TB INVESTMENT — MORE THAN JUST GILDING ELI'S LILLY

In a R200 million investment and empowerment initiative, South Africa has been chosen to manufacture multidrug-resistant tuberculosis (MDRTB) drugs and will late next year supply the entire continent and South America.

Confirming that the operation could be up and running by as early as June 2004, Sipho Moshoane, Corporate Affairs Director for Eli Lilly, South Africa, said this country was chosen because it had the necessary infrastructure, faced a 'very relevant' TB problem and was a regional and continental power.

Also, the Center for Disease Control, one of the partners in what is a global Eli Lilly initiative, had offices in South Africa. 'Head office was looking for regional bases where the quickest start-up was possible,' he explained.

One of the few 'transfer of technology' programmes in the global pharmaceutical industry, the project is part of a R500 million public/private initiative by the drug giant. Its partners include the World Health Organisation (WHO), the United States Department of Health and Human Services Centers for Disease Control and Prevention (CDC), Harvard University Medical School and Perdue University.

The entire project aims at training enough health care staff and to increase sufficiently the supply of critical drugs needed to treat MDRTB so that it can reach the WHO goal of 20 000 patients annually by 2012.

Moshoane said it was 'possible' that the drugs, capreomycin and cycloserine, would be cheaper locally because South Africa would have a currency advantage. Until now they have been produced only in the UK. However, he said he was 'mindful of not raising (price) expectations'.

South Africa will be the first of four global MDRTB drug production nodes. Russia will produce for Eastern Europe, China for itself, and India for Asia.

Cycloserine is already registered in South Africa and the capreomycin application is being prepared for registration so that approval can coincide with the upgrading of the plant next year.

The local production facility will create 'up to 100' jobs while a 'Centre of Excellence' will be set up for the whole of Africa, in partnership with Harvard University, in order to train and impart best practices in TB treatment for African health practitioners.

Moshoane said the plant and the Centre of Excellence would be housed together on one of two sites in Gauteng. A similar Centre has been set up in South America with Harvard University. It will be working closely with local experts and the South African Department of Health.

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Up to 10 full-time staff from Eli Lilly's overseas manufacturing plants will be posted locally for 4 years to give technical assistance and training. Being the first to come 'on stream', would give South Africa a major advantage in export opportunities. The WHO intends to oversee distribution of the drugs to those treatment facilities that have the appropriate infrastructure to manage the DOTS-Plus programme.

South Africa suffers from one of the worst TB epidemics in the world and according to the Department of Health, there has been a ten-fold increase in TB infections over the last 2 years, with almost 1 000 people now dying every month. The lack of co-ordinated and managed TB control programmes in South Africa as well as increasing rates of HIV have led to the widespread emergence of MDRTB.

Moshoane described the project as 'multi-dimensional — we'll also be looking at treatment, surveillance and evaluation'. Compliance was 'the very reason why,' the Centre would be established.

'Our South American experience has taught us that it's an educational thing. We need to collectively share experience with other health workers in this country and this continent and adapt to local conditions to see what works. For example, we use shopkeepers for compliance here — we need that central forum to see what's working and what else we can do. The government by its very nature will provide infrastructure and we will provide skills and health workers,' he said.

South America has taught Eli Lilly that running 1 week - 3-month TB courses for health workers, with an emphasis on enrolling patients into why they need to take their medication for 18 months, is critical.

There is no generic registered for cycloserine but a capreomycin (injectable) generic is registered overseas. 'As far as we know, there are no moves to register generics for either locally,' Moshoane said. He had not spoken to government about HIV/AIDS yet, 'firstly because Eli Lilly has limited capacity and knowledge and secondly, these MDRTB drugs are small in terms of our profile and revenue — we're more geared towards oncology, mental health and men and women's health'.

The 'New Heights' empowerment company will be chaired by Dr Ntuthuko Bengu, a Harvard-trained managed health care expert,

anaesthetist and pharmaco-economics researcher. Bengu told the *SAMJ* in mid-July that an interview was 'about 2 months premature'. 'We're only just getting into top gear, entering agreements and finalising funding. I'm not keen to go into detail because we haven't communicated our plans to government and I don't want to surprise them.' He said that long before it was registered, cycloserine had been made available to the government in terms of a special Section 21 agreement, but this had meant Eli Lilly could not promote it. 'Now we'll be looking at promotion, but you really don't want to hand it out like candy — you have to be extremely sensitive to protocols — our main customer will be the government, the mining houses and the private sector.'

He was reluctant to reveal the names of his 4 proposed fellow directors because some were resigning their present posts and had yet to tell their employers. 'I just don't have their permission and there's obviously sensitivity,' he said.

His prediction with current lead times was that the manufacturing plant would be churning out the MDRTB drugs by 'the second half of next year'.

Chris Bateman

The South African Medical Journal

100 years ago: **Case of needle in the knee joint stimulating tubercular disease**

ARNOLD H WATKINS, MD, FRCS

A female aged 18 months came under my care at the Kimberley Hospital on 16 July on account of a swollen and stiff left knee thought to be due to a broken needle having run into it on 11 June. The only evidence in support of this idea was that a broken portion of needle had been found on a sack on which the child was playing when it suddenly began crying and complained of pain in the knee, and that from that time the knee had been swollen, stiff, painful, and kept in a flexed position.

I had some doubt about the needle, being in the knee when I saw it. It presented the typical appearance of a tubercular joint, but the skiagram taken at the hospital plainly shewed a portion of needle buried deeply at the inner side, and almost behind the joint. On 20 July, I opened the joint by a straight incision on the inner side, in the axis of the limb. The synovial member was oedematous, but there was no pus in the joint. The needle was not easy to find, as it lay very deeply, and could not be felt at any stage of the operation, but, keeping straight on the line indicated by the skiagram, I cut into the epiphysis of the femur, and, just below the cartilage came on a small cavity, in which about half an inch of a fairly thick darning needle lay embedded. The operation wound healed per primam, the temperature, which had been slightly raised, became normal, and, when the child left the hospital on the 30th of the month, the swelling of the knee was very much reduced, and the joint could be freely moved with very little pain to the patient. There is every reason to hope that a perfect joint will result.

This is most clearly a case in which the roentgen rays were of the greatest value, as, even had one been sure of the diagnosis, it would have been impossible to have found the needle, had it not been that the skiagrams taken in two planes gave one the exact position in which it was located.

50 years ago: **The ultra-violet fluorescence of the tongue in African children**

The ultra-violet fluorescence phenomenon of the tongue was described a quarter of a century ago by Hymans van den Bergh and more recently Tomaczewski has studied it, both in health and in relation to certain diseases. Van den Bergh described a more or less visible red fluorescence of the tongue.

Tomaczewski noted that when the tongue is observed through a magnifier, the fluorescence is seen to be composed of small discrete fluorescent points, which he believed to correspond to the filiform papillae. The incidence of fluorescence is greatest in the age group 0 - 20 years (89 %), but with increasing age, the incidence declined to 47% in the 81 - 100 age group.

Tomaczewski states that the fluorescence is due to the bacterial production of porphyrins; there is, however, no evidence as to the origin of these compounds, which might be synthesized by bacteria, or decomposition products of haemoglobin derived from food or from the host. The significance of the porphyrins is also obscure at present.

Finally, the macroscopic appearance of the tongue bears no relation to the incidence of fluorescence, for tongues which appear normal often exhibit no fluorescence. There seems to be, however, according to investigations now in progress, a broad correspondence between the incidence of fluorescence and the ratio between the number of filiform and fungiform papillae per unit area of the tongue surface (papillary ratio) as calculated by the tongue print method.

(*Abstract from original article.*)