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NACI Annual Biotechnology Workshop Proceedings

"Translational Research: from laboratory to industry"

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SESSION ONE: WELCOME AND OPENING ADDRESS

1.1 Welcome and Introduction (Prof Michael Pepper)

Professor Michael Pepper welcomed participants on behalf of NACI.

He explained that NBAC and all the other NACI sub-committees had been disbanded in favour of project teams. The present Bioeconomy Strategy team was formed to look at ways in which it can assist the Department of Science and technology to implement the new Strategy.

He outlined the aim of the workshop: to address the opportunities and problems associated with moving research from the laboratory to industry. Regarding the Bioeconomy Strategy he said that it was necessary to look critically at the old Biotechnology Strategy, to see what can be learnt from government and the private sector, and then to comment on the new Strategy which will have a great focus on the private sector eg SME's with the aim of growing the economy through innovation.

1.2 Opening Address by chairman of NACI Dr Steve Lennon

THE MAIN FOCUS OF THE NEW BIOECONMY STRATEGY IS ON IMPLEMENTATION.

Dr Lennon commended the excellent turnout at the meeting.

Regarding the termination of the NACI subcommittees he commented on how committees can develop a life of their own. What has been created now is a Bioeconomy project team with the focus on implementation but at the same time building on the amazing work done by the National Biotechnology Advisory Committee.

Under the old Biotechnology Strategy, which identified the need for an advisory function, the NBAC was set up within NACI. It comprised an incredibly dedicated and committed group of people who gave advice to three Ministers, namely Mangena, Pandor and now Hanekom. That advice has been very wide ranging from the fundamental role of biotechnology in the SA economy, stem cell research, some of the institutional hiccups that we have in the system at the moment and most recently issues of biosecurity and to do with food security. These are all areas that have been taken very seriously by the ministers to whom the advice has been given but we haven't always been successful in the implementation of the recommendations given. This is in part because we are not very good at integrating across various disciplines, various government departments and various sectors in South Africa. This is something that we need to give attention to as well as focussing on giving advice related to implementation of the Bioeconomy Strategy. The focus should be on the alignment between it and the National Development Plan (NDP).

Some of the key issues identified by the NDP are:

- The creation of jobs. Biotech can be a massive job creator. South Africa's technological balance between the Intellectual Property that we import versus that which we export is appalling. Biotech can change that and at the same time create an enormous number of jobs.

- To change the skill profile of the country. We cannot as a sector sit back and say educational institutions are not delivering so therefore where are we? We have got to take ownership of that and find ways to improve skills whether it is through providing bursaries, giving in-house training, or partnering with the Department of Higher Education or other institutions to create the kind of skills we need to support the bioeconomy. There are many mechanisms available in South Africa to develop skills, something we need to consider.

- The NDP also refers to the manufacturing sector, another area for creation of jobs, for growing exports and for improving the quality of life of all South Africans. But what does this have to do with biotechnology? There are massive

untapped opportunities in the manufacturing sector; it is an area where a lot of innovation is required. The sky is the limit.

- Exploitation of mineral wealth in the country and the beneficiation of that wealth. Great strides have been taken in the area of biotechnology in the mineral processing field, but here is a lot more that can be done.

- The green economy is a very exciting area. There is a role for biotechnology in addressing problems we have to deal with every day. Whether it is in the production of alternative energy sources, for example biodiesel, whilst at the same time reducing CO_2 footprints, or it's the clean-up of environmental spills (oil spills for instance), we know that it works. It has been widely used and is common practise nowadays. Cleaning up of water, water pre-treatment, treatment of waste and just the fundamental improvement in the way that we do business. The green economy has massive opportunities

- Food security. Great progress has been made in agro-processing, the production of drought tolerant and insect resistant crops, and increasing yield.

So we all know that if we look at these opportunities, if we look at the NDP and at the Bioeconomy Strategy we see that the two go hand in hand. The latter is about making the former work and we are going to make the Bioeconomy strategy work! After having done a lot of talking, planning and consultation it is time to get doing in spite of the institutional weaknesses that we recognise. It is a matter of saying I am going to do it and I am going to work to change the system so that it works for us.

Take ownership and play a role now in implementing the great opportunities for the role that biotechnology can play in South Africa. Globally we have just scraped the surface of its true potential. We have the core foundation in place. We have the skills, the innovative ability in the value chain to move from creativity to commercial enterprise. They are not very strong in places but the Bioeconomy strategy is there to strengthen them. What will make the difference is human endeavour and as we have got plenty of that, hopefully in 10 – 15 year time when people talk about models of socio-economic success globally

they will turn around and say let's try and emulate what South Africa has been able to do to grow their economy on the back of advanced technology and in particular on the back of biotechnology.

So once Cabinet has approved this strategy let us stop the talking and put our weight behind it and make it happen.

1.3. The Brazilian Bioeconomy System: An International Perspective – (Gabriela Cezar)

INNOVATION CAN BE DONE ANYWHERE - ROLE OF VENTURE CAPITAL

If one looks at places like South Korea, and the difference that the bioeconomy and the innovation-based economy has made to job creation; to the shift from a commodity based economy, it's amazing. One of the essential engines that makes this happen is venture capital. There is a need to recognize that there will be no growth of the bioeconomy and of biotechnology-based companies without virtual capital and investors willing to take the risk. Institutional investors such as public institutions for example should be willing to take the risk.

How this was done in Brazil? Why, who are the investors and what is their profile?

US$150 million in venture capital was raised. The top investors are a combination of both public and private investors. The Brazilian National Development Bank (BNDS) is the top financing vehicle for the Brazilian economy. Out of that $150 million, $40 million came from BNDS. It did this side by side with private investors, such as Pfize, and the American Development Bank.

The key elements of why it was decided to raise venture capital, and some of the key factors that drove the interest of the investors, were firstly that Brazil has now an ideal ecosystem for technology development. But when there is talk about technology, time is of the essence due to global competitiveness. All nations have recognized the

transformative role of the bioeconomy in job creation and in development. So Brazil with these series of factors has now an ideal ecosystem.

Secondly, what one could call the tipping point, was the adoption of TRIPS, the international agreement for intellectual property. Intellectual property and patents can be referred to as a currency in this industry. You have to value your inventions. Brazil adopted TRIPS in 1996 and this was seen as a turning point for foreign investors and for the growth of the industry. Some of the technological and healthcare accomplishments in Brazil have reached global competitiveness. So for example there are several FDA-approved clinical trials using Brazilian technology developed in Brazil. We also have hundreds of FDA-approved clinical trials on-going in Brazil, which speaks to the quality of the health care, regulatory systems, hospitals and the quality of the personnel and the talent that is in the country. There have been some landmark deals. For example, Monsanto acquired two Brazilian starter companies, Allelyx and Canavialis, around sugarcane, biomarkers and molecular biology. The deal was worth more than $250 million for two Brazilian start-ups. As a result there has been international interest in some of the technologies developed on the ground. There is therefore world class medical technology, experience in manufacturing, an increasing demand for biofuel. One can also recognize the enormous potential of South Africa in this respect.

Brazil's Venture Capital Fund is actually a life sciences fund. The portfolio is allocated to be around 70% investment biotechnology related to health care and 30% in green energy and renewable energy. And the country really does have some competitive advantages in areas such as genome research, stem cell research, vaccines and neuro sciences.

Pfizer has a different strategy along the lines of growing the bioeconomy. It has implemented and made a significant commitment to make this happen in the non-US market by establishing a group called External R & D Innovations. It's a worldwide research and development unit that is exclusively dedicated to external innovations. This is very interesting and the first of its kind within large pharmaceutical companies. Pfizer built this team with scientists that have extensive knowledge of biology as well as business experience and they have started to create opportunities globally. The

group has close to 50 associates but there is an earlier a group called Strategic Partnerships that is implementing this group around the world. These are colleagues in different areas of the globe. I am heading up Brazil and Latin America and would love to initiate some of these activities in South Africa. The working relationships in South Africa are not far from how biotechnology initiatives are expanded making direct investments from venture capital. Our model goes all the way from research collaborations (for instance incubators), direct venture investments through Pfizer ventures, licenses, out-licenses, and all the way to mergers and acquisitions.

The idea is to create a new era of innovation. Some of the major research areas in Brazil are in neuroscience, oncology, information, and there is a strong focus on vaccines. There is also have a new research area: orphan and rare diseases. Pfizer ventures have just signed an important collaboration for sickle cell anaemia and haemophilia.

The pharmaceutical industry is one of the four pillars of the government in its new economic policy. Brazil is a large market, 200 million people with their resources and a growing market. However, in concrete terms, what actions have been taken by the federal government in addition to the availability of capital. Here are some examples:

The first is the implementation of the law saying that the government will grant up to 200% tax exemption for any investment made in innovation. Now we have companies all the way from manufacturing, not just bio-pharmaceutical but across the board. We have manufacturing companies that produce refrigerators telling us how they are into innovation even to the processes of assembly lines. We have several car assembly companies in Brazil incorporating innovation to take advantage of these tax incentives.

The second one: the government will pay more money for medicines that have been manufactured in Brazil, or with relevant technology. It will pay up to 20% more for the medicines it purchases if the medicines are manufactured in Brazil. This has been a real boost for the growth of the pharmaceutical industry and for partnerships between Brazilian pharmaceutical companies and foreign-based ones.

Number three: the tender system was eliminated from the Ministry of Health in September 2012. The Ministry is now exempt from the need of a public tender to

partner with private companies. As long as there is significant technology transfer from a private company to a public laboratory (meaning the Ministry), the government can sign the partnership. We have seen several of these signed.

There is a research centre financed by the State Secretary of Health and the State of Rio de Janeiro. It is going to focus on three key areas: nerve sciences, stem cell therapy and sports medicine. Sports medicine is supposed to be the biotechnology reference consortium for the World Cup and the Olympic Games. So a partnership was signed with Pfizer who do not actually have a research programme in sports medicine. One of the things they are doing in building the strategy is forming global company partnerships all over the world even though it's not in their R&D pipeline. They have been able to put together a brain-imaging company that spun out of Harvard and also has operations in Israel and other countries and that is addressing the unmet medical needs of head injuries during sports, especially soccer. So FIFA actually had a conference around these unmet medical needs. There is clearly a need to better diagnose head injuries in sports. So this is a high visibility R&D initiative and the initial investment was $50 million.

In Summary, Biotechnology is the vehicle to feed, fuel and heal the world. But the time to act is now, because we are talking about technology which if you wait too long is going to become out-dated. One cannot think about it too long in terms of technology development or investments. These three issues that we have outlined here are the issues that are urgent; feeding, fuelling and healing the world. But you also have to recognise that there are no borders anymore. Brazil is competing with India and China, and South Africa is too. You have to choose your partner; you have to get it done. So the main driver is that all your investments and innovation are an engine for long term exponential economic development. We all know that when we create circumstances for talent development, when you are putting students through masters' programmes and PhDs the salaries that the students are going to be able to secure for themselves, their families and their communities are going to be very different. So it brings about exponential economic development.

What has helped Brazil is re-alignment between the public stakeholders, BNDS, the Ministries of science and technology, health, industry, trade and commerce, for this

initiative towards the growth of an innovation-based economy. This has undoubtedly played a vital role in the development of the industry.

If you want to be global player, if you want to be an innovator you need to act like one. You have to integrate the various elements of an innovation-based economy into working practices. Brazil is extremely bureaucratic. For instance a study is being done in partnership with the National Cancer Institute. It is a sequencing study to understand the prevalence of the mutation. It is non-invasive, we are not extracting blood from patients; it's just an authorization for a piece of the tumour that was removed. But just to get the authorization we have been waiting for a very long time. And while we wait the science is moving, technology is moving forward and our competitors are certainly getting it done faster. So such challenges have to be faced head on in order to be globally innovative. Regional challenges have to be addressed. We have to be transformative. To integrate some of these key elements of the global bioeconomy into the workplace the first requirement is an entrepreneurial culture.

Recognising the value of intellectual property was a turning point for Brazil. Before the adoption of TRIPS and intellectual property policies, there was no bioeconomy. That's the case for healthcare, for life sciences and for bioenergy, which is an extensive area with huge competition. For example enzymatic processes with extraction of energy from cellulose: that's worth lots of money and that's biotechnology for you. If you are developing it you have to protect it.

Venture capital is key; acknowledge the fact and face the reality that there is risk. There is technology risk, market risk, and investment risk. Are you going to just sit and watch? We have to recognise and manage risk. Risk is manageable. When we talk about risk one also has to be flexible, so choose to partner with the best. If you are going to do tech transfer, work with the best, but have flexibility. One of the practical things about the Brazilian law changes, exempting the tender system for example, was the ability to have up-front transparent dialogue and negotiation between the private and public sectors.

SESSION TWO PRESENTATIONS AND DISCUSSIONS

2.1. NATIONAL BIOTECHNOLOGY STRATEGY – GLAUDINA LOOTS

This is a policy framework to create incentives to grow the biotechnology sector.

Under the 2001 Biotechnology Strategy of biotechnology innovation centres were established: BioPAD, Cape Biotech Trust, LIFElab and PlantBio, plus the National Bioinformatics Network and the Public Understanding of Biotechnology Programme. These BICs create several platforms, spin-off companies as well as commercial products and services, promoted knowledge of biotechnology, intellectual property management and commercialisation, and improved public understanding and awareness of biotechnology.

“Bioeconomy" refers to activities that make use of bioinnovations, based on biological sources, materials and processes to generate sustainable economic, social and environmental development. It provides an economic engine for the new economy which will in turn provide a basis for future growth.

Science-based "biosolutions" can be used to:

- manufacture high-value protein products such as biopharmaceuticals and vaccines;
- produce biofuels;
- improve and adapt crops;
- remedy industrial and municipal waste;
- reduce production costs;
- reduce environmental impacts;

- improve the quality of products;
- improve the performance of a range of economic sectors.

In order to do this the following are required:

- Establish a coordinating committee to advise, guide and monitor agricultural innovation.
- Establish a network of agro-innovation hubs that enhance technology transfer and extension.
- Determine strategic projects.
- Undertale crop/livestock improvement both for biotic and physical stresses associated with climate change (including indigenous crops).

There are three specific sectors for the South African bioeconomy which are not static and may change over the course of time.

1. AGRO-PROCESSING INITIATIVES (AGRICULTURE)

- An integrated food and nutrition research programme
- Animal vaccine capabilities; for example horse sickness vaccine
- Energy-crop initiatives
- Biocontrol and biofertilisers
- Aquaculture
- Soil conservation
- Water resource management
- Build high-value skills and capacities to enable agro-innovation
- Co-funding initiatives for innovation

2. HEALTH STRATEGIC INTERVENTIONS

- Develop improved therapeutics and drug delivery systems to address priority diseases
- Develop new and improved vaccines and biologics
- Develop improved diagnostics
- Develop improved medical devices
- Build clinical research and development capabilities
- Establish pharmaceutical manufacturing. At present we have 3.3 million people on antiretroviral treatment and we are dependent on Indian companies for the bulk of these medicines.
- Funding of masters and PHD students shouldn't be in our jurisdiction; that's the NRF's job.

3. STRATEGIC INDUSTRIAL AND ENVIRONMENTAL BIOTECHNOLOGY PROGRAMMES

- Integration
- Strengthen and develop bio-prospecting capacity and capabilities
- Strengthen local bioprocessing capabilities
- Develop integrated bio-refineries from bio-based feed stocks
- Strengthen wastewater research, development and innovation
- Strengthen waste research, development and innovation

- Synergies with enabling and emerging technologies.
- Establish an advisory committee for industrial bio-economy

COMMENT: I want to congratulate you on an exceptionally good document and on a job very well done**.**

2.2. AN ANALYSIS OF THE 2001 BIOTECHNOLOGY STRATEGY (a private sector perspective) – Dr. Neville Comins

The Biotechnology Strategy of 2001 was the first to be developed under the concept of a National System of Innovation and in this way was ground-breaking. However, we must ask a number of key questions. Firstly, what have we learnt from it over the years and secondly, how much of that learning has gone on into the current thinking? Strategies are something we do extremely well in South Africa but a strategy is only as good as what you do with it. So what did we do with the 2001 strategy, what did we learn from it and where do we go from here? The approach I have taken is based on the following framework:

i. Strategy
ii. Implementation
iii. Actions
iv. Outputs
v. Review.

Firstly, let's look at the strategy process. What we have just heard about Brazil was the dynamic role displayed by entrepreneurs and business people. When we put our team together to look at the biotechnology subject, which is a knowledge-based one, we choose the team dominantly from the academic and R&D sectors. Why do we leave out the business people? Is it because they get in the way or they ask different questions? The document in 2001 specifically stated that this strategy was primarily aimed at government, its associates and institutions including public sector funding

agencies. Then each sector of the strategy was divided into categories that are the primary means by which 'government' can influence the development of biotech. What would you feel like if you were a business person or entrepreneur reading that strategy? You would put it down because it does not apply to you!

The stated intent of the strategy was to make a 'significant contribution to national priorities'. Thus, investing in biotechnology R&D must be based on an explicit national goal of selecting projects and commercializing these in both local and international markets. Did the strategy focus on this? Indeed, there was acknowledgement in the strategy document that there was an unfocused approach and a low level of commercialization. There was poor interaction and poor networking among knowledge generators and users. There was the idea of lack of critical mass - all the classical things. The strategy was supposed to meet national imperatives, job creation, rural development, crime prevention, human resource development, HIV and AIDS, ultimately leading to economic growth. But we have to decide what we are going to do. What are the real objectives amongst all these issues?

The Strategy, does examine a number of case studies on the approach to biotechnology in Brazil, Cuba and some other countries. Clear emphasis is given to the benefits of creating focus in the programmes with specific defined priority outputs. In the South African Strategy, however, there was a lack of such focus.

Looking now at the 'Implementation' of the Strategy, one of the main recommendations was the creation of a National Biotechnology Advisory Council (NBAC). This structure had a specific role of focusing on national proprieties and promoting coordination. This did not happen until 2007 when NBAC was created by NACI, so there was a significant gestation period before we had any sort of structure and even then, it did not serve the original purpose.

In the interim, the BRICS - the Biotechnology Regional Innovation Centres, and other interventions around human resource development were created, but without the proposed oversight function in place. Additionally, the strategy did not have significant recommendations on efforts to generate an industry for them to work in, but never-the-less they were implemented! The only industrial opportunity in the Strategy was a

proposed intervention by DTI to try to attract foreign investors, anchor investments. The one challenge with that approach is that you need to have something on offer. Investors only come when they see the 'cookie jar', so unless you have got a cookie jar, the investors are going to say, nice climate, Cape Town looks nice, competes with Rio - but that's all.

Looking further at the recommendations of the Strategy, we did say we were going to create biotech industries, but at the time of writing there was only one listed third-generation Biotech Company, so we had a pretty small base to go from. Going deeper into the recommendations, there were nine interventions on policy and legislation, some of which I suspect are still on the agenda for the new Bioeconomy Strategy. A further four related to enhancing international cooperation for intervention and financing, two more on new and innovative financing, one on ethics and a further two on public understanding. These involved a number of different government departments - the same ones still mentioned in 2013. There were 'specific responsibilities' assigned to those departments. The question is: what was the driving mechanism for achieving success and who was coordinating?

Moving now to the 'Actions' stage. How do you get people to come on board? Thirteen years later there is still no implementation plan, and there never was one. The plan in place for marketing and technology focus was extremely vague. If you don't know what you are going to be doing, you cannot write the implementation plan. No time lines were specified because the Advisory Committee was not appointed and there was no governance structure to coordinate and focus activity. Why was the decision taken not to appoint the NBAC at the outset? Thus most of the recommendations remain just that.

One of the most important steps, before contemplating a new strategy, is that of 'Review'. How many reviews did we do on the BRICS? What exactly did we learn? How can we implement better ideas when we actually don't have a history of what happened? Is it too late to find out what happened? If we went to each of the companies that were funded by the BRICS, found the people and asked them for their experience, we would probably learn more about what to do in the next decade in a day than we will in five years of rediscovering the wheel. We should have been going

through a clear cycle but instead of completing the learning, we are actually starting another cycle. How many mistakes are we going to repeat? Do we have the resources in South Africa to tackle that whole new strategy as described or does somebody really need to sit down with a careful mind-set of saying what are the most important things; prioritising, looking at capacity, looking at the resources to demonstrate the power of biotechnology.

Hindsight is 2020 vision. It's easy to look back and be critical. There are so many things we did wrong and one of these was not to thoroughly review. Review and learn I would say now should be the greatest conclusion. The 2001 strategy really was a valiant effort. It came at a time when there were no other strategies. It was the first and it was a great effort. It however did not define a focus and its analysis seemed to think that government was the only barrier that it needed to overcome. But the real question will be, if you analyse it, would business invest in that strategy? And my answer is no. The question with your new Strategy is: will businesses invest in that now?

An interesting example from which to learn is the Philadelphia Science Centre. They have a physical structure and they have some universities attached. They also have a system where there is a pull-out from those universities at an appropriate time in the R&D to move into a cycle of product development. What is important about this is that the science centre is a partnership of 34 institutions; they are all active participants in its success. In South Africa a partnership of 34 institutions would be very difficult to contemplate. Everybody working at that science centre knows exactly where they fit in, and to which stage of the development. So the one lesson, which has been said so many times, is that this is a multi-disciplinary field, you need cross-linkages; you need to put your minds together. The Science Centre 10 years after creation was turning $5 billion a year from start-up companies that had spun out of the 34 institutions. Where in Gauteng is our equivalent of the science centre; where in Cape Town; where in KZN; why can we not collaborate? Another lesson is the tools as were described from Brazil. They look at the whole life cycle, including the tools and finance available at each stage So I think the point is - if you are going to go with the new strategy, you as a scientific community must make up your mind that there will be no solo operations. You are going to work together to meet specific goals. In Brazil's case, pulling people

together to meet objectives was a fundamental goal of their innovation system. We just have not got there yet and biotech could become a very good role model for other sectors.

2.3. DTI POLICY FOR PHARMACEUTICAL INDUSTRY –Ms. CLAUDY STEYN

There is a need to ensure we are positioned for the future.

Challenges: lower prices and falling exports of platinum, minerals and metallurgical commodities; rising costs of imports of crude oil and refined fuels. There is a structural imbalance – SA exports minerals and low-processed metallurgical commodities, and imports technology and labour-intensive products.

The SA GDP growth slowed down in the third and fourth quarters of 2012. It is necessary to grow the economy at 6% p.a. to keep pace with the global economy, reduce unemployment and create jobs for new university and college graduates.

There is a deteriorating trade balance (-R117 billion for the 12 months of 2012). Medical products, pharmaceuticals, medical devices and medical diagnostics are the 5th largest contributor to the SA trade deficit.

Dtl's industrial policy focuses on high value-adding and on hi-tech including pharmaceuticals, and also on job-intensive sectors of the economy such as agro-processing.

The SA pharmaceutical market was US$4 billion in 2012, the largest in Africa, yet it is only 0.4% of the global market by value, and 1% by volume.

ARVs are the only segment of the market where SA is the world's number one, attracting local and foreign investment. We have 25% of the developing world's ARV market.

There is an increasing dependence on imports. South Africa lacks innovation although in the chemical sector they have home grown intellect.

The South African Intellectual Property (IP) system and policy are not informed by other national policies that seek to address national objectives (such as healthcare, economy, education, agriculture, arts and culture, protection of the environment and bio-diversity etc.). There is no coordinated approach on IP matters by the various government departments and other organs of state.

This makes it difficult for South Africa to have a common approach internationally and be able to extract benefits from the IP system.

Objectives:

- To complement other progressive economic national policies.
- To encourage coordination within all spheres of Government.
- To encourage the IP policy to interface with all sectors of the economy.
- To influence regional and international formulation of treaties in the best interests of South Africa.

There is a need to create the necessary infrastructure and incentives for patenting.

In South Africa a patent is granted for 20 years from the date of publication of acceptance of the application in the Patent Journal, with no provision for extension. Generally a patent may only be enforced nine months after it is granted.

A patent can only be challenged after it has been granted – there is no provision for pre-grant opposition. A patent may be challenged at any time after the grant, by any person, on the grounds that the invention was not new at the date of application or that it was obvious. The Patents Act (Chapter 10, articles 61 to 64) also specifies the formal grounds on which a patent may be revoked, such as incomplete disclosure of the invention, insufficient clarity of the claims, fraudulent or false statement or misrepresentation in the application.

The Court of the Commissioner of Patents is the court of first instance in all patent-related matters. The Court decision can be appealed, with leave, either to a provincial division of the High Court and thereafter to the Supreme Court of Appeal, or directly to the Supreme Court of Appeal.

South African patent order is often dubbed as a “weak patent system with strong enforcement”, as the substantive examination of patent applications is not carried out by CIPC, a South African patent is intrinsically vulnerable.

The grant of a South African patent does not guarantee that the invention is new or non-obvious, that the patent will be valid in other jurisdictions, that the patent cannot be revoked, or that the exploitation of the invention will not infringe on existing patents in South Africa or elsewhere.

Big question 1: Does South Africa have the capacity to examine 10,000 patent applications per year? Starting from examining pharmaceutical and biotech / life science patent applications? Is this an opportunity for academia?

Big question 2: Should the South African IP policy encourage compulsory licensing of medicines and biotech inventions?

SESSION 3: PRESENTATIONS AND DISCUSSIONS

3.1. THE SIX NODES OF INNOVATION (Dr. Antonel Olkers)

Innovation The word innovation probably means different things to many. This word innovation is one of the most mis-used in our current vocabulary, not only in South Africa but internationally. I think if we are going to start talking about a bioeconomy, something that generates benefits or money (I also see money-making as a benefit in the economy), then we do need to make sure that the way we use our language is the same.

What do we mean by innovation? One of the other buzz words that I heard a while ago was the “knowledge economy”. I believe it's a knowledge-based economy because we don't actually want to sell the primary resource. You go from knowledge

to understanding (which is a totally different skill), to insight, to deconstruction, and if you can deconstruct generally you can synthesise. So if you can synthesise new things you have invented - if the outcome is novel.

Now you have generated IP, intellectual capital, and you want to translate it to market capital (because I don't know about you but the city of Tshwane where we stand doesn't accept my IPS payment for my electricity). Now we have innovated. Innovation happens at a very specific point. Before that point it is not innovation. Innovation makes money so it drives the economy. **Inventions cost money, innovations make money**. If we only invent in South Africa we are not making money - we have to innovate. Who innovates? Generally researchers invent and entrepreneurs innovate because it is only in the entrepreneur's field that we see the money.

Who operates the translation machine that we put this through? It is not the public sector, neither is it the academic sector, nor the private sector. Yet in our 2001 Biotechnology Strategy we didn't really recognise or articulate it as well as we are doing it now in the new Bioeconomy Strategy. If you want to translate your knowledge to ultimately spin the economy around, you definitely want to make sure that you spend the time. The cost and the complexity increase as you move along the scale but the potential returns on investment fortunately also increase as you move up the graph. If you risk there is reward. It is as simple as that. There cannot be reward without risk, and as a country we need to embrace that risk.

IDO, the world's leading innovation company, says innovation only happens when the viability, the desirability and the feasibility resonate. The six nodes of innovation encompass the following; a concept or an idea, research, development, productisation, then manufacturing. Only after that do you trade with it in the market.

Therefore innovation is not a linear process. It's not a cycle, but a network or a system; a system of innovation, an eco-system. It is a network where all the nodes are linked; it's not only the concept and the research that are linked. The traditional flow has been concept, research, development, productisation, manufacturing and commercialisation, but that's not the only path through this network. In fact all the

nodes are linked. It may be the traditional path but that's not correct because concepts don't always flow to research and it is certainly not a one directional flow.

The input into the idea node is background knowledge. Input is background IP and knowledge, it is global background IP. You know as academics we like to think it's only the science papers, but no, that's only half of the literature; science papers and patents are the background literature. Knowledge - all information that's relevant and that's associated with your idea. But that knowledge must be of quality. Non-quality information is useless; in fact it causes damage because it skews your view of the actual facts. There is no compromise for quality. Therefore we need know-how, knowledge, understanding and insight. Idea evaluation is the process whereby we evaluate ideas so we select only the viable ideas. When I started in biotech I thought the challenge was going to be generating new ideas. I very quickly discovered that is not the case in business; the challenge is selecting the good ones and then backing them.

In generating an idea it is not that an idea pops into your head and tomorrow you start with research. There is a process behind it that makes it worthwhile. That increases the value of that idea until it is a mature idea that actually has innovation potential to generate a benefit, or money in the market. You have to determine what the market needs. It's great to ask them what they need but make sure that what they tell you they need is really what they need. You need to verify that the idea can indeed be taken through innovation and that it will satisfy the stated need. The output is then a fully matured idea and in theory it's now ready to enter the research phase. The idea can be sold; it has value; you can trade with it, and you can attract potential investors with it because it didn't just pop into your head. You have worked with it through the process. Thus the output in the idea node is a mature idea.

Next is research, the input clearly is the mature idea. The process is the scientific method because this is the only method in the world that can guarantee for you a valid scientific result. Invalid scientific results do not attract investment; valid scientific results do. The output is a valid research result that has potential for development and can solve a particular problem.

In development, the input (you won't be surprised) is that valid research result. Where further research is needed it's all applied. We test key aspects of the envisaged product and there's a risk, of course, involved in it - but so there is in all of the nodes. We verify that it actually solves the problem of the market. We must verify that this research result, if we productise it and go on through the process of innovation, will actually solve the market need. And the output, of course, is proof of concept. Now for the first time you have proof of concept.

R&D is not a single concept. We talk about it as though it is, but each component takes very different skills. Research and Development often do not happen in the same institution. With research, the input is a concept and the output is the valid research result. With development we arrive at proof of concept, and for the first time we know that the solution can be addressed. This is critical.

One of the problems that we have in terms of innovation in South Africa, is that the public, academic and the private sectors are not talking to each other. This is one of the reasons for the confusion around the differences between R and D. I've asked university professors what they understand by R&D and they often tell me they do both, while they are actually only doing R. The private company people tell me they do R&D but actually they only do D. Therefore it is no wonder we think we don't need each other! The private sector thinks they can do all of this on their own and the academic sector thinks exactly the same. This is not true, it's false. So with the new Bio-Economy Strategy we need to recognise this, fix it and move on.

When we look at productisation the input is the proof of concept, the process is a mature idea, there are valid research results and there is proof of concept to a product that actually has market pull. You can't get to productisation with a product that has no market pull and think you can fix it. The market will decide by itself when it's ready. So already at idea evaluation the idea should not have progressed to research if there's no market pull. You have to ask the market, for instance, in what shape or form will they embrace the product and you will get design input at this point. Some simple examples: is it a liquid; is it a solid; will people rather prefer it as a tablet; does it need to be transparent or colourful, hard or soft; all of these things can kill your product if you don't pay attention to them. It may be an excellent drug, but people are

not taking it because it tastes vile and they can't swallow it. The output? For the first time you have a prototype after productisation, I take tremendous pleasure in the fact that the word productisation has the word product in it. The whole purpose of innovation is to take a product or service to the market.

Manufacturing: the input is this prototype and you are now ready to make many of it. If you don't pilot it you will be in deep trouble! The new Strategy speaks of pilot plants. Then comes scaling up, one of the most difficult things in manufacturing; to scale up without losing quality and if you start to out-source part of your manufacturing then it becomes an even bigger challenge. So what is the output? The output is a fully manufactured product standing in the store room ready to be sold. It is ready for the market launch.

Then comes commercialisation. Commercialisation is not innovation; innovation is the network. You input the manufactured product now into the market and it's a business process. Your business model may be one of many self-distributions; you may contract it out or you may want to set up franchises. You are going to sell it so your pricing and marketing are critical aspects. Packaging: many, many successful products don't make it in the market because of packaging - it's critical. What is the output? For the first time there is money or benefit on the table. The output of commercialisation is money with benefit into it.

So the innovation network is clearly not a pipeline, or a cycle. It is a network, somewhat unorganised but a very dynamic process. But remember sustainability; sustainability is key in all the nodes of the network.

There are outside factors that also impact on innovation. The IPR Act of 2008 is forcing scientists in this country to become aware of intellectual property. We can't have innovation without it. Legislation is critical; in its absence fly-by-nights are advantaged and the vulnerable public is exploited. Ethics: if you compromise ethics at any of the nodes it contaminates the entire innovation process. And finally, the private sector will not participate or invest without certainty: they are not adverse to risk but want to at least know that success is one of the ultimate options.

Inventions cost money. If we want to make money and derive benefit we have to commercialise. Without it the invention potential is lost, products will not reach the market or grow the economy. The people of our country will see zero benefit from our investment if we don't do it, so we have to nurture the entire innovation network with funding support but also with vision and leadership.

3.2. SETTING UP A VACCINE INDUSTRY (Dr. MORENA MAKHOANA)

Vaccines do not solve all healthcare problems, however they are a fundamental pillar of any government programme. All governments have what they call an expanded programme on immunisation; some of them call it differently but it's a set programme that they have invested in. With vaccines we can add more, sometimes by adding combinations because as we discover new vaccines we want to prevent more diseases. Very few will be like smallpox where you end up not actually having to use it.

Although governments may not always have the budgets to take care of all of their vaccines this is what keeps the vaccine industry alive as the impact is so demonstrable. We are part of the pharmaceutical world but we need to remind ourselves to what extent vaccines are different. In terms of targets they focus mainly on prevention and not necessarily on treatment, even though going forward there are therapeutic vaccines in the pipeline for particular cancers and other diseases. However these will take time.

Government is the central purchaser and the level of acceptance of side effects is much lower than for other types of injections. You are usually injecting vaccines into healthy infants compared with somebody, for instance, in ICU being treated for a life-threatening disease. If they are injected and have a big red mark on their arm no one will be perturbed. They will ignore it if helps them to get better. However with vaccines you take these infants and they come out with what we term a mild reaction, but this can become a major issue as to what the vaccines do. So the level of acceptance of side effects is low, especially among mothers who feel the pain on behalf of their infants.

We deal with biologicals therefore the manufacturing process is a lot more complex than with chemical pharmaceuticals. The regulations are a lot more complex where you can't mix particular processes, so the investment is high. One must understand that whenever you set up in industry, which is what we think government was trying to do when they set up Bio-Vac. Although it forms part of the pharmaceutical manufacturing landscape, you are essentially setting up an industry requiring regulatory authority. We must explain this to the Medical Control Council in that they will have to put their stamp first before any other regulatory authority comes and inspects it. That's quite daunting for some regulatory authorities.

Establishing a vaccine industry means prices should go down as volumes go up. As Bio-Vac we've been setting up vaccine manufacturing but the world is moving on, it's not waiting for Bio-Vac. That's something we need to be cognisant of. Our costs are going up, there's regulation and skills are changing. But the world is moving on and prices are going down. So if you think of producing a product today what is the demand going to be in 2018? These are the realities of the world we live in.

Part of the dilemma is that many vaccines are targeted at children, and when you have a child you are not looking at the total population but at the number of births. So as we set up and think of innovation we also need to be realistic of what's happening globally because we are not the only ones who are thinking of setting up a manufacturing facility. As the world is moving on and has gone probably one or two steps ahead, how do you catch up? Do you niche yourself or do you become broad? There is a need to work with government institutions, product development partners and with multi-national companies that are aiming to tap into the emerging market and assist as part of their development framework. So that's quite important in terms of how we look at things going forward.

When Bio-Vac was set up it was idealistic. We needed to do everything from research right up to the customer. It was good to dream, because at least it gets you started, but that is exactly where we are now. We are on the eve of commencing vaccine manufacture. If there had been no dream, if we had waited for the ideal bioeconomy strategy, we wouldn't be where we are now. However, we need to be realistic. In research do we have some capacity and we still need to collaborate. Looking down

the value chain you don't just set up it all up and everything goes right. There are all of these other underlying things that you have to set up and if they do not exist, and if we do not obtain revenue, then you will only be putting up the bricks and mortar. You need to set up quality systems, things that you cannot necessarily copy and paste from pharmaceutical manufacturers. Some things you need to adapt for yourself. Where do you get the skills to do the analytical side of development; good manufacturing practice within the biological framework; quality control?

An interesting point is the animal testing element where every batch of vaccine that enters the country needs to be tested. Some of it is lab testing and a lot of them in mice, but they need to be done independently. The manufacturers tests their vaccines before they send them to the country, then the MCC have what they call a National Control Approach that tests independently before release. That adds another step, so if you manufacture a while ago, you are only going to sell your products three or four months later and you are sitting on stock. You have people you are owe but you don't know whether the vaccine will pass or not. You hope that you will pass, because you did your own internal quality control, but this just adds another step to the process.

We also work with multi-national companies and at the moment we have signed up with Sanoffi Heber and we hope to sign up with others as we go along. This is mainly to plug the manufacturing landscape.

There is potential in Africa but wherever you set up a vaccine manufacturer (and this was stated recently by the UNCTD) you need links and you need the regulatory framework. That is what is often missing on our continent. South Africa's a bit better than many other countries but we have our own challenges (and we can write a book about that!)

So what does this mean for the future? There all the vaccines that have already been established, such as measles etc., and then there are the future vaccines such as HIV, TB and malaria. How can we plug into this gap? There is a lot of international work that's been happening and the question is how can we fit in, because these are also South African-specific problems . Do we at Bio-Vac have the wherewithal for R&D on that? No we do not, so we have to partner with others. What's important is to create

the link with the client, with the Department of Health, with whom we must align because at the end of the day we need to make sure that we don't develop a vaccine that's not aligned. Sometimes it's not easy but it's something that, with the help of other stake-holders, we need to do.

QUESTION: if you had to look at the vaccine industry and perhaps look at some of the challenges that you are facing what would be your biggest current challenge?

MORENA MOKHOANA: It's difficult to put them in order of priority but the first is funding. Funding to maintain your infrastructure at the level that is required, and I'm talking about the international level that's required. This requires continual investment and this is just maintaining what you have, maintaining GMP standards. But part of what we do as a public-private partnership we cannot ignore, we cannot just be purely commercial and we need to look also at what's coming up in ten and 20 years' time. Thus the innovation part is important and we need funding for that as well. We have come a long way in experience and I think we're now at the point where we understand the global landscape. We are a lot more realistic and if we were to be afforded the money we now know where to spend it wisely. That's something that when we started probably was not as mature as it is now.

3.3 SOUTH AFRICAN CASE STUDY AND SUCCESS STORY (Dr. MAURITZ VENTER) AZARGEN BIOTECHNOLOGIES

I need to say that we are still on this journey. We haven't made an exit yet so I'm an aspiring bio-entrepreneur. I haven't made money yet, so I want to tell you our story so far and the journey that we've been on with AzarGen.

You must love what you do in order to make money out of what you love. This is very important. Do you have the natural ability to be an entrepreneur? You must be able to adapt to the situation and the uncertainty. One thing is certain, bio-entrepreneurship

is like any entrepreneurial endeavour; there are pros and cons but it's still a business and you need to make money out of it. You need to know whether you have the appetite for risk or you should rather go into a stable job - there's nothing wrong with that. With bio-entrepreneurship there are no guarantees, there's a lot of uncertainty. For those of you who are scientists, you would know that there's a lot of uncertainty in any project, but in bio-entrepreneurship there is something different as you are now dealing with real (investor's) money. Now you are going to have to tell the guys this is what we are going to do in theory, we think it can be done but that's where the uncertainty lies. You need to realise that if you are in this game you need to survive and you need to be able to tolerate that kind of uncertainty. That's one of the lessons I have learned.

How do you start? You may have an idea or a concept from scratch or you may be busy at University with a research project, which may be government funded. But for us there were no clear established route to follow, so we needed to go out and say who's done it before? We did a lot of research into who stood out in the world and the big guys were Genentech, the first true biotech company in the world. They started in 1973 right at the beginnings of biotech. We decided to use the route that Genetech followed, as our model.

It's quite simple: you start with an idea, you start your company, and you go through several trials in the middle acquiring funding, obtaining research results which may be failures, so go back, acquire more funding, get more research results, go back…. There can also be many directions on this side and that is a big challenge especially for the funders as well as the mentors. But entrepreneurs need to understand that they need to succeed through this process - and we know that in biotech the periods are long. This isn't a project started in a garage and the time periods are six years, eight years, ten years. You can either go into manufacturing, and you can keep on partnering, or you can go for a buy-out, the merger and or the acquisition. We have gone through all these models and we did a lot of analysis. But you know the saying 'analysis paralysis', you can keep on doing analysis but at some stage that analysis can cause you not to take a risk. There's a fine line between taking the risk and deciding when not to take the risk. So at the end of the day we just decided "let's just start".

We registered our company in February 2003. We have a name, we have different strengths but what are we going to do and how are we going to do it? Are we going to offer a diagnostic service? Are we going to work on a project and sell some stuff? What are we going to do with our skills, our technical know-how? So very early on we had to define our purpose and define how we were going to carry that out. The driver of this whole project was this one: identify and describe the problem that you are going to solve. Thus we needed to find a problem that we wanted to solve using our business. We needed to show how we were going to solve that problem before we could ask for money.

I just want to re-focus on this because after six years, eight years, when you are still part of the team things can change. The team dynamics change, some guys get settled, some guys they say I can't take the risk any more. We had a lot of heated discussions around our table, but this is the core: all the team members need to be aligned with the overall goal. What helped us a lot in this venture was: every time we would ask ourselves what's in the best interest of AzarGen? Should this decision be taken? So what are we going to do? We tried a few things, we offered diagnostic services for citrus farmers, and we went into negotiations with some agricultural prospect funders. But at some stage we had to sit down and say “Let's be realistic. If we are going to put our time and effort into this we've got to make it worthwhile. So we decided that we would determine the sector in biotech that demands the highest capital and risk but offers the greatest reward - and that is the bio- pharmaceutical sector. How can we align this with what we can do? So we started searching for how we could enter this market.

We thought that although we were not sure about bio-pharming, but we thought that this could be how all vaccines might be made in the future and we decided that this was what we were going to do. We will use plants as bio-factories to express recombinant human peptides and proteins of high value. Now we knew what we were going to do, but we needed to decide how we were going to do it and at which stage of the drug development process. We decided that we would focus on the first “higher risk” discovery phase.

A simplified layout of our plan: We are busy developing a platform using great synthetic biology techniques to express our compounds of interest in plants. We will do the characterisation, small-scale, pilot-scale isolation, then go for a scale-up. We plan to exit post pre-clinical trials. That is the business model of AzarGen Biotechnologies.

From the time we got our first funder in 2004, then again in 2009, a lot of refining came into play. I am now full-time with AzarGen and we've reached our first milestone which is the freedom to operate in the USA. FTO analysis was conducted by a US law firm and facilitated by the law firm, ENS, in South Africa. We are now busy on the experimental side, on the research side. We have learnt a lot of lessons one of which is business acumen. It is the business that will drive this company, not the hot-shot science, because you need to show that you can solve the problem.

One thing is for sure, biotech is not a conventional business. You cannot compare it to IP started in a garage. You need a lot of support, a lot of infrastructure facilities. You need to negotiate with academics at universities, with technology transfer offices. You need to build relationships and collaborate; it's an on-going process. For us at this stage in South Africa we are going for the virtual model. In the virtual model we are a small team doing the core work with another team that can facilitate the IP management, a team that can guide us on the financial and business side and then outsource most of our research activities. The funders realise this as it's crucial to have speed on your side. So we are outsourcing a lot of our activities, either locally or in the US, to get the job done.

You can aim for one of those scenarios such as a buy-out or partnership but at the end of the day you need to know that your business model can change at any time and you need to adapt to that. I have always said that passion will allow you to tolerate this level of uncertainty but I must tell you it doesn't help if you have passion alone, you need to have faith as well and be able to adapt to any situation. We cannot give up, especially in South Africa.

Question: Where is AzarGen's actual lab work done?

MAURITZ: We are renting lab space at the University of Stellenbosch.

Question; So it's done in South Africa. I wondered when you talked about work in America.

MAURITZ: No we outsource activities in America but we rent a lab bench and glass house space in Stellenbosch.

Question; Your intention is to exit via an acquisition or something like that and you've started the process of promoting yourself. What's happened in that line?

MAURITZ: Yes that's the advice from our IP lawyer and there's the question about pitching ourselves to investors at this stage. But we are staying below the radar; we want to stick our heads up at the right moment and it doesn't help now to go out and tell what we're doing and then we get people interested and they come here and they see that you have developed technology, but not at a significant (commercially viable) level and then you have lost their interest. You want to be ready on the IP side and the proof of concept side. What we are doing is having discussions with law firms in the US about just what is the IP landscape at this stage, how should we go about it and then at what stage should we stick our heads out and start talking about partnerships.

Question: How are you going to recover the money you put in? How will you prove its worth? And how do you intend to manufacture your product?

MAURITZ: To answer your first question: to help investors make a decision to work with us, we had to present similar examples of Pharma/Biotech Merger & Acquisition (M&A) deals. With most of them the deal offered three, four, five or even more times the Return on Investment (ROI). However, usually the deal value mentioned is known as the "headline deal", but that's not the money that you will initially receive. The overall headline deal usually consists of an upfront cash payment (5% to 9% of total deal value) followed by royalty payments. However, in the bio-

pharmaceutical sector, with so-called blockbuster drugs, the ROI is usually a lot higher than the initial investment/s for development and Clinical trials. With the long drug development process and patent protection for only 20 years, drug companies usually receive ROI in the last 5 to 8 years of marketing the drug prior to patent expiration. With an average cost of $1,3 billion to develop a drug some Pharma giants such as Pfizer can cover those initial development costs with a blockbuster drug such as Lipitor that brings in more than $1,3 billion per annum. There are a few other examples of blockbuster drugs that produce a significant return on investment. However, here in SA we can't compare with the Big-Pharma model, developing novel drugs from bench to FDA approved. However, we have targeted the discovery drug development phase and aim for an exit after pre-clinical trials. We believe that such an exit deal will offer a return on investment in SA. This is a long term commitment and the goal is to secure investment, not only for the current R&D phase, but for the next phase of development prior to exit. Therefore, in the biotech sector, one cannot settle for a "flash in the pan" deal. You need to calculate the long term risk and what the overall cost will be before you exit. Therefore, the entrepreneurs and investors need to be aligned on what it will take to cover all those costs.

Your second question, with our current business model, we need to conduct FDA approved pre-clinical trials and there are only a few institutions in the world that are FDA accredited for pre-clinical trials for the disease sector that we are in. Therefore, it would make sense to outsource our manufacturing, using a cGMP approved service provider followed by an FDA application for pre-clinical trials. This whole FDA process needs to be facilitated by FDA consultants. If this process was possible to conduct in South Africa it would be awesome, but at this stage it is not realistic and we are in the process to explore options on where in the world we are going to do it. Our market currently is in the US so we will probably target US companies to outsource our manufacturing and pre-clinical activities.

Question I've got a technical question. What advantage does making your compound protein in plants have over other expression systems?

MAURITZ: Well for one the current expression systems used by, for instance, Genzyme is typically CHO cell culture systems and so there might be contamination such as allergens or other animal-derived contamination. Then there is cost. Compared with putting up the CHO system, a plant system is predicted to be about 25 % cheaper. There is also no contamination such as might be derived from a bacterial system such as Genentech's been using. With plants there are also the options of transient or transgenic and you can play around quite a lot with the protein structure. But plant systems are still complex enough to give you a complex molecule versus micro-organisms such as bacteria.

QUESTION: Can you define the yields of common proteins, or does it vary from protein to protein?

MAURITZ: Yes it varies and it's usually very low. It also depends upon the system you are using. If it's a transient system you can achieve very high yields, but because you are creating a new entity every time (every transformation event) it can become a regulatory complication for FDA regarding batch consistency. We aim to test our expression platform in stably transformed plants and although it may produce relative low yields, it might still be worthwhile to pursue due to the low manufacturing costs.

Question: For us to realise value we have to operate our IP outside the country. Is there any way to realise value back home?

MAURITZ: Guidelines have been published recently in December on the IPR Act which will influence businesses funded by Government. This publication is the first of a series of guidelines (from our understanding) on how IPR act and Government funding will influence the valuation of businesses locally and the effect for 3rd party acquisitions. As we understand, specific Government funding avenues might influence the exit deal and

also the exit valuation. Although there are still a lot of uncertainties regarding this process and the ultimate effect on the exit deal, especially to foreign parties, we aim to go ahead with our activities in South Africa and we hope to make a dent in the SA biotech sector. At this stage we hope that the Government will accommodate an exit deal as long as money will be coming into the country.

COMMENT: This is a general comment on the unintended consequences of the IPR situation. Is the new Bioeconomy Strategy going to tackle these issues? You only need one case where the money gets completely obliterated to kill off any enthusiasm for our entrepreneurs to go for big stakes. We have a rule of trying to keep things at home in a global world and perhaps this is something that needs to be put into the Strategy as this could be fundamental in limiting where investment takes place and whether any entrepreneur is willing to operate in South Africa. Because the next thing is for that entrepreneur to get on an aeroplane and fly to another country where they don't have this restriction and that will be the worst possible scenario for South Africa. This issue could be catastrophic.

3.4 QUESTIONS AND DISCUSSION (OPEN FLOOR)

COMMENT: I would like to reflect on the key messages that we heard starting with Antonel. Regarding the six steps of innovation her message is clear: there are nodes which are critical in terms of the working system of innovation; it's not a linear process but an iterative one. Clearly from one of the diagrams that she drew it also gets messy and we've seen also from Mauritz' presentation that it is not an easy path. You get some money, you do some work, you achieve some success and you move

on to the next stage. You have some failures and then you've got to keep on going back. I think the key message that came out was the importance of Intellectual Property both as an input and an output and I'll come back to that.

We then moved on to Morena's presentation. For most of us the vaccine industry is perhaps one that we feel we don't understand that much. It is quite important to outline the differences between the pharmaceutical industry as we know it and the vaccine industry. Also in terms of the markets, who is going to buy the product? It is quite clear that perhaps in the vaccines sector it's the government that is going to buy the products and therefore there is a need to align ourselves to understanding government strategy and government procurement policies. If government is funding these things how does it then enable procurement down the line? There are complexities in terms of the eco-system, the regulatory environment and the fact that we do require a lot of support along the way. For instance the determination of the market in terms of the number of births as opposed to the number of people that could potentially have the illness and the fact that the more you get these vaccines out the price starts to come down.

The key message that seems to come across is collaboration and the need to develop partnerships. From Mauritz's presentation we captured the passion in terms of what really makes our entrepreneurs successful. Again we go back to the definition of innovation that Antonel gave: invention costs money, innovation makes money. Also the fact that in terms of those particular six nodes or steps in the innovation value chain you require different sets of skills and that's a very important message linking to those six steps: that it's different sets of skills at the different stages. Mauritz's presentation also highlighted that in terms of putting together the team they had to look at the different kinds of skills that would be required to be successful in the market.

The key message coming through the IP awareness is that you must know where you are going to make your money. You have to start with the end in mind and somehow determine where in that value chain you are going to make money. We also see the message of out-sourcing; if we are going to be doing virtualisation and out-sourcing then the issues around intellectual property come in. If one looks at the IPR Act, and perhaps this is one of the most important things around this particular piece of legislation, it is not different to Bayh-Dole. If you study Bayh-Dole you will realise that it does not allow for disposal of IP. Have a look at it and the question is why should we ask for something different from what some of the global players are asking?

The message from Gabriella was also the TRIPS Agreement. Look at the flexibilities of the TRIPS Agreement and the question is are we utilising those flexibilities? There's a need for approval in terms of IP being sold off-shore so that somehow the value is realised. Somebody is able to capture what value is coming on board and the guidelines that NACI is putting out are becoming clearer in terms of at what stage and what you need to articulate in terms of the IP going abroad. We've seen the shift in terms of the Reserve Bank. Some of you would remember that about three years ago you could not move IP abroad. We've see a shift in terms of our Courts around determining how you can dispose of IP. Again there's been this thing that IP is capital and therefore this is the disposal of capital. In terms of that particular piece of legislation in the IPR Act it is important to be able to align all these other regulatory issues.

It's important for the people who are looking at the Bioeconomy Strategy to take a very objective view of IP and also to look at what is happening globally. Let's not allow a few people to determine a particular path that is not going to be to the benefit of this country. I think we have to take a holistic, long-term view. The solution must be a South African solution. We can take the lessons from best examples, not best practices. It's really best examples where we see them abroad and that's really where

the Bayh-Dole also provided some best examples in terms of the IPR Act.

COMMENT: I think we should really be serious about what we can manufacture in South Africa. We shouldn't let all manufacturing go ahead.

COMMENT: A comment on Neville's talk. I think a key criticism that we must take is that we have a government that is not very transparent. A key issue in the Biotechnology Strategy was that there wasn't an implementation plan. The agencies were the BRICS and they drew up business plans which were then vetted by the DST. There have been reviews of the BRICS and their projects, but these are unfortunately are not in the public domain. This I don't understand.

QUESTION: Regarding the Brazil model: this is one of the developing countries with a level of wealth. Is there any direct focus or deliberate link between the client and the developer, so products developed in Brazil will be absorbed? Not that there's a guarantee but is there that link?

GABRIELLA:There are no guarantees but in some instances entities foster the biotechnology links themselves. So, for example, the two super biotechnology companies that were founded with the Brazilian traditional pharmaceutical share-holders, right after the dates of implementation, were already involved in the PPD. So you can say that there is a direct role of an important stake-holder, which is the Ministry of Health, for the production or the absorption of a next generation drug. But the opposite is also true in the sense that, for example the change of law that eliminated the need for tenders, was actually a circumstance of technology because the Ministry recognised that it needed next generation technologies and that the former tender system was not working. Therefore the did this in order to execute negotiations in a more streamlined manner and to bring those competencies to the country. It wasn't a push from the buyer, it was actually a push from the technology. There are some initiatives from the start that already come with the buy-

in word from the government as was the case with these two. This is all public information. These two super Brazil biotech companies started with purchase contracts.

QUESTION: I would like to know how Brazil is able to compete with the North American and European markets considering that it's a developing country. My concern is do you have the skills to compete? My second question is if you don't have the skills how are you making the market find skills to help you?

GABRIELLA: Great question! How do we compete with more developed countries? This comes back to something that was said here but with which I disagree: that the value of a South African company, for example, is greater in the United States or other markets than it is here. This goes back to the fact, which has been demonstrated by concrete actions, that the value of innovation today has no borders. So yes, Brazil can compete with more developed markets and one example is the fact that Monsanto, which is one of the largest multi-national companies in the world. Purchased two Brazilian start-ups for a significant market value. What we see happening in the world today is that it doesn't matter if you have new molecules in South Africa, if you have true innovation in South Africa in my view that innovation will be valued at top currency wherever it's coming from here or Brazil or India. We don't have all the necessary skills in Brazil to compete in all the segments of the production chain, we have gaps in bio-manufacturing. The company that I mentioned, that has a FDA-approved orphan drug eligibility status, is actually manufacturing in the US. But what's wrong with that? You have to accelerate your research efforts, but you don't need to recreate every single step. You need to bring in as much key technology to reduce your foreign dependency, but the bottom line is that you need to accelerate the research and sometimes you have to out-source. The example that Mauritz just gave is called Vit Coes, Virtually Integrated Pharmaceutical Companies, as opposed to Fip Coes, which was the old model of Fully Integrated Pharmaceutical Companies.

SESSION 4: WAY FORWARD AND CLOSING REMARKS

4.1: WAY FORWARD AND RECOMMENDATIONS (Prof Michael Pepper)

Prof Pepper thanked all participants and presenters for contributing excellently.

There are two key documents that anyone working in this space really needs to be very familiar with, the National Development Plan and the Bioeconomy Strategy (which has been in the making for several years).

Important things to come through were:

- The importance of taking ownership. We need to take ownership of what we're doing and not sit back passively and wait for things to happen.
- The Bioeconomy Strategy will accommodate just about everything that any of us wants to do. Its purpose though is not to make everybody happy because you know you can't please everybody all the time. Therefore it is going to be important to focus and prioritise in this Strategy. We need to undertake a market research survey, which has never been done in the three sectors that the Strategy speaks to, Health, Agricultural and Industrial/Environmental Biotech so that when the funding comes we know exactly where to direct it. It is important that we do prioritise and that we do undertake some sort of formal assessment of where the key opportunities are in this sector
- Incentives. The speaker from DTI mentioned that the pharmaceutical manufacturing base has been eroded and that 37 manufacturing plants closed down between 1995 and 2005. Many if not most of those companies were involved in the synthesis of API's and in closing down those companies we not only lost all the revenue that came from them, we also lost 6,500 jobs. However, we also now have to import all our API's and this contributes very significantly

to our trade deficit. We need to critically look at the legislation and the IPR Act plus many other pieces of legislation; the National Health Act, the Bio-Diversity Act, the Companies Act and the GMO Act.

Part of the NACI Bioeconomy Project team's goal at the moment is to critically look at the legislation to see whether it promotes or hinders the emergence of the Bioeconomy Strategy. If we really see that there are things that are problematic we have to do something about it.

We need to pay more attention to incentives. We are an emerging market, we are an extremely resourceful nation, and we manage to do a lot with very little. This speaks very well for what lies ahead of us. We recognise that we are in a global market and there are no borders to what we do, so we need to take that resourcefulness, combine it with the extensive natural resources that we have (we are perhaps the richest country on a square kilometre basis in terms of bio-diversity) and we need to look out at the global market and see how we can capitalise on these resources, not only human but also natural.

- Very important also is to accept that this field we involves risk, so accept risk. We tend to be very risk averse but we need to embrace the risk and manage it. We need to integrate it into what we're doing, so involve it in all the calculations that we make going forward. It was very encouraging to hear that the DST is looking at setting up a Venture Capital Fund, because as you know there's virtually no venture capital in South Africa for biotechnology.

We need to find ways of implementing the Strategy it's not simply a question of having a great document that reads well, that covers all the bases. We are going to have to work hard from here on and be proactive in making sure that the Strategy can be implemented. Together with implementation goes M and E, monitoring and evaluation. We need to constantly have monitoring and evaluation processes in place to make sure that as we apply this Strategy we're achieving the objectives that we set out in the beginning.

4.2. CLOSING REMARKS – Ms. Kelebogile Dilotsotlhe

Ms. Dilotsotlhe thanked the organisers of the program.

She also thanked each of the presenters for their insightful contributions;

- Professor Michael Pepper for setting the tone at the beginning and helping to identify the way forward.
- The Chairperson of Council, Dr Steve Lennon, who had one message: focus on the Bioeconomy Strategy and link it to the NDP. What does NACI have to do from here? The Council provides DST with credible policy advice on the bioeconomy and that is greatly assisted by meetings such as this.
- Gabrielle Cezar set the scene with those issues that are enablers, those that are disablers and those that create an environment conducive for venture capital and the innovation space.

She went on to thank every speaker and participant and concluded by saying that the outcomes of the workshop would definitely assist NACI to shape and sharpen its policy advice to the Minister of Science and Technology.

ANNEXURE A: ACRONYMS

API's	Active Pharmaceutical Ingredients
AIDS	Acquired Immune Deficiency Syndrome
ARV	Antiretroviral Drug
BIC	Biotech Incubation Center
BioPAD	Biotechnology Partnership and Development
BioVac	The Biovac Institute
BNDS	Brazilian National Development Bank
BRICS	Brazil, Russia, India, China, South Africa
CIPC	Companies and Intellectual Property Commission
cGMP	Current Good Manufacturing Practice
CHO	Chinese Hamster Ovary Cell
CO_2	Carbon dioxide
CSIR	Centre for Scientific and Industrial research
DOH	Department of Health
DST	Department of Science and Technology
DTI	Department of Trade and Industry
ENS	Edward Nathan Sonnenbergs
FDA	Food and Drug Administration
FIFA	Fédération Internationale de Football Association
FIP COES	Fully integrated Pharmaceutical Companies
FTO	Freedom to Operate
GDP	Gross Domestic Product
GERD	Gross Expenditure on Research and Development
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practices
HIV	Human Immunodeficiency Virus
ICU	intensive care unit
IP	Intellectual property
IPR	Intellectual Property Rights

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KZN	KwaZulu-Natal
MCC	Medicines Control Council
MRC	Medical Research Council
M&A	Merger and Acquisition
NACI	National Advisory Council on Innovation
NBA	National Biodiversity Act
NBAC	National Biotechnology Advisory Committee
NCI	National Cancer Institute
NHRC	National Health Research council
NDP	National Development Plan
PDP	Partnerships for Productive Development
PhD	Doctor of Philosophy
QC	Quality Control
R&D	Research and Development
ROI	Return on Investment
SA	South Africa
SME	Small and Medium Enterprises
TB	Tuberculosis
TRIPs	International Agreement for Intellectual Property
UCT	University of Cape Town
UNCTD	United Nations Conference on Trade Development
US	United States
USA	Unites States of America
VIT COES	Virtually Integrated Pharmaceutical Companies
VCF	Venture Capital Fund