Launch of ACT subsidy fund planned for 2008

For more information on ***Saving lives, buying time*** see http://www.nap.edu/books/0309092183/html/

For more information on **presentations from the Amsterdam meeting** see http://www.rollbackmalaria.org/docs/events/2007amsterdam/amsterdam2007.ppt

A new global fund to subsidise artemesinin-based combination therapy (ACT) could be up and running as soon as next year, according to delegates at a high-level meeting organised by Roll Back Malaria (RBM) and hosted by the Dutch government in Amsterdam in January.

The meeting brought together malaria experts, policy makers, and representatives from non-governmental organisations, funders, and malaria-endemic countries to discuss details of the subsidy fund, first proposed in the report *Saving lives, buying time* published by the US Institute of Medicine in 2004.

In the report, economist Ken Arrow suggested that flooding the market with low-cost ACTs would reduce the risk of resistance to artemisinin developing, by reducing use of artemisinin monotherapy. Following the Institute of Medicine publication, the World Bank commissioned additional research to support Arrow's hypothesis and won funding from the Gates Foundation to flesh out the plans.

Andreas Seiter, Senior Health Specialist at the World Bank, explained that drugs would be subsidised high up in the distribution chain. "In principle, the high level subsidy would lead to much lower prices for ACTs, available to all buyers", Seiter said.

However, the plan would not guarantee better access to ACTs. Seiter believes that without making supply chains more efficient and educating consumers "there is a risk that middlemen capture part of the subsidy and retail prices do not come down sufficiently to put these drugs into reach for the poor".

Another key issue in the fund's design will be to ensure that it complements existing funding mechanisms. "Our assumption is that the ACT subsidy will be managed by an existing institution", said Seiter. "It is not the intention to create another organisation".

A detailed plan for the subsidy is due to be finalised in June. RBM estimates that between US$80 and 100 million would be required for the fund in 2008, with $250 million every year from 2009 onwards.

Graciela Diep, of the Drugs for Neglected Diseases initiative, said the Amsterdam meeting was important for galvanising support for the subsidy idea. "At the beginning of the meeting people were a bit suspicious because they thought it might just be subsidising a drug company", she said. "But what these discussions have really shown is that if you want to hit the 60% of people who self-treat for malaria you really have to tackle this cost issue in pharmacies. That's what came out of Amsterdam".

Hannah Brown

Curbing false positives and pseudo-epidemics

A B Dowsett/Science Photo Library

"Pseudo-epidemics" may be on the rise because of an "over-reliance" on molecular diagnostic tests, suggested an article in *The New York Times* (Jan 22, 2007).

The article described how experts at Dartmouth-Hitchcock Medical Center (Lebanon, NH, USA) reacted to what was believed to be a "huge whooping cough outbreak" in April, 2006. Nearly a thousand health-care workers were tested; 142 people seemed to have the disease; thousands received antibiotics and a pertussis vaccine. Yet, 8 months later, Dartmouth officials were "dumbfounded" to learn that not a single case of pertussis had been confirmed by culture. The pseudo-epidemic had occurred, said experts interviewed for the article, because health officials "placed too much faith in a quick and highly sensitive molecular test [PCR] that led them astray." The test, and a "home brew" of others like it that are given and interpreted in a non-standardised way, were blamed for the false positives.

The type of PCR testing that led to the Dartmouth debacle was not identified in the article. But the type matters, David Perlin, (Public Health Research Institute Center, Newark, NJ, USA) told *TLID*. So-called "classical" PCR amplification, in which "positivity" is assessed based on the size of identified DNA fragments, gives "notoriously poor" results; spurious, hard-to-quantify fragments tend to cause "lots of false positives", Perlin said. By contrast, real-time PCR relies on secondary probes that are sequence-specific, so the rate of false positives is considerably lower. "But the best way to reduce false positives for pathogens you're not sure about and that are difficult to grow, such as *Bordetella pertussis*, is to use multiple targets", Perlin emphasised. "You're not just amplifying a single fragment, but rather multiple targets to reduce the probability of error".

Indeed, the Dartmouth team used PCR with only a single target, US Centers for Disease Control and Prevention's (CDC) Katrina Kretsinger told *TLID*. When CDC was called in to confirm the outbreak, "we did PCR using two different targets, which did not confirm the Dartmouth results; we drew serum to look for IgG against pertussin, and did not find increased concentrations; and we also looked at clinical symptoms and did cultures", she said. CDC and its partners recently launched a validation study of a specific testing protocol for unknown pathogens; however, results won't be available for several years. Until then, Kretsinger urged, "we have to look at the big picture and use all available data".

Marilynn Larkin