

Merck's appetite for African microbes

by Edward Hammond

With the rise in infections resistant to current drugs, few would discourage the identification and development of new antibiotics. Often, these come from natural sources, such as soil microbes. The pharmaceutical company Merck has recently found two promising new antibiotics by studying molecules produced by bacteria from African soils. These are under patent claim and, the company says, may become widely used medicines.

Under the United Nations Convention on Biological Diversity and its Nagoya Protocol on access and benefit sharing, the rights of the country and people(s) that provide samples that yield new drugs must be respected. This includes the need for prior informed

consent and mutually agreed terms for use of biodiversity. Yet an investigation into Merck's new drugs from Africa uncovered no evidence of the existence of such arrangements for these two new drugs.

Kibdelomycin from the Central African Republic

With 2012 revenues of over \$47 billion, Merck is the world's fifth largest pharmaceutical company. Operating with its Spanish subsidiary, the US-based giant is advancing patent applications on the drug called kibdelomycin, which was found in a soil bacterium (*Kibdelosporangium* sp.) collected in a forest of the Central African Republic

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(CAR). The circumstances of the collection, including the date, precise location and collector, have not been made public.

It is a case of possible biopiracy in which the company has far greater economic clout than the country from which it has obtained a product. The CAR gross domestic product of \$2.17 billion is the equivalent of less than two-and-a-half weeks of Merck's revenue. Another stark comparison: Merck CEO Kenneth Frazier earned over \$13 million in 2011, the average annual income of enough CAR citizens to fill a football stadium – over 30,000.¹

Isolation of kibelomycin appears to have been made in cooperation with the Medina Foundation, a publicly supported research organization in Granada, Spain. Before 2008, Medina's facilities and microbe collections were a Merck research unit. The company gave the unit away, creating the foundation with the University of Granada and its regional government. The foundation is now independent, although Merck maintains strong representation on its board (four of nine members are Merck employees).

Medina prides itself on "a long history of international bioprospecting" and its large collection of microbes, which exceeds 110,000 isolates. These the Foundation does not give away; it offers them to other research institutions under licence.² Several Medina Foundation staff members appear among the inventors of kibelomycin in Merck's international patent application, but it is not stated if the drug came from a bacterium in Medina's collection or from another source.³

Writing in *Chemistry and Biology*, Merck scientists claim that the CAR *Kibdelosporangium* is a new species to science, and that kibelomycin is a new

class of antibiotic drugs. The soil sample was "collected in the forest of Pama, a zone of dense, humid vegetation in the plateau of Bangui, in Central African Republic." Touting their discovery, Merck scientists say kibelomycin is the first effective antibiotic of its kind discovered from natural sources since the 1950s, and that "Successes like this have the potential to revitalize interest in natural products-based antibacterial drug discovery."⁴

While Merck may regard kibelomycin's discovery as a great success, it may not be a success for the Convention on Biological Diversity (CBD), to which both Spain and the CAR are Parties. Although Merck freely admits the CAR origin of the drug, no evidence of the company's fulfilment of requirements for access and benefit sharing, including prior informed consent and mutually agreed terms for use, can be found.

Platensimycin from South Africa

Merck scientists are sifting through samples from other parts of Africa too, and have laid claim to another antibiotic, platensimycin, which was isolated from South African soil. The source of platensimycin is a strain of *Streptomyces platensis* from soils in the Eastern Cape.

Merck's patent application on platensimycin⁵ only includes inventors listing an address in the United States; however, its scientific publication on isolation of the drug⁶ includes a number of authors from Merck's Spanish subsidiary (several of whom were Merck employees at the time of the patent application but now work at the Medina Foundation).

Neither the patent nor the scientific publication reveals any more pertinent detail on the origin of the streptomyces strain than

to state: “The original producing strain MA7327 was isolated from a soil sample collected in Eastern Cape, South Africa.”

Key details are thus unrevealed and, like in the case of kibelomycin, no information can be located indicating compliance with the access and benefit-sharing provisions of the CBD.

Current status

Both kibelomycin and platensimycin are in pre-clinical development programmes aimed at producing commercial drugs. Significant research has been conducted on synthetic methods to produce both compounds, as well as to develop and test analogues (derivates) of the originally-discovered molecules.

With financial support from the European Union and the Spanish government, the Medina Foundation continues to look for new drugs in its collections with Merck, as well as seeking to sell access to its microbes to other companies. A recent Medina marketing presentation emphasizes the diverse geographical origin of its microbe collections as a selling point for companies interested in accessing its collections.⁷

But nowhere on Merck or Medina’s websites, not in their patent publications and not in their key scientific publications, can any information be found to indicate that appropriate CBD access and benefit-sharing procedures were followed for kibelomycin and platensimycin.

These cases illustrate yet again the continuing disregard for the CBD provisions by a major corporation, and the inadequacy of regulations in “user countries”. The CBD’s Nagoya Protocol on access and benefit sharing that was concluded in 2010 awaits

the required 50 ratifications by CBD Parties for it to enter into force. Preparatory steps are being taken to implement the Protocol, and the kibelomycin and platensimycin cases reveal the gaps and weaknesses in current national, regional and international regulatory regimes that need to be urgently addressed.

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Endnotes

1. The CAR’s per capita income (2012) was \$442.
2. Fundación Medina (2013). Natural Products Collection (web page), accessed 15 July 2013. URL: http://www.medinaandalucia.es/en/natural_products_collection.html
3. PCT patent publication WO2011079034, published 30 June 2011.
4. Phillips JW et al. (2011). Discovery of Kibelomycin, A Potent New Class of Bacterial Type II Topoisomerase Inhibitor by Chemical-Genetic Profiling in *Staphylococcus aureus*. *Chemistry and Biology* 18:955-65, 11 August.

5. PCT patent publication WO2008039327, published 3 April 2008. A patent has been granted in the United States and Australia, and is pending elsewhere.

6. Singh SB et al. (2006). Isolation, Structure, and Absolute Stereochemistry of Platensimycin, A Broad Spectrum Antibiotic Discovered Using an Antisense Differential Sensitivity Strategy. *J. Am. Chem. Soc.* 128:11916-20, 13 September.

7. Fundación Medina (2013). Helping Science Reach Industry and Society. Presentation for Spanish Bioindustry Association (ASEBIO), March.