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Active Pharmaceutical Ingredient Requirements for the Manufacture of ACTs

Position Paper

Of the RBM Procurement and Supply Management Working Group (PSMWG)

Background and purpose of document

Recent efforts to scale up the use of Artemisinin Based Combination Therapies (ACTs) including the possible launch of the Affordable Medicines Facility for Malaria (AMFm) has led the international community to discuss whether current production of artemisinin, the raw material for the active pharmaceutical ingredient (API) needed to manufacture ACTs, will meet the potential increased demand of ACTs that will be created in the near and intermediate term.

Due to the long planting cycle of *Artemisia annua* and producing finished ACT products of 14 months, early planning for adequate supplies of the API is needed to ensure that sufficient buffer stocks of good quality product needed for the actual production stage are available. This will eventually lead to a more stable market reaching an equilibrium between supply and demand.

The purpose of this document is to inform key stakeholders of the potential API requirements needed to produce forecasted estimates of ACTs, as well as key actions that need to be taken to achieve the required production.

Target audience

RBM Partnership, AMFm, policy makers and pharmaceutical manufacturing companies

Current situation of API for ACT manufacture

The current expected production of artemisinin in 2008 is estimated at 30-40 tons (reference?). The existing current global pipeline of artemisinin is difficult to ascertain, however, it was estimated at approximately 40 tons in June 2008 (reference?). This includes existing stocks with extractors and ACT manufacturers. This stock is rapidly decreasing as manufacturers continue to procure the API to produce ACTs. These 40 tons will need to cover the demand from June 2008 until a new crop is planted, harvested, extracted and available for the production of ACTs.

It must be noted that the estimates above are based on limited information of stock held by the two major ACT producers and the assumption that the farmers are given off-take guarantees and contracts from extractors and/or manufacturers.

Given the planting cycle of the *A. Annua*, decisions on the surface areas that need to be planted with *A. Annua* in the major producing regions will need to be made **before the end of 2008** in order for planting to begin in early 2009 (depending on the planting region). This new crop will then have to be harvested and extracted and the first new batches of finished ACTs will only start to become available at the end of the first quarter of 2010.

The quantities needed for manufacturing the ACTs will depend on which of the two main ACTs used in Africa; artemether/lumefantrine (AL) or artesunate/amodiaquine (AS/AQ) is being considered as well as the respective quantities of adult versus child dosages.

Nevertheless, we can estimate that to manufacture:

- 1 million treatments of AL, manufacturers would need 0.57 tons of artemisinin
- 1 million treatments of AS/AQ manufacturers would need 0.4 tons of artemisinin.

And that one ton of artemisinin will yield:

- 1.76 million treatments of AL or
- 2.5 million treatments of AS/AQ.

AL is the first line treatment for uncomplicated malaria in the majority of malaria endemic countries in Africa, we therefore assume that most of the market for the API will be for the production of AL. The 70 tons of artemisinin available from the existing API pipeline and the 2008 crop will thus yield approximately 140-150 million treatments of AL. This will need to cover the demand until the new batches of ACTs from the new crop which will be planted in early 2009 start to become available in April 2010.

The AMFm which has an expected start date of April 2009, estimates a minimum demand of 20 million ACT treatments for the first year. These quantities will be needed in addition to the current estimates of utilization under existing donor funding mechanisms. The current requirements under these existing financing mechanisms are estimated at 130 – 150 million treatments per year. Therefore additional demand created by initiatives such as AMFm has the potential to lead to a global shortage of ACTs. In addition, it must be noted that ACT production is spread out over the year making it impossible to supply this massive demand in April 2010 with the ACTs produced from the new crop.

Position of the RBM PSMWG

The PSMWG strongly recommends that the global RBM Partnership take urgent action to ensure that adequate planting of *A. Annua* occurs by the end of 2008/beginning of 2009 to ensure that adequate API is available in 2010 for the production of ACTs. A lack of action on this issue is likely to result in a significant supply shortage of API and hence finished ACT products in 2010. In addition to severely compromising the strides made in the reduction of mortality and morbidity due to malaria in recent times, a global shortage and poor delivery will also compromise confidence in and the success of malaria initiatives including the AMFm.

In order for this to occur, *A. Annua* growers, extractors and pharmaceutical companies need to have accurate forecast information for timely ACT market planning as well as a security of long term orders in order to contract farmers for planting the seeds and to ensure adequate manufacturing capacity.

The following actions need to occur in the immediate term (before mid December 2008):

- Obtain support from major actors supporting and financing malaria programs including the Global Fund, PMI, World Bank and the major bilateral donors
- Obtain information on eligible manufacturers and products for AMFm
- Confirm quantities, types of treatments and a timeline for implementation of AMFm
- Obtain more actual, evidence based information from the pharmaceutical industry on the supply of ACTs and existing pipeline of API
- Urgently disseminate information on this supply situation as widely as possible
- Agree on a working model for estimating ranges of requirements of API in collaboration with the Forecasting Task Force of PSMWG
- Ensure that adequate quantities of seeds are planted in early 2009
- Task a group of experts to design a business plan, including the private sector and (local) formulating industry (ideally a three year framework agreement to be agreed with the pharmaceutical industry, supported by all presently known approved sources, including a frame work supply arrangement and plan of action. This agreement needs to be supported by a firm budget and some payment guarantees for producers

The following actions need to be planned for the intermediate term (December 2008-April 2010):

- Consider a risk sharing strategy such as an API bank may be required. This may guarantee demand minimums to the eligible ACT producers, which will in turn enable them to provide API supply contracts to the extractors and planters.
- Explore the possibility and feasibility of an independent supply organization similar to GDF, either as a new set up or managed by an existing organization.

The PSMWG urges key stakeholders of the RBM Partnership to take this issue forward as a matter of urgency to ensure that the global malaria community continues to makes strides in the reduction mortality and morbidity due to malaria.

This document was drafted by the following members of the RBM Procurement and Supply Management Working Group:

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