

Artemisinin Consortium Meeting with Key ACT Manufacturers

- Date:** June 19, 2007 (with organizers meeting at 1800hr on 18th and dinner at 1900hr on the 18th)
- Location:** MMV Offices, Geneva, Switzerland
- Participants:** MMV (Host), Institute for OneWorld Health/Amyris Biotechnologies, York University, Bill and Melinda Gates Foundation
- Invitees:** Sanofi Aventis, GSK, Novartis AG, Holley Pharma, Sigma-tau (declined), Shin Poong Pharma, Mepha, Pfizer

CMC Regulatory Consultant (George Aynilian, confirmed); WHO representatives to be confirmed (Lembit Rago, Arata Kochi, Hans Hogerzeilh)
- Objectives:** Bring together major, producers of ACT's to:
- Inform them of plans, timing, and goals for low cost alternate supplies of artemisinin
 - Understand the needs and expectations of ACT manufacturers ("our customers"), their specifications for incoming artemisinin and the analytical procedures they will use
 - Understand regulatory constraints on integration of new artemisinin options into the supply chain
- Materials:** To be provided in advance: IOWH & York overview and background information, manufacturer's overview of their marketed or pipeline ACT products, relevant regulatory guidance, discussion questions, etc
- Outputs:**
- CD with all the presentations – Maud C
 - Two page document summarizing conclusions, list of actions with person responsible, items needing more discussion, date and place of any next meeting – Rapporteur/IOWH rep/Chair to draft, circulate to organizers, finalise
- Rapporteur:** Jaya Banerji

Draft Agenda

1. 0800-0830: Complete loading of all presentations on to Meeting laptop
2. 0830-0845: Introductions/finalization of agenda - Chair
3. 0845-0900: BMGF Malaria Strategy/Role of Grantees – Tom Brewer
4. 0900-0915: MMV synthetic peroxides – Carl Craft
5. 0915-0945: Program presentation by IOWH – Nina Grove
6. 0945-1015: Program presentation by York – Maggie Smallwood
7. 1015-1045: Morning Coffee/tea break
8. Manufacturer Presentations on malaria/ACT(s): overview, general information about supply chain, regulatory approach (CMC and product registration), etc
 - i. 1045-1100: GSK
 - ii. 1100-1115: Holly
 - iii. 1115-1130: Mepha
 - iv. 1130-1145: Novartis
 - v. 1145-1200: Pfizer
 - vi. 1200-1215: Sanofi Aventis
 - vii. 1215-1230: Shin Poong
9. 1230-1330: Lunch
10. 1330-1630: Discussion of questions attached to agenda in the light of the morning's presentations – All
11. 1630-1700: Tea/coffee break
12. 1700-1725: Draft conclusions, list of actions with person responsible, items needing more discussion – Chair/Rapporteur
13. 1725-1730: Date and place of next meeting, if required - Chair
14. 1730: Closure – Chair

Discussion Questions

A. Questions on current supply:

1. What is your long term forecast for artemisinin supply needs?
2. Does your company buy artemisinin derivatives as API or do you buy artemisinin starting material and convert this to API yourself?
3. What criteria do you use in choosing a source of artemisinin supply?
4. Do you use a single supplier or multiple sources?
5. Do you buy their entire production?
6. Is the seasonal nature of artemisinin supply an issue?
7. Under what conditions do you store and ship your plant material or API?

B. Questions on current quality/regulatory issues:

1. What quality criteria do you have for incoming artemisinin over and above those stated in the monograph?
2. What sort of problems do the differences in the quality of artemisinin present to your company?
3. Would introduction of a more rigorous standard than the existing monographs be an advantage?
4. Are there any particularly problematic plant-derived contaminants in artemisinin?

C. IOWH Questions Specific To Microbially-Derived artemisinin:

1. Do you agree with the IOWH-proposed Regulatory strategy?
2. What is your preferred Regulatory approach for substitution of plant derived for microbially-derived Artemisinin in your existing or pipeline ACT(s)?
3. What analytical information beyond what has been proposed will you need to pursue the chemical equivalence strategy?

D. York questions specific to new, high yielding Artemisia varieties.

1. Are there any regulatory implications in using a new variety?
2. What information do you need from us about the new varieties?
3. Do you need to know any information about the phytochemistry of new varieties with respect to other metabolites?
4. Can you think of any other implications (either good or bad) that high yielding varieties might have for you?
5. Would you be willing to test artemisinin extracted from novel varieties to see whether it met your standards?
6. Are there any steps that might be taken to help ensure high-yielding varieties of Artemisia are only used in the production of good quality ACTs?

D. Concluding Questions:

1. Is there interest in development of a monograph with standards/specifications for artemisinin beyond what currently exists today?
2. Is there interest in developing a consensus substitution strategy or should each ACT manufacturer develop their own substitution strategy?
3. If consensus would be useful, is there agreement on the regulatory body where this could be discussed?
4. What are the key gaps/concerns with these new technological approaches?
5. What can be done to address these issues now?
6. What do you see as the advantages and disadvantages of plant v microbial v synthetic sources of artemisinins?