what uncertainty does is prevent products from getting to the market. As Dan mentioned, there are things in the lab that could be used in Africa, but it's not that they're over-regulated or under-regulated but nobody even knows what the regulation is. And until you do that, it's a non-answer ends being a no answer. So I think that's something to just keep in mind, that the longer we wait to have this discussion and make some decisions, that ends up being a default "no" to a large extent.

Louise Yes, absolutely. Anything from your side, Dan?

Dan Yeah, I mean one question that often comes up is—How do you know that you haven't done something else to the genome in your editing and that you've created something that could possibly be harmful? And to get to Ren's point is we now have really powerful analytical tools. If we edit a plant's genome, we can sequence it and say—well, we actually only made that precise modification to the genome. Or if that gene modification changes fatty acid composition, we can analyze that and make sure there's nothing harmful there. So I think we have tools and technologies to ensure that the products we create are safe.

Louise That may be kind of guaranteed. Any comments from your side, Ren?

Ren Just make one more comment, and that is, it's the role of the private sector. Since I now left the public sector and joined sort of the private sector, which is my new experience, I see there are private sector companies who are not necessarily for the purpose of making money to develop and applications are CRISPR technologies. I'm quite encouraged, actually. They are really driving down, through competition actually, driving down the cost of sequencing and also syntheses. Synthetic biology—now there's such a trend, so I see positively.

Louise [inaudible] if what you say is that when we work on public outreach and building public support, the private sector has to be part and parcel of that. Public outreach

cannot just be a government issue. Okay, the time has come to open up for questions and comments. Now, in order to give everybody a chance, it's really going to be important that you be brief and that you concentrate on a question rather than on a statement. So I see Ismail Serageldin running to the microphone. Can I have a show of hands of other questions, or have you been… Yeah, I'm looking at the mic. Okay. Queue up and speak, Ismail first.

Ismail Thank you, Louise. I just have three quick questions to the panel. Number one is—we just finished a major study for the National Academy of Science on human genome editing. Under what circumstances should it be allowed? And there the guidelines are for the research labs and so on and for applications to humans. But nevertheless, in the preparation of that, which took about a year and a half, we were concerned about the appearance of indels, which are unwanted inserts and deletions that occur along with CRISPR.

Secondly. There has been a...—How shall I say this?—discovery that in fact, because CRISPR has become so easy and so inexpensive with the average cost about $200 for a whole kit, including your guide RNA, which you can get on the internet. There's a lot of do-it-yourself young people which are reminiscent of hackers who would take their laptops and sit in coffee shops. And they do things and experiment on themselves. They experiment on each other like they would do with drugs. So that this is not going to be contained in that side. And maybe—here's the question for the lawyer—we need a different sort of mechanism as the telephones have allowed for apps and for people to design apps for the iPhone or for the Samsung or for whatever, and then get somehow acceptance on some of these things. And I think that therefore that requires thinking outside of the box in both cases.

Louise Next, we are going to collect a couple questions and then let the panel react. Next question. I can hardly see you, so you have to speak up who you are.

Q Hi, Louise. It's Lawrence, Lawrence Kent from the Bill & Melinda Gates Foundation. My question for the panel, and maybe starting with Greg but if others have comments, is about the possibility of developing model regulations and model laws. I think our experience with GMOs was that some very toxic model legislation and model laws were developed through Cartagena, through the African Union and others that really sort of set the baseline in a bad way. And currently, as you described it, we're facing somewhat of a regulatory void when it comes to gene edited products. And a void is dangerous, because others might come in with model rules and regulations that really are designed to block the technology transfer. Are any of you aware of any efforts to develop model laws or regulations, perhaps drawing on some of the Australian expertise?

Louise Thank you. Well, in fact, one could say that the European Court of Justice has stepped into a void already. Anyone have comments, questions? Oh, this side, yes. Go ahead.

Q [inaudible] Thompson, Michigan State. Quick question. If you have an event that's really clean that's something that could happen in nature, what's the plan to regulate something you can't detect?

Louise Really fantastic question. Thank you. Next?

Q Hi. Pedro Sanchez. I'm not a geneticist at all, but I'm getting sick and tired of fears that have been proven wrong by many years of safety and observation that still impede Africans to have the advantages of GMOs. And now with this new technology, it seems to be judged… There needs a lot of safety. At the same time, looking at the medical science, they have used GMOs for a long time. So we don't want GMOs, or some of us don't want GMOs in our food, but we sure have them in our medicine. I think the whole thing is getting a bit ridiculous. It's been a long, long time, and I hope that the world can come to grips with this finally.

Louise I guess you hear from the applause that many people agree, but the trouble is, it's more than just an issue of language. It's an issue of emotion, and emotions don't go away like that. Next question, please?

Q Hi. My name is Jorge. I'm from Alabama, and I'm part of a farmer community. And my question is—with GMO crops, can seeds be used for the next harvest? Because I know I heard like, yes, it can, but after you keep using the seeds, they might not produce well, and after each harvest you need to get new seeds. So I want to know—if you can't reuse the seeds from that crop, how do you keep getting more seeds? And is that efficient to keep buying new seeds instead of using the ones that you just grew?

Louise Thank you. Yes, this raises the issue of hybrid seed, for example. We will get Dan to reply to that in a few minutes. Any other questions? Yes, please.

Q Hi. My name's Jay Edmond McGee. I'm from Minnesota here. My question to you guys was—What can we, the younger generation, do to get these genetically modified organisms better understood by the public? I think there's a lot of skepticism between the less educated areas on GMOs.

Louise Yeah, thank you. A very relevant question. I go back to the other… We don't have anybody in the middle there, so…

Q Can you hear me? Yup, there we go. Okay, my name is Mark Gee, student at Purdue University. And I was wondering—what would your response be to someone who says, "Food security is not an issue in the United States and Europe. Medical issues are. Therefore, we need CRISPR in medical technology but not in food research." Thank you.

Louise Okay, thank you. I'm going to get the panel to give a very quick reaction, just select maybe one or two questions. And we can have another round with the audience. And for the next questions, I want women to start off the questions. What's happening here? The room is all full of women, and we have men asking questions. I cannot tolerate that as a chair. Good. I'm starting with Ren. Ren, any comments from your side?

Ren Yeah, I wanted to pick up the comment or question about is the model lost, or are models sort of a regulations. Of course there are commonalities, right, there are common concerns and considerations, let's say, for developing the methods and regulations for evaluations of these products. However, you have to consider this is country specific, right? Countries are different. They have different legislation systems, different culture and so on. So there is that concern.

Nevertheless, let me just share with you one interesting sort of lesson that we in China we learned when the, let's say the research community particularly has been very much frustrated by the lack of development or lack of progress in approval, government approval, legislation approve for the commercialization of GMOs, let's say transgenic. And one big lesson that was really written by quite a few people on public media was this split, let's say, between scientists and public. There was basically no campaign or let's say no effort of media for educating the general public about the GMOs. So when a scientist presented strong evidence and so on to convince the ministries to have quickly released the approval for the environmental release of transgenic crops. And there was a strong opposing sort of opinion from the general public. So now the science community in China have been saying in conferences, again not on general public media, that we should learn the lesson. And they also quoted, actually, the experience from the United States. I leave it to you to judge whether it's true. They said, "Well, their one big reason for the United States of America being able to, let's say, commercialize these transgenic crops was the advanced public education. That was something quoted from the Chinese media. So now the scientific community is saying that we should make effort now. The anticipation of the availability of gene edited products and services that I want to make emphasis.

Louise Dan, at least you have one question to reflect.

Dan A few of the science questions, I guess. So I mean one of the first ones was, you know—where do you draw the boundary in human gene editing? And generally it's, you limit it to the somatic cells. You don't edit the germ lines if you can pass the change to the next generation. So if you have cystic fibrosis, you try to edit the cells of the lung to cure the disease.

But in contrast, in plants we try to make a stable, heritable modification that would be transmitted from one generation to the next. And so you could in fact grow the seeds over multiple generations. I mean, there are, as you mentioned, hybrid systems where in the progeny of the hybrids over multiple generations may not behave as the parents did, but that's an inherent problem in planting the progeny of a hybrid, and it would persist if you also had a gene-edited hybrid.

And then the final question that I will address is the one concerning—How do you distinguish and edit from natural variation? And I think, you know, the USDA has proposed that, well, if you move… Let's say you have a disease resistance allele in potato that confers blight resistance, and you could edit a cultivated potato to have that same genetic variation. You could cross it in also to create a cultivated potato with that same genetic variation. So really the two outcomes are very similar, and so in some cases it is not distinguishable.

Louise Thank you, Dan. Greg.

Greg So I'm going to try to quickly answer a number of different questions. So Ismail's question about the DIY young people and how do you regulate that—and that's why I think we need to think about regulation more creatively. So we think of regulation usually as a product developer going to the government and things like that. But there are other kinds of regulations. There could be codes of conduct, so we could have general codes of conduct that DIY labs and others use on how to properly use this

technology—what's in bounds and what aren't in bounds, what are the best practices types of things. We could also have licensing things, so when you get the kit from the… Because even DIY people are still going to get their sequences somewhere, something like that, that with that, there comes some licensing, some agreement to use it in a certain fashion and not to do human testing on it or something like that. So I mean if somebody wants to violate and do something illegal, they're going to do it anyway—the laws don't prevent that. But I think we have to think more creatively, potentially, on how do we oversee this, and think about it was overseeing than just regulation necessarily. So that's a question there.

To Lawrence's question about developing model laws or provisions, I'm not aware of anybody doing that now for gene editing around the world. I think most of the stakeholders are still in this battle of—is it a GMO, not a GMO—as opposed to, sit down and think about what is the proper type of oversight that might be needed here. My take with experience from models in the GMO context is, I mean I think the problem with a very prescriptive model law is a lot of countries want their own sovereignty—and so they want to change that, and their changing of that sometimes can be more stringent, sometimes it's going to be less. But they don't want to just adopt something. They somehow think if they adopt it, we haven't put our own thought process into it. So I'm not sure I'm in favor of a whole model law or things, but I think clearly an outline and clearly some of the key provisions about what we're going to do and where the buckets are for the different kinds of things would be important. In terms of regulating something where we can't detect it, that is true, and that becomes an enforcement issue; but we do have laws that do regulate intent. So "pesticide" is defined in the United States as something that's intended to kill a pest. There are lots of things that could kill a pest that aren't pesticides and don't need to be registered because they're not intended to be. And, similarly, food is intended as something to be eaten. So we do have laws that talk about intent. And so could we design a law that talked about the intent? You know, if you intentionally edited something, even if you couldn't detect it, that could be regulated? We could. There are enforcement issues around it. I'm not suggesting we do it; but as a theoretical matter and as a legal matter, one can do that in it—whether that's the right thing to do, that's why we need that discussion.

And finally, just about the question about sort of the medicine dilemma. I think what's interesting about the CRISPR debate is—you know, what happens in the medicine could greatly impact what people's perceptions are in agriculture if we do some things like cure cystic fibrosis or deal with sickle cell anemia. That might pave the way for people to be much more open about gene editing in agriculture when they weren't in GMOs. So these things are being developed simultaneously, and I think the public gets more in the press about CRISPR with medicine. And so to some extent, how they feel how that works, positively or negatively, could affect how it affects agriculture.

Louise Thank you. Yeah, very useful. I have room for two really brief questions, so back to the microphone—ladies only, going to be really strict with you guys. And ladies, you have to run also. Yes, go ahead.

Q I'm wondering in time of still strong prevalence of religion, how that plays a role in public perspectives of genomic editing and how that be combated in media or policy or even just as scientists.

Louise Yes, thank you. Good question. Second question.

Q Florence Mambobo, Africa Harvest. The one, gene editing itself is the background of GMO. Just because you are seeing gene editing, you are really telling the story that you are editing some genes, and that creates that whole story about there is something to be regulated. But if you look at the experience of GMOs in Africa, Africa looks at what's happening in Europe—what Europe has said is going to be GMO, the African countries are going to look at this in the same way. And so we have to figure out… Most important is education, information. Just as companies are investing in new research—and I think this should be [inaudible] have been discussed here—outreach, extension, information. If you are coming with a new product, I think you can't escapreto educate, to inform the consumers and the farmers. But we have to invest in this thing. Thank you.

Louise Yeah, good question. I want the very, very last question on the other side.

Q So Barbarafrom Uganda. I've been listening, and I'm worried, because we are already struggling to get what we call the biosafety laws in place in Africa, and now we are talking of other regulations for CRISPR-Cas or the gene editing. So I'm wondering if we are going to go through this same process, aren't we going to again to miss a lot about this technology? Why don't we find alternative ways of regulation instead of asking for new model laws or laws to be considered for this technology? So I want to agree with Florence. Maybe what we need is to educate more the populations and to be clear on which will be regulated and which ones are almost natural, look like natural that we don't need to regulate them. Thank you.

Louise Thank you very much. All very relevant questions. So my panel gets exactly one minute, and you have to look at the clock to get one minute a person to reply whatever question comes to mind. I'll start with Dan.

Dan A few of the questions' concerns for the public acceptance or how do we get the public to embrace the technology, and I think if you look at the first wave of our technology, we made traits that benefited the farmer—herbicide tolerance, insect pest and pathogen resistance—which is a little bit of a disconnect from the consumer. But if you make a healthier cooking oil reduced gluten-wheat or products that the consumer can see a direct health benefit to, I think that in part could help accept… People could connect to the technology and maybe accept it more willingly.

Louise Thank you very much. Ren.

Ren Thank you. I want to make quickly one point again. That is looking to the future. My suggestion really is for the governments and also even the public to really pay attention to the capacity development, to nurturing and developing the next generation of scientists who can not only research but also the applications, the use of the gene editing technologies, especially for developing countries. Here let me just make a one-minute advocacy for this wonderful initiative called African Orphan Crops Consortium, which was initiated actually by American scientists and together with international, the World and Agroforestry Center in Nairobi. And then their starting point…, two actually. One is to sequence all of these more than a hundred

orphan crops which are used in Africa, and secondly is the nurturing of development of a new generation of plant breeders. That's important.

Louise Thank you, very important. Greg, last but not least.

Greg I'm going to try to respond to Barbara's question. I mean, ideally we shouldn't be writing a law for each new technique or technology, a GMO law; because if we do write that and then we write a law for gene editing, and now five years from now we're going to have some new technique, some new technology. So we should write… If we're going to write any law at all and have oversight, it should be either a product-specific thing—we're looking at food kind of thing—with a technology provision, with giving the discretion to the regulator to figure out which of the products that have different new technologies need oversight at all and what that oversight should be. Because we clearly don't want to keep going back to our parliaments or congresses every four or five years for every new technology that comes along. It's not efficient, and it's really going to hold things back. So the better thing would be to have some broader umbrella and give discretion to the regulators to figure out which products have risks that need any oversight at all.

Louise Thank you. I think we had a fantastic panel, and let me just share with you a few ideas that I retained. Obviously, this is the tip of the iceberg; there is so much more to be said. I think the first conclusion is—We aren't in a regulating void. There are very few country that have been actually regulated something. And the whole question is—How much regulation is needed to make sure, not only that on the one hand science can go forward and find solutions for all these pressing issues, but on the other hand the public is comfortable that it's not being exposed to undue risks? The longer this void continues, the more uncertainty there is with the public, the more risk there is that companies feel uncomfortable, that governments don't know what to do. And that is really a serious situation. So I want you to go home with a sense of urgency there. This is not something that can be left alone for ages. Not regulating means in fact also regulating but regulating in the wrong way, based on prejudice, based on misconception, based on all kinds of things that actually will hamper not only science and public acceptance but also things like trade flows. That is one, I think, important conclusion.

The other one is that it all hinges on public acceptance and that we should not fall into the trap of the mistakes that we've made with GMOs, a mistake that has to do with not explaining enough—and I think these scientists have also been guilty in some ways for remaining too long in our ivory-dome towers and not communicating sufficiently.

Now here's the last, most important comment, and that is: We end on a note of optimism because there is a huge, new generation called plant breeders, of geneticists, of scientists, of lawyers, of economists who really see the importance of moving forward. We see the need not just to work in their own countries but also in other countries. And they will want to move. They don't want to stop. And they need to have the tools and the means to do it but also the security of some kind of agreement that doesn't need to be a legal, regulatory framework but some kind of agreement between governments and countries, including the private sector and NGOs, that we can move forward and that we can put into practice that wonderful experience that we

now have, that we can do something with far more precision and far more accuracy than any other generation has been able to do before us.

So on that positive note, I want you to thank my panel and go away and think about it.