2022 Innovation Council - Bobab discussion about bio-manufacturing in emerging regions

Transcript

Tuesday, 08 February 2022. 15.00 – 16.00 Session was recorded, with link available <u>here</u>

Jen Brant

- > Introduction of Bobab and Innovation Council.
- > Introduction of speakers. All bios are posted on the Bobab website.
- > Kicking off the discussion, starting with Anissa Boumlic: What role does Merck LS play in global value chains for vaccines and other biologics? How you work with governments or companies to extend bio-manufacturing?

Anissa Boumlic

- > The Life Science division of Merck offers partnerships and support to various entities, whether in research, production or institutions, to advance the development and production of biomolecules or, in particular, biological substances.
- > We are also involved in other aspects. We have our own contract manufacturing organization dedicated to outsourcing, for example when companies need to outsource the manufacturing of biologicals, whether it's monoclonal antibodies or viral vectors for gene therapy. And we also provide testing services, for example for all the control and testing procedures that need to be done before a drug is released.
- > We also provide support for facility planning and design in general. So in terms of how we fit into the whole ecosystem, it's not just about technology, which we sometimes refer to as a technology provider or technology solution provider. That's how we see it, but we also actively participate in different partnerships and collaborations, especially to advance manufacturing, and we will talk about that, but also vaccines, because we think it's not just part of the role of a technology provider to participate and contribute to sustainable manufacturing.

Jen Brant

> Follow on question for you, Anissa: How do you work with governments? Can you give us an example?

Anissa Boumlic

> We don't necessarily have a direct relationship with governments. Unless a governmentowned institute or company is developing or producing certain biological products, so the



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relationship we can build is more of a supplier-to-customer relationship. But what we are trying to do is be more part of an ecosystem

> It is really about making sure that we can also offer expertise or thinking for projects that are supported by governments. So we are involved in certain collaborations or coalitions where we also bring in the industry perspective that can help governments understand what challenges they might face.

Jen Brant

 Thanks for this background. Tell us more about the state of place in global biomanufacturing? What is happening in emerging regions already, and what are the trends?
Why are some regions moving faster than others?

Anissa Boumlic

- It is a highly growing market. 10 15 years ago, most of this market was driven by North America and Europe. In the last decades, the low- and middle-income countries, which we call growth markets, have really made great progress, especially China and India. We expect even higher growth from these countries and that is why they have been able to expand their production of vaccines and monoclonal antibodies for oncology in these countries.
- What we see is that the market in Asia in general is growing very fast. And we see not only China and India, but also Southeast Asia and other countries like South Korea. They are also trying to strengthen their manufacturers. What we can see is that in Africa they still have the lowest manufacturing infrastructure, but there are programs and we see initiatives that will allow to increase that level of manufacturing. I think generally all regions are looking to strengthen their manufacturing, whether it's a high-income country or low- and middle-income countries. And we see that the gap between is getting smaller over the years.

Jen Brant

> Turning now to our next speaker, Simon Agwale: What is the AVMI? Tell me about your membership and its collective vaccines manufacturing expertise.

Simon Agwale

AVMI stands for African Vaccine Manufacturing Initiative. AVMI has been bringing together African vaccine manufacturers and groups from the North since 2010. With the aim of building African capacity to develop their own vaccines, membership includes both vaccine manufacturers on the continent and scientists from universities and research institutes working on vaccine-related issues, as well as representatives from regional health organizations such as the West Africa Heritage Organization. Our mission is





essentially to promote the creation of sustainable human vaccine manufacturing capacity in Africa.

Jen Brant

> Let's focus on Africa for a moment. What are some recent advances/successes in enhancing bio-manufacturing in Africa? What were the factors driving success?

Simon Agwale

- COVID-19 has accelerated the number of technology transfers initiated on the continent from only three from before 2020, and the three were basically all in South Africa. And now it's over 10, including announcements by Pfizer, which has partnered with Biovac to produce at least 100 million doses of the vaccine in South Africa, and Johnson and Johnson, and it is believed that all of this will be used on the continent.
- We need to start focusing on upstream manufacturing of medicines and we will have a case study in this regard shortly. We are aiming to take the whole value chain from vaccine manufacturing to vaccine purification to the end of operations. The use of COVID vaccines has been a starting point for this whole project of ultimately setting up end-toend manufacturing in Africa, starting with the research and development and going all the way to manufacturing the vaccine and the development of the process, to the design and construction of the plant.

Jen Brant

You mentioned that there have been three tech transfers before 2020 and then a plethora of announcements since early 2020. Are all of these focused on different areas of the manufacturing process.

Simon Agwale

- \rangle The previous tech transfers were all downstream process or fill-finish operations.
- > With COVID it is a mix, you have both the upstream, which is the production of the drug substance, and then the downstream or fill-finish operations.
- If you look at all the announcements, you can see that the biotech players are looking more into the upstream process, not only for COVID, but also for other diseases. Most initiatives start with fill-finish and then move to backward integration. One focus is on mRNA based COVID vaccines. They are looking at doing the clinical trials of the vaccine that they did this year.

Jen Brant

> Thank you. Just to go back to Anissa for a moment: Simon just gave a lot of different examples of things that are happening across Africa and in different regions. How might one define the success of a production capacity expansion, for example? Based on what



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criteria, and can you tell us the story of some of these projects, you know, how they started, what are some of the factors that are leading to success, and where do you see them evolving?

Anissa Boumlic

- So if we want to look at the continental level, we should look at the percentage of biological products that are produced on the continent. So, while today, as Simon mentioned, we have limited production of less than 1%, the success of this continental strategy is that at least 60% of vaccines are produced on the continent. So that's the target that we're aiming for, and that's considered a success. And that's for 2014, so it's going to take a few more years to reach that milestone, although maybe we can reach it sooner.
- I think the pandemic has acted as a catalyst. We are seeing first signs of success in terms of the beginning of technology transfers and partnerships (and I think that the collaboration between Sanofi Pfizer and Biovac was considered a success on the continent even before COVID it was the first time there was a partnership between international vaccine companies and a local company in Africa.) But what we're going to see next is how that model can be a little bit more sustainable, and that's what Simon mentioned for the next step of success, which is when you have the production of the complete biologic product from upstream to downstream to filling all on the continent. We're already seeing that in Egypt with monoclonal antibodies, and we're seeing that with certain vaccines as well, like in Senegal, for example. But there is definitely a need to increase the ramp-up points. I think the next milestones are to create a local ecosystem where governments create the right regulatory pathway, the right incentives for manufacturers, and the right access to market for manufacturers, and we have started to see that in certain countries. That's the example of South Africa.
- Another success metric for me is when all the conditions are in place to facilitate entry into biologic medicine. In addition to access to regulations and markets, there are other elements that we can look at as success or metrics of success, such as trade barriers that need to be changed. We now know that it is also more difficult for countries within the continent to exchange freely, so we need to look primarily at the scale that is required to make this business sustainable. You have to have access to more than just your own country as a market. So there are also those elements that need to change, and there is a lot of infrastructure in Africa in general. Projects going forward will support that as well. That includes, of course, the African trade projects and the African regulatory authority. All of that will also be taken into account, even though it's not directly related to production, but those are also successes, criteria and milestones that will help achieve that goal.





> Questions about enabling policy environments certainly open up the opportunity to have Professor Mark Schultz come in. Mark, to get started, I'd like to ask you about the key findings of your research that are included in the recently published IP and COVID report.

Mark Schultz

- It's a pleasure to be here and learn from my colleagues on the panel. I think one of our key learnings was that intellectual property was not an obstacle, but rather a facilitator in every innovation step necessary to combat the COVID pandemic. It facilitated the creation of technology platforms like mRNA, vaccine development, and vaccine manufacturing. And why was it a facilitator? Because property rights create exclusivity, of course, but they also encourage investment and create the necessary environment for collaboration. And I think that leads to another realization related to that. We found that there is a great deal of distributed innovation, and that distributed innovation requires collaboration at every stage. In other words, different players had different parts of the solution, and they had to work together to achieve the result.
- If we look at technology platforms, for example mRNA, there were many precursors to > this technology. You could go back to the discovery of mRNA in the early 1960s, where the key components were created in university labs that allowed this technology to become a practical technology. But then the private sector picked up this technology and licensed it, often in the form of patents, to startups that then invested billions of dollars and many years of applied research to create the mRNA technology platforms, which fortunately were ready when we needed them. Companies like Biotech and Moderna were crucial actors in the development of the COVID vaccines, which also required a lot of collaboration and investment. An example of that collaboration is the collaboration with Pfizer-Biotech. They had to work together and the intellectual property rights created the trust necessary to share some of the most proprietary technologies, and also the manufacturing of the COVID vaccines required collaboration. And we found over 40 manufacturing agreements for the five leading vaccines that we could find in the public record by the end of last summer, and they were global, on every continent. Essentially everywhere there were collaborations, as Simon described them, also for the production of key components of the vaccines. And some of those collaborations or with natural and historical competitors like Pfizer, AstraZeneca, and others, they had to collaborate with some of their biggest competitors, which would not have been possible without a trusting environment including IP.
- I think we were surprised at the extent and depth of the collaboration. How many different parties brought together different parts of the solution. We learned that biomanufacturing is an increasingly innovative activity, where many different parties bring different parts of the solution, and they all have their own intellectual property. It's not just a vertical solution with one company developing the technology, developing the





Jen Brant

So we have Simon, who listed quite a number of different partnerships involving small companies, local partners, and then global multinational companies, major innovators that have become very well known, especially after the COVID pandemic. So you're saying that intellectual property is an important part of the environment that allows these partnerships to thrive. What types of intellectual property rights are we talking about? Can you tell us a little bit more about the IP/collaboration dynamic?

Mark Schultz

- I think that these are usually patented technologies that are often developed within the framework of research institutes. And these are usually the first building blocks of a technological platform. And in order for those building blocks to be turned into practical solutions and commercialized, a lot of investment is required. So they are usually patented and either licensed or transferred to a start-up or a larger company, which then, because of the confidence it has in those patents, is likely to invest money and other resources to develop the technology further. As I said, it took another decade after the basic building blocks of mRNA technology were created and another decade of applied research and commercialization to get to the point where we were able to develop vaccines. Another essential form of intellectual property is trade secrets.
- Trade secrets include proprietary information developed in the research and development process. The things that are not yet inventions may never be inventions because they are dead ends. But even knowing what a dead end is valuable information. And when you gather information about how it works for a particular therapeutic or vaccine. And then you develop proprietary manufacturing processes and related know-how - all of those things can be protected by trade secrets. And I think we sometimes worry that secrets have a bad reputation, but we should remember that trade secrets are different than secrets. Trade secrets are legal protections for proprietary information that companies guard closely, but the law protects them, and unlike protection by concealment, trade secrets allow you to expand the circle of trust. As long as one gets the consent of others to keep that information secret, through a contract. You can share it, and that's what Pfizer has done, for example, in expanding its manufacturing capacity by working with manufacturing partners.
- Pfizer is documented to have shared thousands of pages of proprietary information, many dozens, perhaps hundreds of things that they consider trade secrets, all with the knowledge and protection of trade secret law that has allowed them to expand manufacturing capacity worldwide using trade secrets.





Simon, Mark has raised the role of know-how and the role of knowledge transfer in tech transfer partnerships. Is it shared, through some of these technology transfer partnerships, in both directions?

Simon Agwale

- Before I answer that, it's important to mention some of the challenges that local manufacturers face. Vaccine manufacturers are generally reluctant to engage in technology transfer because they have to make large investments in human resource development and equipment procurement to achieve improvement. So basically technology transfer means transferring experience to the local manufacturers, and we need to close existing skills gap by transferring the technologies or know-how from the experienced manufacturers to the local manufacturers.
- It should be a win-win situation, where both parties win, the recipient and the donor, and then it becomes a successful partnership. The government needs to create a natural environment and then provide some incentives. Like advance purchase commitments, market assessment, innovative financing - these are all strategies that we can use to mitigate the risk.

Jen Brant

> Anissa, you have also mentioned market shaping. Can you comment on that point, the need for intervention in that way?

Anissa Boumlic

- I think what Simon mentioned is that there have been some private companies in the past in some countries that have ventured into the biologics space. And what happened in the process is that, again, going back to economies of scale, it's obviously very difficult to compete. If you make small volumes of biomedical products, you can basically get a better return on investment than if you make large volumes. But when you start, you usually start small, right? What has happened in the past with insulin is that certain companies have tried to manufacture insulin in different countries, in Africa, in the Middle East, and in other countries in other regions. And what happens is when they realize it's completely open. Of course, if there are our old tendered base procurements, and of course, any outside company can come in because that company has a large production area and maybe can get better prices.
- > Then it becomes very difficult for a small company trying to enter this field to get competitive prices. So different countries have different strategies. There are countries in Africa that have decided to close the market or to dedicate a certain part of the market to companies that produce locally. That's what we call national preference. And that's not new. China has been doing it for a long time, guaranteeing a certain percentage of the





So you will come to an agreement with the manufacturer in advance. So you're not only giving him access to the market, but you're also making sure that you have access to the vaccine. So there is also this relationship with the manufacturer. These obligations are not new. For example, we know that in the past GAVI has agreed with certain companies to access a certain number of vaccine lots, which also secured the market, because as a company you also want to make sure that it is something that is viable for you. So those are the kind of processes and measures to ensure sustainable production and supply of biologicals.

Jen Brant

> Just to come back to Simon briefly: building on what Anissa said, please briefly tell us about some of the challenges that you see in this area, particularly in Africa, in terms of expanding infrastructure for biomanufacturing. Maybe you can give two or three of those as illustrative examples and also give us an idea of how those might be addressed.

Simon Agwale

- > The first is the initial investment. This is a big challenge. Because the initial investment is huge. You need at least \$50 million to \$200 million to build a mini-production facility, and it's not going to be ready in a year or two.
- > And then you also have to train your staff. You have to recruit trained personnel and so on. So this huge investment gap is very risky for local manufacturers, and we see this as the main risk that discourages vaccine manufacturers from participating in technology transfer.
- > So we think that the solution, as proposed by Anissa, is to find innovative financing that covers this risk. Because, you know, we can't do it without that, we can't get to where we want to go, and that's the biggest challenge we've seen with manufacturers in terms of content.
- > IP is less of an issue. We can always license in technologies, as Mark mentioned, or alternatively, depending on the technology we're talking about, we can develop an appropriate design. But what is interesting is that most of the vaccines that are currently used on the continent are not of a particular design, so that should not be a barrier to entry. So we should focus more on the know-how, because even if these exemptions are granted, how are we going to do that if we don't have the know-how? I think we should focus more on the know-how instead of focusing mainly on the intellectual property exemptions.





Jen Brant

Interesting: you mentioned risk. This could also relate to the IP questions. For example, would you consider abandoning patents and IP – for instance, as a result of the proposed TRIPS waiver – as something that could be perceived as risky and could slow down technology transfer? Mark, what is your sense?

Mark Schultz

- A proposal for a waiver would allow governments to suspend intellectual property rights or in some way try to require the transfer of know-how, and I think that certainly creates a riskier environment. I think we need to think first about how new innovative technologies are developed. Biologics are not like small molecule drugs that are synthesized by a fairly well-known process and manufactured by a fairly well-known process. Each of these new biologic treatments was a new step in technology, and they required large investments from the beginning. And those investments won't be made if potential investors think they might lose their investment. BioNTech and Moderna were startups, and it wasn't long ago that Moderna, for example, was founded in 2010 with billions of dollars of other people's money, and those investors aren't going to decide not to invest out of spite.
- Abandoning intellectual property is a tough proposition because things like abandoning intellectual property make the investment riskier. When you invest in a biological product, you have to accept that the investment is likely to fail. Most potential treatments don't come to fruition. Most companies are not successful. But you accept that when you invest. What you can't accept is that if you are successful, your investment will also be withdrawn. Then there is no more profit. And so you decide to invest somewhere else. That's exactly the problem. The money goes somewhere else, it goes somewhere safer, somewhere less productive for humanity, it goes into lifestyle brands or food and beverages instead of risky pharma startups.
- Without IP, companies may collaborate less, they might go slower, they might monitor things more carefully. They won't work with manufacturers and countries that they think are risky because they've waived intellectual property rights. And that, I think, is the risk: that we get less investment, less collaboration, less commitment to solving a problem. Not divesting out of malice, but rather out of the logic that you have to protect your investments. You know, the last thing I want to say is that venture capitalists have told me "I love investing in this sector. I feel like I'm doing something good". But they point out that they don't usually invest their own money either. "I usually have to raise an investment fund, and part of that money is a pension fund. So when I raise money from pension funds, I'm putting people's pensions at risk, and I can't in good conscience put people's pensions at risk for things that could be taken away from them." So yes, there is capitalism here. Yes, there is a profit motive, but it's more complicated than that. People



have responsibilities, and so innovation and collaboration are stifled when we give up intellectual property rights.

Jen Brant

So there is a delicate balance and we have to make sure that people are able to invest and reap the rewards of that investment. A question for you, Anissa. We have been dealing with a lot of challenges in this area. Tell me, from where can we draw some optimism? What are the strengths of vaccine manufacturers and other players in Africa in particular, what are we building on, and how are these local partners contributing to some of the longer-term regional and even global goals?

Anissa Boumlic

- First of all, there is already a foundation in Africa. It's not like we are starting everywhere and everything from scratch. So there is already a pharmaceutical industry that has a foundation especially in certain countries like Morocco. We also mentioned South Africa, Senegal, and other countries. So there are manufacturers that used to be more in classical pharma production, though Mark already mentioned that small molecules are not comparable to biological products. But nonetheless we have seen that the evolution from small molecule production and knowledge and know-how to biologics is possible also since there is already an existing infrastructure, there are already regulated markets, and some countries are already exporting on the classical pharma side for other highly regulated markets.
- Secondly, we have already mentioned that COVID-19 has acted as a catalyst. So the strength that we see is that there are certain countries that have immediately developed a strategy with a longer-term goal, so not just short-term legislation, and not just on COVID, but also on other vaccines. Based on the biological targets, they basically realized that there is a big weakness in their countries, but also on a continental level, and this is not just a thing that will help a country and private companies to participate and invest more because they see that the environment is changing. They see that more work is guaranteed. So BioNTech and Moderna have ventured out of oncology and vaccines. I think they recognize the importance of building these partnerships and taking them to specific countries, obviously being selective. I mean, as a pharmaceutical industry player, you select the market that you think is promising, you see more risk and less risk and you make your decisions accordingly.
- What we see now is that because of the COVID situation in Africa, that American, European, Chinese companies also want to work with African countries. They know that they can get access to a big market. I think that is the other side of the coin that we have to take into account: these are countries, and it's a continent, with a high population and also a very young population. One thing I would add as a strength is that things are changing because the environment is changing and there are more opportunities for



biotechnology. We are also seeing a number of Africans who were educated outside of Africa or even working outside of Africa coming back to the continent.

And I think that's a wealth of knowledge. And experience that will come back to the continent, assuming, of course, that they have opportunities, and we're already seeing that in most of the projects that Simon mentioned, there are local Africans who have had experience in big pharma or in engineering who will come back and support those local projects. So we shouldn't underestimate that either. That's the role that returnees will play in shaping this market, because they bring the innovation and also the knowledge. When I left Morocco, I was still young. At that time, there was no biotechnology in the country. And that's the reason why I left the country, because I wanted to pursue that. But now that we see biotechnology being produced on the continent, I'm sure many Africans will be interested in joining this effort.

Jen Brant

And what about Simon's background, as a long-time university researcher in addition to entrepreneur. What is the role of the universities and their researchers, I mean. Many countries have excellent university research programs. What role do these factors play in the equation. This is a question for you, Anissa, and also for you, Simon.

Anissa Boumlic

I think a lot of Africans are left behind because it wasn't possible to get a degree specializing in bio-manufacturing or biotechnology. That's right. Some countries have started to include that now in their curricula. You know, we need engineers. We need engineers in a variety of areas to support the expansion of biotechnology, and Simon will be able to add to that. The good news is this is part of the continental strategy, to make sure that the workforce is strengthened at the university level, but also in research and development to make sure that there is more innovation on the continent for endemic diseases that are particularly important to the continent. Simon, feel free to add to that.

Simon Agwale

> The African CDC is really addressing that because, as you know, the diseases in Africa are not necessarily the ones that plague the West. So there is a need to build research and development capacity to enable the continent to address the particular diseases that are endemic to the continent. And to do that, above all, you need the involvement of universities to continue to do research and development and to develop vaccines against the diseases that are currently plaguing us. If we look at the Indian model, for example, and that's why we're pushing and supporting biotechnology on the continent, most of the R&D funding and clinical trial funding in India is coming from the local biotech companies that are developing their own vaccines, and they're spending over \$200 million to \$300 million every year on clinical trials because manufacturing is not very successful. So the governments in Africa may not have those resources to strengthen the capacity of the







universities to invest in doing the clinical trials for product development that are needed for vaccine manufacturing. So once local bio-manufacturing capacity is established and becomes profitable, they naturally begin to support universities and other institutions in their research and development efforts.

Jen Brant

Yes, that makes sense, a mutual alignment, flow of knowledge and expertise, creation of centers of excellence – with a role for IP. Last question, Mark, what are intellectual property considerations that might be relevant to this question as to how researchers, universities and the like fit into the ecosystem?

Mark Schultz

- Businesses look at the IP environment of a particular country before they decide whether or how to invest in production. They distribute, they set up operations, they look for local partners, and the way they partner is influenced by the IP environment. So the greater the trust that you create, the more likely it should be worth the investment. And you know, there's even research that shows that the stronger and more effective the intellectual property environment is, the more likely smaller local manufacturers are to benefit. For example, if you go to India and you want to partner with a very large company like Tata, you would probably like to partner with that company because it's almost like a contract between two large countries. But if you choose smaller companies to work with, then you think more about the IP environment.
- > So the quality of the partnerships increases and the transfer of know-how increases with the trust in the IP environment. But that's not to say that intellectual property is the beall and end-all, because you also need confidence in the court system, infrastructure, trained workforce. There are so many other things, but intellectual property is just one of the key requirements that you don't want to be without or you will lack an important element.

Jen Brant

Our speakers have mentioned the pandemic several times. Can we have one last round of closing thoughts. What can we learn from the pandemic? What can we take away to create the right conditions as different actors in these ecosystems to scale up biomanufacturing in the medium and long term, especially in Africa? Let's start with you, Simon.

Simon Agwale

AVMI believes that this pandemic has opened our eyes to the importance of local vaccine manufacturing. We now need to move beyond finishing and also to start manufacturing medicines. Otherwise, we could end up with complex factories on the continent, but no







product that can be filled. We need to have all parts of the production process in Africa, and we can do this.

Jen Brant

> Anissa, what's your thought?

Anissa Boumlic

- > The last message I want to convey is something that we haven't spent too much time on, but I think it's important to mention that Africa is not going to start from scratch. So, we are in a position where manufacturers and, of course, governments can benefit from the latest technology, and I mean, we could see that with the pandemic, everybody said mRNA was all the rage, but mRNA has been around for 20 years. And Africa is not going to wait another 20 years and can already start developing mRNA vaccines and biologics and other biologics on the continent. I think the pandemic has highlighted the importance of continuing to innovate, whether it's a high-income country or a middle-income country.
- I think technological innovation is key to always staying agile and taking advantage of these iterations in innovation and adopting them as quickly as possible. I mentioned mRNA, but Simon mentioned single-use technology, so we are looking at the next generation of processing, so what we call the industry of the future or "Industry 4.0". That is something that I think they have generally learned the lesson, that we need to be able to take advantage of innovation and make better and faster biological products. Thank you.

Jen Brant

> Okay, Mark, any closing thoughts on lessons from the pandemic that can help us to extend bio-manufacturing capacity to new regions?

Mark Schultz

Sure. I think a key moment in this pandemic was the fact that governments, with their upfront purchase commitments, helped ensure that companies knew that if they invested quickly in developing vaccines, they had someone who promised to buy them, and yet they didn't completely forgo the risk of the investment. In many cases it was necessary to develop a vaccine that worked, but when it was developed, the government promised to buy it, and that was important to know that you wouldn't be rejected in favor of another vaccine that had a few percentage points more efficacy. However, that was a double-edged sword. The advantage was that it encouraged vaccine development. But the problem was that these manufacturers, these innovators, had contractual obligations to certain countries that were entitled to the vaccine supply. And so they had priority there at times, it wasn't perfect. They were vaccinating parts of their populations that





were far less at risk than unvaccinated people around the world. So what is the solution to this problem? I think we need to look for policy solutions where there's more global or regional cooperation, so that African countries work together to create a purchasing pool to have more leverage. That's it. We need to work harder to make these global cooperation efforts happen. We need to work better and make commitments so that innovation is encouraged and everyone has equal access.

Jen Brant

> Thank you.

Closing of the event.

