

PHARMACEUTICALS

Corners are cut in order to bring drugs to Africa

Treatments against tropical diseases are being launched without western regulatory scrutiny

When a French pharmaceutical company teamed up with a Swiss charity this month to launch a low-cost malaria drug for Africa, the news caused as much concern as rejoicing among international health experts.

Asaq – named after its two constituents, the drugs artesunate and amodiaquine, combined into a single pill – offers a relatively affordable and simple treatment for a parasite that kills more than 1m people a year and causes substantial economic upheaval.

To its champions, it marks a first success for one of a growing number of “product development partnerships”, twinning the Drugs for Neglected Diseases initiative (DNDi) in Geneva, a non-profit organisation that co-ordinates academic research groups, with Sanofi-Aventis, the French pharmaceuticals producer.

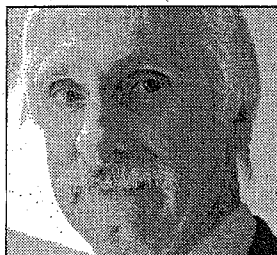
“We urgently need to increase usage,” says Bernard Pécoul, head of DNDi, who expresses his frustration that despite successfully treating patients with similar combination drugs for malaria since the early 1990s, uptake in affected parts of the world still remains limited today.

But to its critics, Asaq is a step backwards, because its developers opted to bypass the stringent standards of

developed-world regulators and instead gained quick approval in Morocco, based on relatively limited scientific data.

At the core of the debate is the tension between a desire to save as many lives as quickly as possible and a concern to ensure that patients in the developing world do not receive medicines of poorer quality and efficacy than would be approved in richer countries.

“We realise that Sanofi’s aim is to get the drug launched quickly. However, applying a different standard for drugs aimed at Africa invites unnecessary questions,” says Chris Hentschel, head of the Medicines for Malaria Venture, another non-profit group, which is developing a range of treatments for the



Reformulation: Bernard Pécoul

parasite. His and similar research groups have been created since the late 1990s to fill a gap: developing innovative treatments for

“neglected diseases” in the developing world for which the markets are too modest to interest industry. The aim was to meet western

standards, ending an era of second-rate “poor drugs for poor people”.

But as private philanthropic support for such drug development partnerships has gathered pace, matched by a consciousness of corporate responsibility on the part of the drug companies, regulators have proved slow to respond to the resulting pipeline of experimental medicines and vaccines nearing launch.

One problem for such developers is that the regulators’ assessment of the relative balance of risks and benefits of a new medicine or vaccine in the developed world is not the same as for their counterparts in poorer countries, because of the greater burden of disease and the lower level of medical resources available.

For example, when Wyeth’s pioneering RotaShield vaccine for rotavirus – a gastric infection that causes thousands of hospitalisations each year but very few

deaths in the US – was linked to an extremely rare but serious side-effect in 1999, the company withdrew it from the market.

But in the developing world, where rotavirus causes up to 500,000 deaths a year and access to hospital care is less easy, the side-effects have since been judged to outweigh the risks. That is one reason why GlaxoSmithKline sought regulatory approval first for its rival Rotarix vaccine in Mexico, in 2004.

Mr Pécoul from DNDi cites a similar reason for why, after initial talks with the MHRA, the British drugs regulator, about authorising Asaq, he decided to go elsewhere. It told him that he would need to conduct a full and lengthy clinical trials because the treatment contained artesunate, which is not yet approved for use in Europe, where malaria is rare.

Since 2004, the European Medicines Agency (Ema) has launched a partial

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solution with a special regulatory pathway for drugs for the developing world, dubbed Article 58. The US Food and Drug Administration is considering a similar approach.

The Ema has already approved three drugs using this approach. GSK this week applied to it for approval of Globorix, a combination vaccine to protect against multiple childhood diseases including meningitis.

A second task for regulators is how to evaluate drugs that are reformulations of existing medicines. Mr Pécoul argues that Asaq falls into this category. It combines in a single pill two malaria treatments that have been shown to work in the developing world. Asaq was developed because patients often abuse the existing treatment – and risk triggering drug resistance – by taking the artesunate while throwing away the amodiaquine, which has unpleasant side-effects.

However, Brian Greenwood, a malaria expert at the London School of Hygiene and Tropical Medicine, says: “When you combine two pills, one drug can affect the other and you can get reduced activity, different absorption rates, stability and reactions.”

A final difficulty for regulators is safety surveillance after the launch of new medicines in the developing world, where there are limited systems to pick up side-effects that could trigger withdrawals or require prescription practices to be modified. “When you are putting the drug into the bush, you have a much more serious responsibility than you do in Europe,” says Lembit Rego, who scrutinises drug applications for the World Health Organisation.

Attention will now turn to his agency, which needs to study Asaq before many donor agencies and developing-country regulators will purchase it or approve its use.

Meanwhile, Mr Hentschel says he has faced questions from donors inspired by Asaq’s fast-track tactics but insists on taking a more cautious approach.

“Millions of people depend on anti-malarials to save their lives and we would feel more secure if a stringent regulatory authority reviewed the history and clinical data and gave its stamp of approval,” he says.