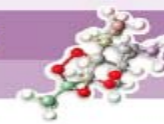


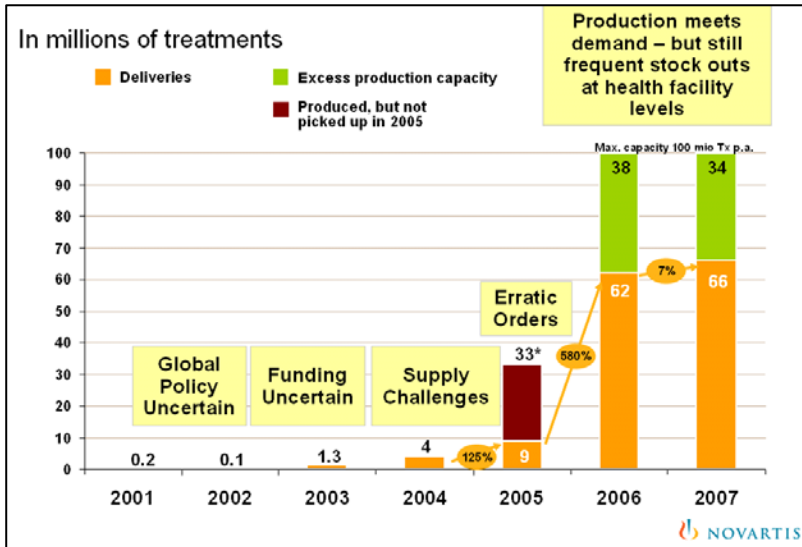
ARTEMISININ ENTERPRISE CONFERENCE 2008

David Clayton

on behalf of the Artemisinin Enterprise



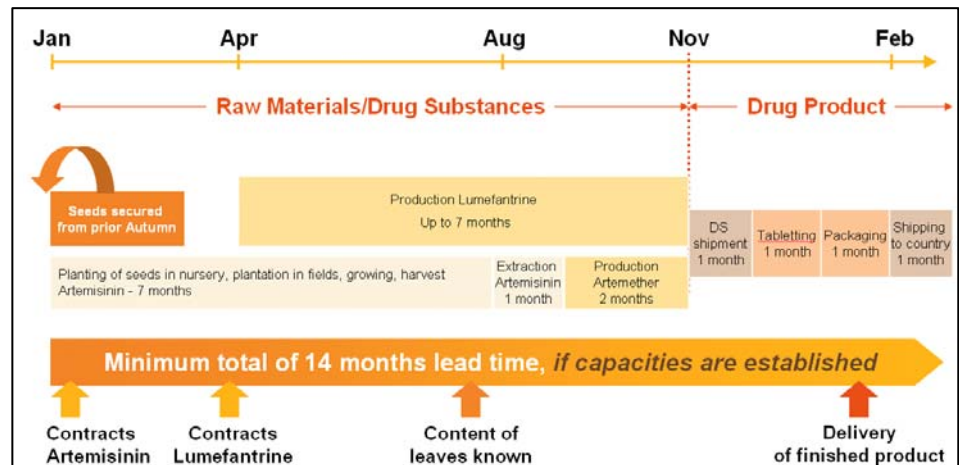
ARTEMISININ SUPPLY – THE CHALLENGE



- Rapid increases in volume demand
 - maybe unparalleled in history
 - no generally accepted forecast for future needs

Current production is

- expensive
- has long lead times
- is unreliable in quantity and quality



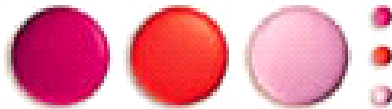
ARTEMISININ ENTERPRISE

CNAP

CENTRE FOR NOVEL AGRICULTURAL PRODUCTS

BIOLOGY TO BENEFIT SOCIETY

THE UNIVERSITY *of* York



Medicines for Malaria Venture



BILL & MELINDA
GATES *foundation*

- supported by the Bill & Melinda Gates Foundation
- a portfolio approach to address the need for affordable ACTs
- complementary technologies working in different ways and at different points in the artemisinin supply chain

THE 2008 ARTEMISININ ENTERPRISE CONFERENCE

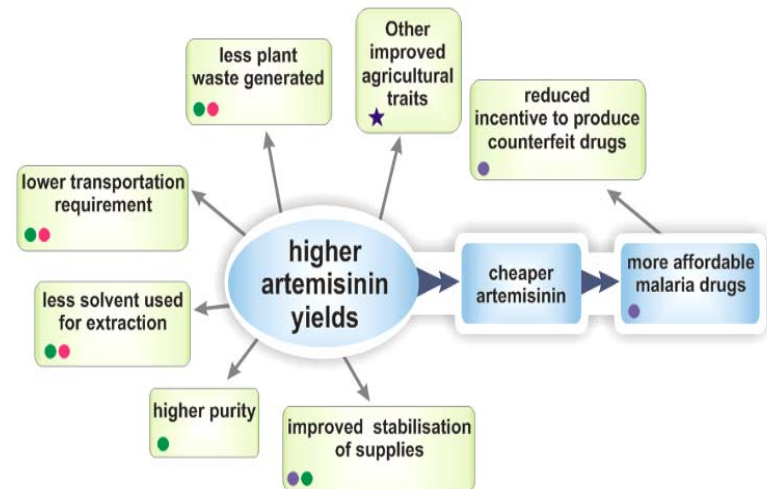


CNAP ARTEMISIA RESEARCH PROJECT

- to develop new varieties of *A. annua* with increased yields of artemisinin.

- A *annua* has not benefited from domestication - modern molecular breeding can lead to rapid development of a robust crop
- Screening variation can identify high yielders that become parents to new hybrid varieties with improved performance

increased yields are not generated by genetic modification

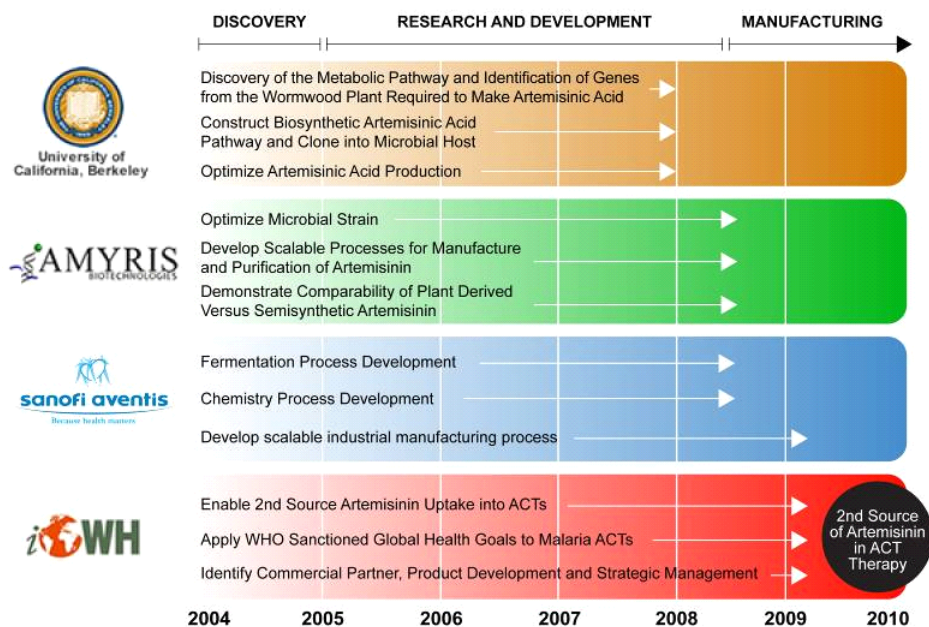


key:
● benefits to malaria sufferers
● benefits to ACT supply chain
● benefits to the environment
★ benefits to growers



IOWH: SEMI-SYNTHETIC ARTEMISININ

- **Objective: a complementary source of artemisinin**
 - A non-seasonal supply
 - Rapid response to changes in demand
 - Supplements plant-derived artemisinin derivatives
- **Artemisinic acid derived by fermentation of genetically engineered yeast**
 - Subsequent chemical conversion to artemisinin

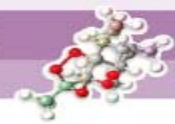
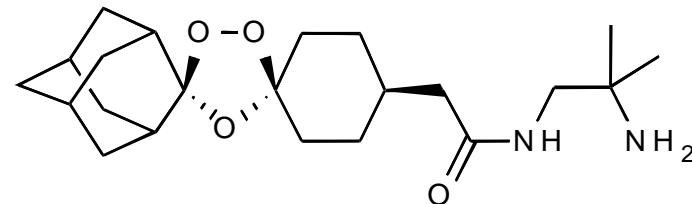


- **4 partners with complementary expertise**
- **Reduces the length of the supply chain by up to 90%**
- **Promise of 99.6% purity**
 - plant-derived 97.8%

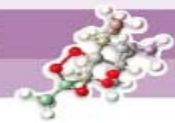
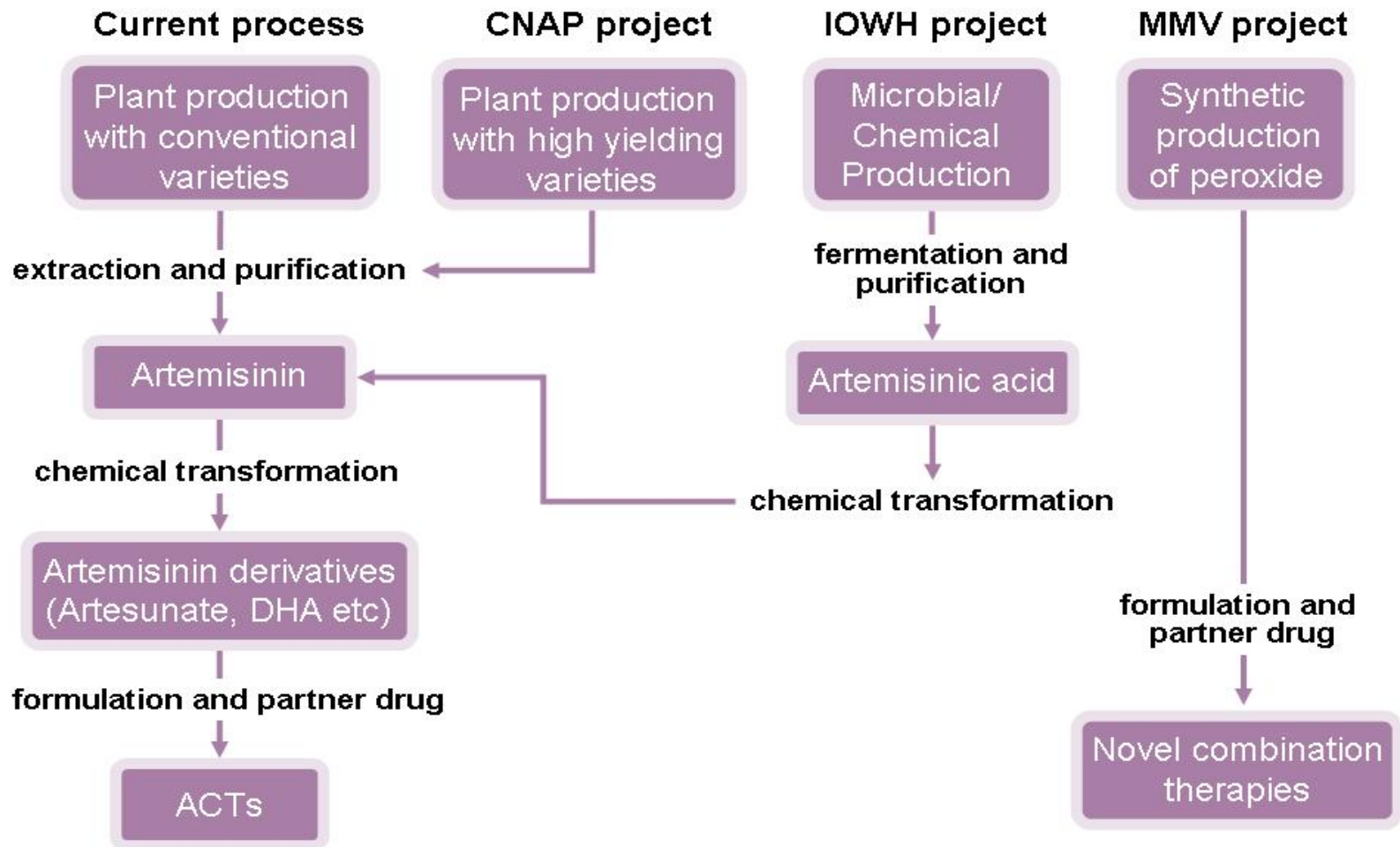


MMV: SYNTHETIC ENDOPEROXIDE

- Objectives:
 - identify a new class of fully synthetic endoperoxides
 - more potent than the currently available artemisinin derivatives in reducing parasite burden
 - low cost (< \$1 USD per treatment when used in combination)
 - provision in combination of a single-dose oral cure for patients with uncomplicated *P. falciparum* malaria (and possibly *P. vivax*)
 - potential for prophylactic treatment and intermittent preventative treatment in pregnant women and infants (IPT_p and IPT_i)
- Builds on experience with RBx11160:

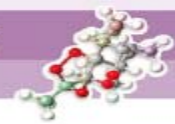


The ACT supply chain; role of the new technologies



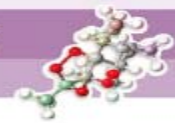
AE CONFERENCE - 2008

- **Third annual AE Conference - University of York October 8-10**
- **Broadened participation -**
 - **Artemisinin growers & suppliers**
 - **Industry representatives**
 - **Policy-makers, regulators**
 - **Product development partnerships**
 - **International organisations and sponsors (RBM, WHO, Global Fund)**
 - **Researchers**



CONFERENCE OBJECTIVE

- To: update the wider malaria community on the progress and timelines to delivery of outputs from the AE Enterprise projects**
- To: invite stakeholders to assess the impact of the three new AE technologies on the ACT supply chain**
- To: ask the stakeholders to make recommendations on how best to ensure smooth and effective integration of the new products into the supply chain so that they can contribute to the envisaged demand for ACTs**



Key milestones

CNAP:

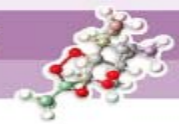
- delivery of registered hybrid seed with 2% artemisinin content by the end of 2011

IOWH:




- semisynthetic artemisinin produced in 100,000L tanks between 2011 and 2012.

MMV:

- development of a combination product and the product ready for launch by 2015



IMPACT OF AE TECHNOLOGIES

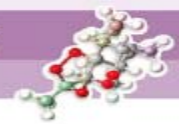
Impact			
Reduce lead-time for antimalarial drug supply	No change from current plant-derived artemisinin	Fermentation reduces lead-time by ~90% compared to plant-derived	Totally synthetic production should reduce lead-time by ~90%
Reduce cost of antimalarial drugs	Higher yields reduces cost/kg of artemisinin	Cost advantage over plant-derived needs to be clarified	Premature to estimate cost – target to at least match current ACTs
Stabilise artemisinin supply	Higher yielding varieties will restore confidence of farmers: fewer farmers needed to meet demand	Fermentation can be used to smooth variations in demand & respond to rapid upscaling	Increased choice of drugs will increase resilience in the supply chain
Stabilise market demand	Stabilisation of supply and reduced cost will increase and stabilise demand		
Quality of antimalarials	Reduced cost of effective antimalarials will drive out counterfeits and artemisinin monotherapy		



POTENTIAL CHALLENGES IN THE INTRODUCTION OF THE NEW AE TECHNOLOGIES

Market Issues:

- Keeping farmers & derivatisers engaged
- Developing credible forecasts
- Stabilising price, demand, and supply in artemisinin market
- Increasing competition of high quality ACTs
- Controlling access only to quality manufacturers
- Engaging global stakeholders



POTENTIAL CHALLENGES IN THE INTRODUCTION OF THE NEW AE TECHNOLOGIES

Technical Issues:

- Regulatory & pharmacopeial status of artemisinin
- Impact on existing regulatory approvals of changing source of artemisinin
- Variations in yields and impurity profiles between geographies



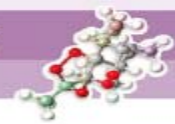
RECOMMENDATIONS FOR AE PARTNERS

- **Ensure outputs exclusively benefit the manufacturers of high quality ACTs**
- **Develop an effective, joined-up communications strategy across the three projects**
- **Establish a regular Stakeholder Forum**



RECOMMENDATIONS FOR CNAP

- **Develop new communications networks**
- **Enhance farmer and extractor knowledge, confidence and participation**
- **Assess the impact of new varieties on impurity profiles for API manufacture**



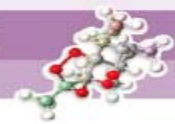
OTHER AE RECOMMENDATIONS

IOWH:

- Forward-looking communications to ensure clarity on prices, volumes and impacts**

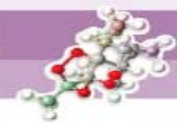
MMV:

- Information to stakeholders on progress with new synthetic peroxide**



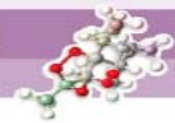
RECOMMENDATIONS FOR THE MALARIA COMMUNITY

- **Develop agreed set of planning assumptions for demand forecasting (RBM/UNITAID)**
- **Develop action plan to mitigate future supply/demand mismatches (RBM PSM)**



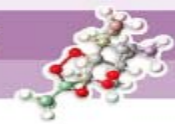
RECOMMENDATIONS FOR THE MALARIA COMMUNITY

- **Scale-up RDTs in parallel with treatment strategies for patients who do not have malaria (RBM)**
- **Maximise the benefits of the AE technologies by minimising harmful alternatives (RBM PSM, MMV Access team)**



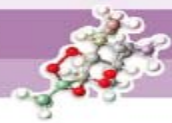
RECOMMENDATIONS FOR THE MALARIA COMMUNITY

- **Achieve consensus that artemisinin should be considered a starting material (Regulatory bodies)**
- **Consider pathways to sustainable and appropriate local production of ACTs (Donors and regulatory bodies)**
- **Review current extraction capacity (RBM PSM)**



CONCLUSIONS

- AE innovations can significantly improve the ACT supply chain
- Needs timely and effective technology introduction
- Stakeholder confidence needed to realise full potential of the new technologies
- Time-limited opportunity to deliver success



THE 2008 ARTEMISININ ENTERPRISE CONFERENCE

