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Briefing document

**The status of genetically modified (GM)
pharmaceutical crop research
in South Africa**

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CONTENTS

• What are GM pharmaceutical crops?	3
• Determining the status of GM pharmaceutical crop research in South Africa	3
• Pharma-crop facilities in South Africa	5
• Conclusion	7
• Recommendations	7
• References	9
• Annexures 1 and 2	10

THE STATUS OF GENETICALLY MODIFIED (GM) PHARMACEUTICAL CROP RESEARCH IN SOUTH AFRICA

WHAT ARE GM PHARMACEUTICAL CROPS?

Genetically modified (GM) pharmaceutical crops are crops which have been genetically engineered / modified to produce pharmaceuticals. These pharmaceuticals can be vaccines, antibodies or therapeutic proteins. The crops are often known as “pharma-crops”.

Pharma-crops are a contested and little-known terrain, with remarkable benefits being claimed for them in South Africa – edible vaccines that will be easy to consume, vaccines to alleviate the desperate HIV/AIDS situation, supply of low cost drugs, added value to crops ... whilst other voices ask about contamination of the food supply and the environmental and social costs of this technology.

Internationally, commercial GM plant-derived pharmaceuticals are not available, but there are GM plant-derived pharmaceutical proteins which are said to be approaching commercial release.¹ But what is the situation in South Africa? What sort of research is being done, where is it being done, who is funding it, what plants are being used, what pharmaceuticals are being produced, at what level is the research being done?

DETERMINING THE STATUS OF GM PHARMACEUTICAL CROP RESEARCH IN SOUTH AFRICA

What is the reality in South Africa? The regulatory framework governing GMO's in South Africa requires that:

- i) permits are needed to “... import or export from the Republic of South Africa, or develop, produce, use, release or distribute any genetically modified organism in the Republic of South Africa”...², except in the case of:
- ii) GMO's that are “... used under conditions of contained use in academic and research facilities, and for those organisms listed in Table 3 of the Annexure”³.

The list of permits issued from 1999 to date, by the Department of Agriculture, are on the Department's website. Permits are given for Contained use, Trial release, General release and Commodity clearance. None of the permits, and there have been many of them, have been for GM pharmaceutical crops.

¹ “Plant-derived pharmaceuticals – the road forward.” *TRENDS in Plant Science* Vol. 10. No.12 Page 580 December 2005

² Department of Agriculture. 1999 Regulations within the framework of the Genetically Modified Organisms Act (No. 15 of 1997): Regulation 2. (1)

³ Department of Agriculture. 1999 Regulations within the framework of the Genetically Modified Organisms Act (No. 15 of 1997): Regulation 2. (2)

A list with certain details of the 48 academic and research facilities that have been registered with the Department of Agriculture from May 2000 to January 2006, was made available by the Department. According to the Department's Standard Operating Procedures for (academic and research) facilities, an import permit or a permit authorizing contained use is not needed, provided that:

- (a) The GMO will only be used within a research or academic facility;
- (b) The activity is for research or academic purposes only;
- (c) The confined area within the facility is a laboratory or growth room;
- (d) The confined area within the facility is a greenhouse (glasshouse), provided that the greenhouse (glasshouse) is not used for bulking-up or commercial production purposes;
- (e) The facility is registered in terms of Regulation 4 of the GMO Act;
- (f) The level of containment is not higher than 2, which has been verified by the Advisory Committee during registration of the facility;
- (g) The GMO will not be removed from the facility or released into the environment;
- (h) The responsible individual in charge of the facility implements the necessary measures to effectively contain the GMO at all times.⁴

A contained use permit is required once the research is scaled up from basic research to product development, or when conducting the activities in a greenhouse or when the containment level is 3 and above.⁵

If the facilities are working on GMO's on an ongoing basis, then they need to renew their registration on an annual basis as registration is valid for a maximum period of one year.

The 48 facilities that have been registered, but not all of them currently, are housed in 26 institutions (see Annexure 1). The details given for each facility usually included information on the location of the facility, the responsible person, type of facility, containment level, purpose of genetic modification and a list of genetically modified organisms.

Of the 48 facilities, 33 were contacted to check if they were involved in GM pharmaceutical crop research. This was done as it was not always possible from the information provided by the Department, to determine whether research was on GM pharmaceutical crops or not. For example, in the section on the purpose of genetic modification, "crop improvement strategies", "introduce high price products into plants", "production of proteins" may be given or in some cases no information was provided. The remainder of the facilities were not contacted because it was clear from the information provided that they were not involved in GM pharmaceutical crop research. Of the 48 facilities registered, two have GM pharmaceutical crop research projects that fall under their jurisdiction. These are listed here, with their involvement in GM pharmaceutical crop research discussed later on:

1. CSIR-BIO/CHEMTEK Department (Brummeria) as one of the partners of the Pharma-Planta Consortium
2. University of Cape Town, Department of Molecular and Cell Biology (Rondebosch) with their Plant-Based Vaccines Group

⁴ Department of Agriculture: Standard Operating Procedures for implementing Regulation 2(2) of the Genetically Modified Organisms (GMO) Act, 1997 (Act No. 15 of 1997)

⁵ Department of Agriculture: "Application to register a facility for activities involving genetic modification"

It should also be noted that none of the organisms listed in Table 3 of the 1997 Regulations or in the annexure of the previously mentioned Standard Operating Procedures, relate to GM pharmaceutical crops.

PHARMA-CROP FACILITIES IN SOUTH AFRICA

1. Pharma-Planta

Pharma-Planta is a research consortium representing 39 academic and industrial institutions, 38 of them from Europe and the CSIR (Council for Scientific and Industrial Research) from South Africa (see Annexure 2). Pharma-Planta was launched in 2004 and is funded by the European Union, under the Framework 6 programme for Research and Development, for an amount of 12 million Euros over five years.

The mission of the Pharma-Planta Consortium is “to develop efficient and safe strategies for the production of clinical-grade protein pharmaceuticals in plants, and to define procedures and methods for the production of these proteins in compliance with all appropriate regulations”.⁶ The pharmaceuticals planned are for vaccines and treatments against major diseases including AIDS, diabetes, rabies and TB.

Although the CSIR has been working on genetically modified maize, grain sorghum and millet for many years and has “expertise, infrastructure and production capabilities for breeding and bulking up of genetically transformed maize”⁷, the work under the Pharma-Planta project is at a basic research level. The staff consists of two doctoral and two M.Sc. graduates and one greenhouse assistant. The research is on transforming maize to produce antibodies that have neutralizing activity against HIV, and on transforming tobacco to produce antibodies that have neutralizing activity against rabies.

The change from basic research to product development is contingent on the outcome of the exploratory work. It is anticipated that this shift will only be made in the fifth year if all goes well. Currently there are no plans for field experimentation or general release.⁸

In 2004, it was postulated in the United Kingdom that as a result of the Pharma-Planta work that “Scientists will probably carry out the first field trials (of vaccine-producing plants) in South Africa in 2006, because researchers feared the possibility of crop vandalism in the United Kingdom, where some activists have in the past destroyed GM crops”⁹. However, the CSIR has stated that no decision has been made as to whether South Africa will be the test site for the first pharmaceutical crops.¹⁰ Spain and the United Kingdom were mentioned as other possibilities besides South Africa for this.

It was emphasized by the CSIR that issues around food security would be dealt with, that different regulations are needed for pharmaceutical crops as opposed to food crops and that Standard Operating Procedures for the Pharma-Planta project are being worked on.

⁶ <http://www.pharma-planta.org/description.htm>

⁷ CSIR media statement “The CSIR, South Africa and Project Pharmaplanta” July 2004

⁸ Dr Rachel Chikwamba, CSIR pers. comm. 23 February 2006

⁹ Steve Connor “GM plants will be used to create Aids vaccine”. The Independent, 13 July 2004

¹⁰ Dr Dusty Gardiner, CSIR pers. comm. 14 Dec 2005

Funding for the Pharma-Planta work in South Africa is from the CSIR and the EU. There are no commercial partners and no multinational involvement. The level of funding is contingent upon the outcome of the exploratory research that they are currently involved in.¹¹ However, a figure of between R5 – R10 million was mentioned for the 5 year project.¹²

2. Plant-Based Vaccines Group

This is an informal grouping in the Departments of Molecular and Cell Biology (MCB) and the Institute of Infectious Diseases and Molecular Medicine (IIDM), in collaboration with the BIOVAC Institute.

The Plant-Based Vaccines Group is working on a Human Papilloma Virus (HPV) plant based vaccine and a HIV plant based vaccine. In both instances the plant used is tobacco, *Nicotiana tabacum* and *Nicotiana benthamiana*.

There is also a plan to attempt to produce influenza virus haemagglutinin protein in plants soon as well as short chain variable region antibodies derived from chickens. There are no plans for field trials as the intention is for the plants would be grown in an indoor or quarantine glasshouse.¹³

a) Human Papilloma Virus (HPV) plant based vaccine

The status of the work has changed from pure research to largely developmental with two candidate vaccines for HPV (HPV thought to be the major cause of cervical cancer). The one vaccine is a novel chimaeric capsid protein produced via recombinant baculovirus, whilst the other is a conventional capsid protein vaccine produced in plants. Scale-up of production and purification is being investigated. The vaccine has been in animals (mice) and there is the intention of non-human primate trials soon and only after that could consideration be given to human trials.¹⁴

This research is currently funded through the Innovation Fund of the National Research Foundation (NRF) / Department of Science and Technology (DST) and the Poliomyelitis Research Foundation. Previous funding was from The Technology and Human Resources Industry Programme (THRIP), managed on behalf of the National Research Foundation on behalf of the Department of Trade and Industry (the dti) and the Cancer Association of South (CANSAs).

b) HIV plant based vaccine

The status of this work is preliminary and is funded by the SA AIDS Vaccine Initiative (SAAVI).

3. Other facilities

There has been some interest expressed in genetically modified pharmaceutical crops by other registered facilities, but at present there are no plans to do this work. In one facility, the ARC-Roodeplaat Vegetable & Ornamental Plant Institute, it was noted under the Purpose of Genetic Modification "... is also involved in the development of transgenic plants as biofactories for the inexpensive production of high value proteins

¹¹ Dr Rachel Chikwamba, CSIR pers. comm. 23 February 2006

¹² Dr Dusty Gardiner, CSIR pers. comm. 14 Dec 2005

¹³ Prof. Ed. Rybicki, UCT pers.comm. 27 February 2006

¹⁴ Prof. Ed. Rybicki, UCT pers.comm. 27 February 2006

such as vaccines, enzymes, etc.”. However there are no plans at Roodeplaat to work on pharmaceutical crops in the foreseeable future.¹⁵

CONCLUSION

Currently there are no genetically modified pharmaceutical crops grown in South Africa. Of the 48 academic and research facilities that have been registered with the Department of Agriculture to work on genetically modified organisms, only two are directly involved with genetically modified pharmaceutical crop research. These are the CSIR with their European Union funded Pharma-Planta Consortium and the Department of Molecular and Cell Biology of the University of Cape Town with their Plant-Based Vaccines Group. Although there has been some interest expressed by some of the facilities to do GM pharmaceutical crop research, currently there are no plans to do this work. Recommendations coming out of this work on “The status of genetically modified pharmaceutical crop research in South Africa” follow:

RECOMMENDATIONS

1. In-depth studies of GM pharmaceutical crop research in SA

In-depth studies need to be done on the GM pharmaceutical crop research done at the two facilities (CSIR and UCT’s Dept of Molecular and Cell Biology). The claims that are made for the research should be analysed, the risk assessments obtained, the finances detailed and the links with partner organizations (inside and outside the country) mapped. It would be important to know what research work the partner organizations are doing and the details of the genetically modified organisms shipped to SA.

In the case of the CSIR, it would be important to gain access to the Pharma-Planta consortium agreement or at least key portions of it – at the moment it is not able to be made available and neither is the technical information relating to the project.

2. Informing the public

The public needs to be informed about issues (environmental, social and health) around GM pharma crops. The public need to have easy access to better information than the web hype of edible vaccines in bananas and quick fixes to solve the devastation caused by HIV/AIDS and TB.

National government’s regulatory system does not facilitate easy access to information around GMO work, but national government has a responsibility to the people of South Africa to make them aware of the issues and particularly those issues around food security. Pharma crops are different to food crops and there is always the risk that there will be contamination of the food supply.

It is recommended that there is a high profile national forum where issues around pharma-crops are raised and that national government makes a concerted effort to see that concerns around pharma-crops are addressed at all levels of government (from policy makers to the agricultural extension officers).

¹⁵ Dr Kobie Theron, Roodeplaat Vegetable and Ornamental Plant Institute, pers. comm. February 2006

3. South Africa's biosafety system

South Africa's biosafety system is widely regarded as being weak (e.g. in terms of liability, public participation, access to information) and the current system does not adequately cater for pharma-crops. The recommendations are:

- i) easy public access to risk assessments
- ii) that the biosafety system is developed to provide proper protection in terms of GM pharma-crops, e.g. with respect to food security, liability, Standard Operating Procedures, human and animal health and environmental impact assessments.
- iii) that South Africa's weak biosafety systems and lack of capacity should not be allowed to be exploited by research partners outside the country, e.g. if it's not possible to do the field trials and commercial growing of pharma crops in Europe, then it should not be possible here.
- iv) that the largely self-regulated research done at the registered research and academic facilities should at a far earlier stage be actively regulated by national government and that there should be public participation and easy access to information at a far earlier stage as national interests of food security, human health and environment are at stake. (It would also mean that the millions of rands needed for this type of research could be diverted at an earlier stage, if it was found that the research is, for example, going to negatively impact on food security.)

4. Contamination of Food supply

There is widespread support for not putting pharmaceuticals into food plants. If there are mistakes in the US, (e.g. with Prodigene Inc.'s volunteer transgenic maize growing in a soybean crop one year after the pharmaceutical maize was harvested¹⁶), which is supposed to be better equipped than South Africa, there will be mistakes in South Africa. Contamination of the food supply can occur in the field, mixing of seed, harvesting on the farm, shipping, handling and storage.

The recommendation is for no pharmaceuticals in food plants, which means no edible vaccines and no pharmaceuticals put into food crops where the pharmaceutical is later extracted! Don't use food plants for pharma-crops.

5. Financing of GM plant-derived pharmaceuticals

The claims of cheap GM plant-derived pharmaceuticals (vaccines, proteins ...) through GM pharmaceutical crops needs to be assessed. The costing of this from staffing, infrastructure, research funds, production and commercialization, liability and social and environmental impacts needs to be included. Much public money is going towards this work. Should this be the case? Will the products do what they say they will do and will the products be "safe"?

¹⁶ "Plant-derived pharmaceuticals – the road forward." *TRENDS in Plant Science* Vol. 10. No.12 Page 581 December 2005

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Freese, B. & Caplan, R. "Plant-made pharmaceuticals Financial Risk Profile". January 2006. Friends of the Earth and U.S. Public Interest Research Group.

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Ma, J K-C, *et al* "Molecular farming for new drugs and vaccines. Current perspectives on the production of pharmaceuticals in transgenic plants". *EMBO Reports* 6: 593-599. 2005.

Mayer, S. "Non-food GM Crops: new dawn or false hope?" August 2003. Part 1: Drug Production. GeneWatch UK Report.

Websites

www.mcb.uct.ac.za/plant_vaccines.htm Plant-Based Vaccines Group

www.nda.agric.za Department of Agriculture, South Africa

www.pharmaplanta.org Pharma-Planta consortium

www.pub.ac.za Public Understanding of Biotechnology (PUB), Department of Science & Technology

www.twinside.org.sg Third World Network

Annexure 1

LIST OF FACILITIES registered with the Registrar of the Genetically Modified Organisms Act, Department of Agriculture May 2000 – January 2006¹⁷

	NAME OF FACILITY	AREA and postal code
1.	AECI-BIOPRODUCTS (PTY) LTD (see also no. 13)	Umbogintwini 4120
	AGRICULTURAL RESEARCH COUNCIL (ARC)	
2.	ARC- Grain Crops Research	Potchefstroom 2520
3.	ARC-INFRUITEC-NIETVOORBIJ	Stellenbosch 7599
4.	ARC – Livestock Business Division Irene	Irene 0062
5.	ARC-PLANT PROTECTION RESEARCH INSTITUTE (Onderstepoort Veterinary Institute)	Onderstepoort 0110
6.	ARC-PLANT PROTECTION RESEARCH INSTITUTE	Pretoria 0001
7.	ARC-ROODEPLAAT VEGETABLE & ORNAMENTAL PLANT INSTITUTE	Pretoria 0001
8.	ARC-ROODEPLAAT VEGETABLE & ORNAMENTAL PLANT INSTITUTE	Pretoria 0001
9.	AMPHIGRO CC	Monument Park 0181
10.	BIOVAC INSTITUTE	Pinelands 7430
	CSIR	
11.	CSIR-BIO/CHEMTEK Department	Brummeria 0148
12.	CSIR-BIO/CHEMTEK Department	Modderfontein 1645
13.	CSIR-BIO/CHEMTEK Department	Modderfontein 1645
14.	FRONTIER LABORATORIES CC.	Dennesig 7601
15.	MEDICAL RESEARCH COUNCIL	Tygerberg 7570
16.	MOLECULAR DIAGNOSTIC SERVICES	Westville 3630
17.	NATAL BIOPRODUCTS INSTITUTE	Cape Town 7000
	NATIONAL BIOPRODUCTS INSTITUTE (name change from above)	Pinetown 3600
18.	NATIONAL HEALTH LABORATORY SERVICES	Johannesburg 2000
19.	OUDSPAN CITRUS CENTRE	Centralhill 6006

¹⁷ List compiled from information supplied by the Registrar of the GMO Act on 10 January 2006.

Note: renewals and new applications may have been received since this date, registration is valid for a maximum period of one year.

20.	PANNAR (PTY) LTD	Greytown 3250
See 1.	SOUTH AFRICAN BIOPRODUCTS (was AECI-BIOPRODUCTS)	Umbogintwini 4120
21.	SOUTH AFRICAN BIOPRODUCTS APPLYIT (PTY) LTD	Westway 3635
22.	SOUTH AFRICAN BIOPRODUCTS	Umbogintwini 4120
23.	SOUTH AFRICAN BIOPRODUCTS	Umbogintwini 4120
24.	SAPPI FORESTS (PTY) LTD	Howick 3290
25.	SA SUGAR ASSOCIATION EXPERIMENT STATION	Mount Edgecombe 4300
	UNIVERSITY OF CAPE TOWN	
26.	UNIVERSITY OF CAPE TOWN (Department of Molecular and Cell Biology)	Rondebosch 7000
27.	UNIVERSITY OF CAPE TOWN (Department of Human Biology)	Observatory 7925
28.	UNIVERSITY OF KWAZULU-NATAL	Pietermaritzburg 3209
29.	UNIVERSITY OF FREE STATE	Bloemfontein 9300
30.	UNIVERSITY OF PORT ELIZABETH	Port Elizabeth 6000
	UNIVERSITY OF NORTH WEST	
31.	UNIVERSITY OF POTCHEFSTROOM now University of North-West (Potchefstroom campus)	Potchefstroom 2520
32.	UNIVERSITY OF NORTH-WEST	Potchefstroom 2520
33.	UNIVERSITY OF PRETORIA	Pretoria 0001
	UNIVERSITY OF STELLENBOSCH	
34.	UNIVERSITY OF STELLENBOSCH (Institute for Plant Biotechnology)	Matieland 7602
35.	UNIVERSITY OF STELLENBOSCH (Institute for Wine Biotechnology)	Stellenbosch 7599
36.	UNIVERSITY OF STELLENBOSCH (Department of Microbiology)	Matieland 7602
See 15.	UNIVERSITY OF STELLENBOSCH (Medical Research Council)	Tygerberg 7570
37.	UNIVERSITY OF STELLENBOSCH (Department of Medical Virology)	Tygerberg 7570
38.	UNIVERSITY OF STELLENBOSCH (Agricultural Research Council – INFRUITEC)	Stellenbosch 7599
39.	UNIVERSITY OF STELLENBOSCH (Dept of Biochemistry)	Matieland 7602
40.	UNIVERSITY OF STELLENBOSCH (Department of Genetics)	Matieland 7602
41.	UNIVERSITY OF STELLENBOSCH (Department of Genetics)	Matieland 7602
42.	UNIVERSITY OF STELLENBOSCH (Department of Genetics)	Matieland 7602
43.	UNIVERSITY OF STELLENBOSCH	Matieland 7602

	(Department of Genetics)	
44.	UNIVERSITY OF THE NORTH (Biotechnology unit)	Sovenga 0727
45.	UNIVERSITY OF THE WITWATERSRAND (Department of Molecular Medicine and Haematology)	Wits 2050
46.	RHODES UNIVERSITY (Department of Biochemistry and Microbiology)	Grahamstown 6140
47.	UNIVERSITY OF JOHANNESBURG (Department of Biochemistry)	Auckland Park 2006
48.	VINE VET (PTY)LTD	Paulhof 2056

Annexure 2

PHARMA-PLANTA Members of the Consortium¹⁸

- Fraunhofer Institute of Molecular Biology and Applied Ecology, Aachen, Germany
- St George's Hospital Medical School, London, UK
- Rheinisch-Westfälische Technische Hochschule (RWTH), Aachen, Germany
- National University of Ireland, Maynooth, Republic of Ireland
- John Innes Centre, Norwich, UK
- Centre de Cooperation Internationale en Research Agronomique pour le Development (CIRAD), Paris, France
- Oxford Brookes University, Oxford, UK
- University of Warwick, Coventry, UK
- Universität für Bodenkultur, Vienna, Austria
- Polymun Scientific Immunbiologische Forschungs GmbH, Wien, Austria
- Università Degli Studi di Verona, Verona, Italy
- Ente per le Nuove Technologie, l'Energia e l'Ambiente, Rome, Italy
- Diamyd Medical AB, Stockholm, Sweden
- Universite Blaise Pascal Clermont-Ferrand II, Aubiere, France
- Institut National de la Recherche Agronomique, Paris, France
- University of Cambridge, Cambridge, UK
- University of Glasgow, Glasgow, UK
- Ruprecht-Karls-Universität Heidelberg, Heidelberg, Germany
- Universite Catholique de Louvain, Lovain-la-Neuve, Belgium
- University of Leeds, Leeds, UK
- Consiglio Nazionale Delle Ricerche, Rome, Italy
- Council for Scientific and Industrial Research (CSIR), Pretoria, South Africa
- Rothamstead Research Ltd, Harpenden, UK
- Universite de Neuchatel, Neuchatel, Switzerland
- Max Planck Institute, Potsdam, Germany
- Trinity College, Dublin, Republic of Ireland
- Institut für Pflanzengenetik und Kulturpflanzenforschung, Gatersleben, Germany
- Vlaams Interuniversitair Instituut voor Biotechnologie VZW, Zwijnaarde, Belgium
- Agricultural University of Athens, Athens, Greece
- Centre for the Management of Intellectual Property in Health research and Development (MIHR), London, UK
- Mosaic Systems BV, Prinsenbeek, The Netherlands
- Univeritat de Lleide, Lleida, Spain

¹⁸ <http://www.pharmaplanta.org.consortium.htm>