NOTE TO WORLD HEALTH ORGANISATION
ON

INTEGRATION OF *ARTEMISIA ANNUA* INTO THE STRATEGY AGAINST MALARIA IN AFRICA[1]

1. Executive Summary.

1.1 Natural plants are a common good and at the disposal of humanity as a whole. No one can prevent people from growing and using *Artemisia annua* L. for one's well-being or to protect oneself against diseases. While the on-going programmes using Artemisinin-based Combination Therapy (ACT) to treat malaria in Africa have booked impressive progress, there are indications that several components of the programme are not sustainable: drug resistance may be emerging thereby threatening long term efficacy, and there is excessive dependence on limited foreign aid resources.

1.2. The issue then is whether it is justified for the World Health Organisation (WHO) to maintain its reservations on integrating the use of natural extracts or dried leaf[2] consumption of *A. annua* against malaria and other tropical infectious diseases against which the multiple components of the plant have demonstrated efficacy. Thus far there is no scientific proof that the integration of the plant and/or its extracts into the overall global strategy against malaria would actually threaten the efficacy of the current ACT programme, the latter being based on artemisinin, a single component of the plant. The current request is based on the findings that the plant is generally recognized as safe (Graz; Duke 2001; US FDA CFR), therapeutically effective, more cost effective and because they contain polytherapeutics, less sensitive to emergence of drug resistance than the two-drug ACTs. The plant is also more readily accessible to derelict and isolated families that fall beyond the reach of the on-going programmes.

1.3. If WHO were to lift its reservation, it would accelerate large scale distribution of the plant first through farm cooperatives and school gardens promoted by UN organisations (Food and Agriculture Organization (FAO), World Food Program (WFP)) and other Non Governmental Organisations (NGOs) like CARITAS, More for Less or IDAY[3] and thereby teach the young population to grow and use the plant correctly. This would relieve budgetary constraints preventing malaria eradication campaigns to reach all potential victims of the disease and release resources to tackle not only malaria, but also Neglected Tropical Diseases (NTD), enhance local agriculture, and help raise education standards in Africa. Integration of *A. annua* into the overall strategy against malaria in Africa seems to be necessary if the continent is to achieve by 2030 several of the United Nations (UN) Sustainable Development Goals (SDGs) related to malaria as well as those related to the health of pregnant women and small children.

2. Current Programmes to stop malaria in Africa.

2.1. **Successes.** According to the last WHO report on malaria (2015) the number of malaria cases globally fell from an estimated 262 million in 2000 (range: 205–316 million), to 214 million in 2015

[1] This note was prepared by Professor Pamela Weathers, Worcester Polytechnical Institute (USA), Dr Lucile Cornet-Vernet, Founder of « More for Less » (France), Professor Ahmed Hassanali of Kenyatta University (Kenya) and Jean-Jacques Schul, Chairman of IDAY-International , aisbl.

[2] Throughout the text, « dried leaves » is meant to cover « dried leaves and small stems ».

[3] www.iday.org

(range: 149–303 million), a decline of 18%. Most cases in 2015 were estimated to have occurred in the African Region (88%). The total number of deaths decreased in Africa from 694,000 in 2000 to 292,000 in 2015 (average between 212,000 - 384,000). The number of children aged between 2 and 10 infected by malaria dropped from 33% in 2000 to 16% in 2015. The causes for this reduction are due to increased use of bed-nets (69%), medication (21%) and in-house sprayings (10%). Early diagnostic tests increased from 36% in 2004 to 65% in 2014.

2.2. **Failings.** Still only 55% of the at-risk population sleeps under bed-nets (68% of the children) and while in 2014, 52% of pregnant women received a pre-birth preventive treatment, only 17% received all 3 prescribed treatments. Vaccines are still far off. One case in four is still treated with means other than those recommended by WHO. The overall reduction in mortality rates in the main infected countries is declining due to inadequate coverage, with a few exceptions, e.g. Burkina Faso. In Africa, only 269 million people out of the 834 million living in malaria sensitive areas have access to the official treatments; 15 million pregnant women and an estimated 68 - 80 million children out of the 92 million suffering from malaria still do not have access to medicine.

2.3. Resistance. Resistance to insecticides sprayed on bed-nets are reported in 3 countries out of 4. According to WHO, drug resistance is reported only in Asia and includes medications other than ACT. The literature, however, suggests there are also numerous cases of ACT resistance or lower efficacy of ACTs in numerous African countries (Daddy, 2017;Mutabingwa, 2005; Van Tyne (2013, Luicer (2015)

2.4. **Counterfeits.** Counterfeits are known to be a major issue in Africa with 50% or more of the malaria medicine being fake with no or limited content of artemisinin. In Cameroun, for example, about half the antimalarial products on the market have been identified as counterfeits. Substandard artemisinin medication is an even more fearful problem as it could aggravate the risk of resistance. Identifying truly illegal operations is always difficult, but the counterfeit market of antimalarial drugs is indeed recognised as a serious drawback to the use of ACTs and for that matter any therapeutic. This needs to be kept in mind as the uncontrolled composition of natural extracts of freely distributed or locally produced medicinal plants is often cited by WHO as an argument against their use. It is, however, a much worse problem with mono- or bi-therapies, since the absence or lower content of one component has much more radical effects than with natural polytherapies, which inherently comprise a large number of effective components.

2.3. **Financial shortages**. Expenditures in the fight against malaria rose from USD 960 million in 2005 to USD 2.5 billion of which 91% was supplied by foreign aid, the bulk of which was mainly directed to Africa. To reduce mortality due to malaria in Africa by 40% in 2020, WHO estimates that it would need USD 6.4 billion/year, in 2025 USD 7.7 billion to reduce it further by 75% and by 2030 USD 8.7 billion/year to reduce mortality by 90% (WHO, 2015). To obtain these amounts, WHO counts on a growing participation of local budgetary allocations that today average in Sub-Saharan Africa already 10% of GDP (UNESCO-UIS reports). Given the current and anticipated political climate in both the USA and the EU, this is an unrealistic expectation.

2.5. **African Initiatives.** China has supported local production of ACTs in particular in Nigeria (Darlymple,2012). Presumably, this could reduce the cost of the medication. The Economic Community of West African States (ECOWAS) is supporting research in the production of sterile anopheles with the hope to destroy the vectors and preventing the dissemination of the disease. The WHO report on larval control, however, provides no data as of yet on this approach.

2.6. **Conclusion**. Under the UN Sustainable Development Goals (SDG) , Member Governments have agreed to: "*By end of 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases (NTDs) and combat hepatitis, water-borne diseases and other communicable*

diseases" (SDG N° 3.3)[4]. Except for the still somewhat uncertain impact of the two last initiatives, it appears that this SDG will not be achieved in a majority of African countries. The on-going programmes, while making major progress, are clearly too costly to succeed in simultaneously stopping malaria and a series of neglected tropical infectious diseases (NTDs), while also reinforcing the capacity of the health services (SDG n° 3.8: "…*achieve universal health coverage, ... access to quality essential health-care services*). WHO indeed assumes that the financial needs of the anti-malaria programme will be covered increasingly by additional local budgetary allocations but this would reduce the means allocated to the reinforcement of the very health services needed to implement the programme.

2.7. In 2011, Richard Horton, Chief Editor of "The Lancet" qualified the official programme "*the Wrong Road* (Horton, 2011). Liverpool University researchers have complained that research on NTDs received inadequate funding because of the concentration of available means on malaria and AIDS control. Linda Nordling (Nordling, 2012), Journalist of "Research Africa" deplored the domination of the shortage of African experts and researchers on malaria in international conferences on the disease and describes how differently it is perceived by Africans. She calls upon African researchers and governments to seek their own solutions to malaria control.

3. The *Artemisia* solution.

3.1. The *Artemisia* genus.

3.1.1. Several members of the *Artemisia* plant genus are used in traditional herbal medicine against infectious diseases. In particular:

- *Artemisia annua* has been used in China for over 2000 years against several infectious diseases including malaria; rich in artemisinin, *A. annua* is used in the production of ACTs.
- *Artemisia afra is* native to South and Eastern Africa where it is also used traditionally against infectious tropical diseases including malaria.
- *Artemisia herba alba*, is similarly used in the Mediterranean area.
- *Artemisia cina,* rich in santonin, is used as an antihelminthic drug.

3.1.2. This enumeration is important to keep in mind because it reveals that the accusation against *Artemisia annua* as being an artemisinin monotherapy is unwarranted. The plant contains many other phytochemicals including other terpenes, flavonoids, tannins, saponins, scopoletin, essential oils and zinc that are also found in varying degrees in other members of the genus. Although they do not contain artemisinin, many of these other members of the genus are also effective against malaria. The diversity of these phytochemicals in the *Artemisia* genus also helps explain the numerous reports of efficacy against a range of tropical infectious diseases that are effectively combatted with *A. annua*, including tuberculosis (Zheng ,2016), leishmania (Sen, 2007), schistosomiasis (Hirt, 2003; Keiser, 2012)), typhoid, intestinal worms (Guarrera, 1999), and malaria. Recently artemisinin was also reported to combat tuberculosis (TB) (Zheng et al. 2016) and there is another unpublished report of *A. annua* success vs. TB in humans. There are many other reports of artemisinin and/or *A. annua* extract efficacy against a diversity of viruses and other diseases, e.g. numerous neoplasms.

3.1.3. The polytherapeutic capacity of *A. annua* is also demonstrated by the effectiveness of ARTAVOL, a Ugandan product fabricated out of *A. annua* after elimination of artemisinin to avoid conflict with WHO. The product is known to help a large number of farmers avoid malaria despite the absence of artemisinin.

[4] Which has an impact on SDGs 3.1 (By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 births) and 3.2 (By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1000 live births and under-5 mortality to at least as low as 25 per 1000 live births).

3.2. The Potential and risks of *Artemisia annua*.

3.2.1. *A. annua* offers the best potential in fighting malaria in Africa. With WHO's blessing, it is already widely planted in Africa to supply the pharmaceutical industry with extracted, purified artemisinin. As a result, cultivars well-adapted to tropical climates and equatorial photoperiods are today available and exploited by the local population as a repellent against the mosquito vector and both preventively and curatively against the disease.

3.2.2. Although the plant is relatively demanding in terms of climatic conditions - it needs large quantities of water and sunlight to become established, rich organic substratum and special care to get it started, it has considerable potential because of its yields of at least 2 T/ha, enough to cure > 125,000 persons (Weathers et al. 2014a). Little agricultural area needs to be sacrificed for producing adequate plant material to protect a family. Even larger leaf yields have been obtained from larger cultivated areas in East Africa (Weathers et al. 2014a).

3.2.4. Some key points related to therapeutic use of *A. annua* against malaria:

- Artemisinin delivered via orally consumed dried leaves (DLA) in animal models was ~45 fold more bioavailable than when delivered as a pure compound (Weathers et al. 2011, 2014b).
- Artemisinin delivered as DLA persisted longer in sick rodents than in healthy ones (Weathers et al. 2014b).
- Patients with severe malaria who were unsuccessfully treated with ACT and iv artesunate were cured after 3-5 days treatment of DLA (Daddy et al. 2017, submitted for publication).
- *A. annua* contains many other antimalarial phytochemicals, but with higher IC50s than for artemisinin (summarized in Weathers et al. 2014a). Some of these work synergistically with artemisinin (Elford et al. 1987; Ganesh et al. 2012; van Zyl et al. 2006; Lehane and Saliba 2008; Liu et al. 1992; Suberu et al. 2013).
- Artemisinin delivered orally as DLA tablets cured malaria in adult malaria patients at 74 mg artemisinin delivered over 6 days (ICIPE 2005) and pediatric patients with asymptomatic malaria (Onimus et al. 2013) with no detectable toxicity.
- DLA provided as a once weekly infusion appeared to provide prophylaxis vs. malaria (Ogwang et al. 2011, 2012).
- The above human trials, albeit small, compared favorably with ACTs, but at much lower total doses of artemisinin (summarized in Weathers et al. 2014a).
- In Mali, Dr. Yves Saint-Hillier treated 100 neonates with encapsulated DLA, 500 mg/capsule delivered rectally up to three times daily and observed 100% cure with no fatalities or side effects (MW, 2016).
- Artemisinin delivered as DLA in an animal malaria model was at least three times more resilient against emergence of artemisinin drug resistance than the pure drug. (Elfawal et al. 2015).
- Artemisinin delivered as DLA for 9 days, eliminated parasitemia in an artemisinin resistant mouse malaria model within 14 days, while mice given an equal amount of pure artemisinin showed no decline in parasitemia. (Elfawal et al. 2015).
- DLA tablets have been made and analyzed (Weathers and Towler 2014); a variety of encapsulation technologies have also been tested (Weathers et al. 2014c); all capsules allowed excellent release of artemisinin from the plant material (Desrosiers and Weathers 2016).
- Simulated digestions of DLA increase artemisinin permeability rates in Caco2 drug transport studies by >25% (Desrosiers and Weathers 2017, submitted for publication).
- Based on agricultural field trials and the ICIPE (2005) study it is estimated that therapeutic DLA and tea infusions are highly economical at << $0.50/cure easily meeting the WHO threshold (Weathers et al. 2014a).
- If clonally propagated, *A. annua* produces DLA with consistent artemisinin content (Weathers and Towler, 2014).
- Unpublished analyses showed that both AN and total flavonoid content of DLA remain at stable levels for up to 2 years post-harvest (Simonett et al 2010; Weathers lab unpublished).

- Although few field experiences have been subject to independent evaluations, evidence from independent sources (Ogwang, 2011, 2012) confirm that with non-hybrid seed and cutting propagated *A. annua* administered in the form of tea in schools, corporations and prisons, effective control of malaria and other diseases, including gonorrhea and skin rash, has achieved significant reductions of absenteeism, higher scholastic results (in terms of the number of pupils passing end-of-year tests) (Christensen, 2014; Kago, 2013), reduction in hospital visits for prison inmates (up to 50%), and health cost reductions averaging 64% (up to 80% in two enterprises). Indications are that malaria treatment with ACTs does not produce higher scholastic results.

3.2.4. WHO has expressed reservations against popular use of *A. annua* in Africa and in a number of Northern countries for the following reasons:

- they fear a spread of further drug resistance against the ACTs;
- the uncontrolled posology applied that could exacerbate the development of resistances.
- the uncertain composition of the extracts produced in various ecological environments and limited rules regarding the cultivation and processing methods

3.3 The fear of emergence of new drug resistance.

3.3.1. WHO fears that popular use of *A. annua* with low artemisinin content would create artemisinin resistance thereby impairing effectiveness of the current ACTs particularly if the plant were under a generalised preventive use.

Both tea infusions and DLA are polytherapies. Delivery of tea infusions have proved successful in malaria patients, but only if the infusion is consistently prepared (Zime-Diawara et al. 2015). Although a precise preparation yields maximum artemisinin content that is stable at room temperature for 24 hrs (van der Kooy and Verpoorte 2011), other phytochemicals, e.g. flavonoids, are not well extracted nor stable (Weathers and Towler 2012). However, in rodents given DLA little to no resistance evolved, and certainly much less than to ACTS (Hassanali, 2013, Elfawal et al. 2015; Kangethe, 2016). Furthermore, rodents with artemisinin–resistant *Plasmodium*, were cured after daily treatment with DLA (Elfawal et al. 2015). More recently, DLA capsules were used to treat malaria patients (Tchandema et al. 2016) and DLA tablets were also successfully used in Democratic Republic of Congo on at least 18 patients with severe malaria, some in coma, who did not respond to either SANU supplied ACTs or even iv artesunate (Daddy et al. 2017, submitted for publication). Thus, evidence is accruing that *A. annua* as DLA is clearly not a monotherapy and instead of evoking artemisinin resistance, actually treats and prevents it.

3.3.2. Regarding the impact on humans, to our knowledge, no country– whether in[5] or outside Africa - that has experienced large scale use of the plant against malaria for several years has reported any fatigue or drug resistance. This is likely because numerous components of the plant create a genuine polytherapy; there are >20 different phytochemicals that can occur in *A. annua* that have demonstrated antimalarial activity (Weathers et al., 2014a).

3.3.3. While these observations indicate that the risk of generating resistance with the plant are less preoccupying than the detractors of its use would like to suggest, one cannot exclude the advent of resistance if the use of the plant is generalised especially at prophylactic doses. If the proposal to generalise the use of the plant is accepted, it means that a network of *pharmacovigilance* will have to be established in the participating countries in line with WHO guidelines. Also, the observations would usefully be accompanied by a rigorous verification through clinical tests carried out in conformity with WHO norms in countries where the plant is used to a large extent (Kenya, Uganda, Gambia etc.). In the meantime, however, one finds it difficult to prevent populations protecting themselves with the plant to save precious lives against malaria. There is equal or greater risk that the

[5] *Artemisia annua* is known to being planted for direct consumption at least in Benin, Burkina-Faso, Burundi, Cameroon, DRC, Gambia, Guinea Conakry, Kenya, Rwanda, Senegal, Togo, Uganda. .

pharmaceutical cures become inoperative through emerging drug resistance, a process that is unfortunately already in progress.

3.4. Uncontrolled posology for a curative use of *Artemisia annua*.

3.4.1. The risk that patients take the natural extracts under an uncontrolled and therefore inappropriate posology needs to be considered carefully. It could reduce their effectiveness in cases of crises with potential fatal outcomes. It could also aggravate the risk of generating resistance especially considering that the reputed bitter taste of the dried leaves and extracts may discourage patients from applying the treatment for the number of consecutive days needed to eradicate the infection, especially with children.

3.4.2. The successes encountered so far from the application of natural extracts of *A. annua* suggest that their use remains globally correct and partly dispels the fear of an inappropriate posology on a large scale. The initiation of the use of the plant with children and youth in schools or with farm cooperatives, especially those managed by women helps anchor effective habits into the population. Projects should of course be closely monitored by the local health services, which need to be trained for this type of malaria treatment.

3.4.3. A. annua infusion has been found to remain effective when it is mixed with soft drinks to eliminate the bitter taste, thus making it more palatable for children. Interestingly, in a taste test in the US, about 25% of the population thought the leaves and/or tea infusion tasted good vs. 75% who either were indifferent or found it bitter (see Supplemental online data in Desrosiers & Weathers 2016). Field experiences in DRC and in Benin also showed that children were not disturbed by the taste. They also showed that after taking the infusion for several months, the taste tends to become more acceptable and is no longer an obstacle to regular intake.

3.4.4. The problem should also be weighed against the African tradition of herbal medicine and one can expect that the population at large will quickly adopt the appropriate techniques to enhance efficacy.

3.5. Uncontrolled composition of *A. annua* extracts.

3.5.1. WHO fears that different soil types, climatic conditions and cultivation methods generate different plant composition that could diminish the effectiveness of the plant and by reducing the artemisinin content, increase the risk of drug resistance.

3.5.2. Measurements have generally shown that the plant composition varies widely with soil type, elevation, temperatures during the growth period, stage of growth at harvest and the way the plant is dried, stored and processed. WHO fears, however, are based only on the artemisinin content. Since it is becoming apparent that the therapeutic efficacy of the plant is determined by a broader phytochemical composition than just artemisinin, it is important to establish the window of phytochemical composition that is therapeutically effective. Because so many different flavonoids have antimalarial activity (Weathers et al. 2014a), total flavonoid content along with artemisinin (for *A. annua*) serve as excellent composition markers for establishing therapeutic windows of activity. Identical cultivars of differing artemisinin and flavonoid composition are being tested in the Weathers lab using a plethora of *P. falciparum* strains ± artemisinin resistance (e.g. K13) to establish IC50 values *in vitro* for both artemisinin and total flavonoids. These data will help establish the therapeutic window for both artemisinin and total flavonoids.

3.5.3. On the other hand, *A. annua* leaves and stems are known to loose much of their effectiveness after flowers start maturing and the plant reaches seed production stage. It will be of critical importance to train the population to harvest the plant at the appropriate time. Here again, African tradition with medicinal plants can be counted upon to ensure a fast learning curve and initiating the programme in schools and cooperatives headed by women assisted by regular visits of experts, will

reduce mishaps. Participating countries should set up regular testing of plant composition and verify phytochemical composition according to area, planting season and harvest (see WHO guidelines for pharamacovigilance of medicinal plants). Although the technical methods used to validate ACTS and to validate plant material are not interchangeable, the costs of compositional monitoring of *A.annua* is not to be allocated only to the plant since inappropriate compositions of ACTs also need to be subjected to WHO rules in terms of verification of the composition of drugs available to the public markets and in pharmacies.

3.6. Comparative advantages of *Artemisia annua*

3.6.1. Against these potential risks, the numerous advantages of using natural extracts or DLA of *A. annua* suggest a clear advantage in favor of using the whole plant. Besides its equivalent efficacy, its lesser sensitivity to emergence of drug resistance and its much lower price making it accessible to the poorest and most isolated part of the population, integration of natural extracts and/or DLA of *A. annua* among the weapons used against malaria in Africa carries the following additional advantages :

- Effectiveness against a wide spectrum of other infectious diseases.
- No known side effects making *A. annua* accessible to pregnant women and young children.
- Easy delivery: as a carefully prepared tea infusion, an extract, or as DLA tablets or capsules.
- Its potential for prophylactic use against malaria.
- Its established efficacy as a mosquito repellent[6].
- Its contribution towards raising educational quality when used as repellent and as prophylaxis.
- Contribution to improving community health.
- Economic sustainability as a result of ownership by the local population.

3.6.2. Besides many other microbes and diseases (Efferth 2006, 2009; Sen et al. 2007; Keiser and Utzinger 2012; Michina et al., 2007) research has shown natural extracts of *A. annua* and/or DLA to be effective against two other main killing diseases in Africa, intestinal infections and tuberculosis. It has also been shown to effectively fight bilharzia (Keiser & Utzinger, 2012) and leishmania (Sen et al., 2007) among others. Some in the West as well as in Central and East Africa use it against skin rash, psoriasis, to reduce menstrual pains, and to cure typhoid. The Chinese traditional pharmacopeia ascribes to *Artemisia* plants numerous cures. All indications are that the plant's composition, including its high content of zinc, a known anti-infectious micro-element relatively rare in tropical plants, helps the body build up its overall capacity to fight infections. This advantage must be considered when taking into account WHO's objection against the use of the costlier ACTs against diseases other than malaria, a problem avoided through use of cheap natural extracts or DLA tablets or capsules.

3.6.3. Since whatever toxic components that may be present in natural extracts and DLA tablets of *A. annua* are administered in small concentrations, no significant negative side effects are known or have been observed in human trials. Hence, DLA tablets and DLA extracts can be used preventively and given to pregnant women and young babies (with rectal administration of capsules when oral delivery is not possible). The exact posology still needs to be determined through clinical tests. They should build on the experiences in particular in Mali (Onimus, 2013; MW, 2016) with capsules and other recent or planned trials using tea infusions or DLA tablets.

3.6.4. *A. annua* extracts and DLA tablets are more easily distinguished from counterfeits (Lutgen, 2008) and contents in both flavonoids and artemisinin validated prior to distribution to insure their phytochemical content using thin layer chromatography fingerprints and simple spectroscopy for total flavonoid content.

[6] Research should include tests of the repellent effect of *A. annua* against the *Aedes* mosquito that propagates the Zika virus.

3.6.5. Eliminating malaria from Africa will bring major income increases; it is estimated that malaria costs Sub-Saharan Africa an annual income growth of 1,4 to 1.5% of GDP. More immediate benefits would come from widespread use of the plant in school gardens. Evaluation of two experiences in Kenyan Schools (see above) have shown that while systematic treatment of malaria with ACT does not seem to result in any notable increase in school results while application of *A. annua* did achieve the following:

- cut drastically teacher and pupil absenteeism;
- decreased health expenditures by 64% on average (up to 90% in two schools);
- repellent impact was sufficient in some schools to consider discarding bed-nets;
- prisoners, generally unprotected by bed-nets, had reduced malaria cases by planting *A. annua* around their prisons. Intestinal infections were also reduced by drinking the tea thus reducing visits to hospital by 50% according to the prison director.

Hence, integrating natural extracts of *A. annua* into the panoply of weapons against malaria in Africa, could have major effects on a global scale.

3.6.6. In terms of safety of the products, the plant is quite resilient against plant pathogens and thus because it is grown without herbicides or pesticides, there is no risk of agricultural chemical contamination. The application of WHO's many guidelines on the cultivation, preparation and safe use of herbal medicine should therefore be restricted to natural contamination due to potential poor hygienic preservation during harvest, drying and storage. Since some of the products will be consumed within the producing families, one can assume that the level of hygiene of the product will be equivalent to the one prevailing in the local context and does not present a critical issue. Urban populations, which have little to no access to land for family cultivation of *A. annua*, would more likely use DLA, which require more stringent conditions as noted in Section 4.

3.6.7. Accustoming populations to treat major diseases through locally available means will encourage Africans to develop better community health programmes with their local health services, hereby multiplying the impact of the latter with fewer new investments. Foreign financed programmes will thereby be minimized and hence more easily eliminated over time. Representatives of various organizations combatting malaria who participated at the World Malaria Day Conference of April 2014 at the Brussels Secretariat of the Asian Caribbean & Pacific (ACP) Representation complained about the resurgence of malaria at the end of official anti-malaria schemes. The case of India was cited as symptomatic. By taking ownership of *A. annua* as an efficient and low-cost protection against various tropical infectious diseases including malaria, African civil society will avoid this drawback and raise the likelihood that the anti-malaria programme will be more sustainable than the top-down official schemes. The approach is therefore more in line with the United Nations' sponsored SDGs.

3.6.8. The famous American anthropologist, Jared Diamond[7] noted that most developing countries were located around the Equator where debilitating tropical diseases are endemic. He predicted that lifelong exposure to such diseases was at least as much a causal factor for their poor economic development as bad governance, perhaps even more so. Hence, one can safely estimate that adopting DLA and/or natural extracts of *A. annua* as a complementary weapon to accelerate the elimination of malaria and other infectious tropical diseases will have a measurable impact on the African population, its health services and on the general economy.

4. Respect of WHO norms regarding the use of medicinal plants.

4.1. The programme, if accepted will, however, need to be accompanied by training at health services and schools of the following WHO norms that should be summarized with a special concern for *A. annua*:

[7] *What makes countries rich or poor*" The New York Review of Books, June 7 2012.

4.1.1 Assessing quality of herbal medicines with reference to contaminants and residues.

- Quality control methods for medicinal plant materials
- Good agricultural and collection practices (GACP) for medicinal plants
- International pharmacopoeia, 4th ed.
- Good manufacturing practices: main principles for pharmaceutical products
- Good manufacturing practices: supplementary guidelines for the manufacture of herbal medicinal products
- Guide to good storage practices for pharmaceuticals
- Good trade and distribution practices (GTDP) for pharmaceutical starting materials
- General guidelines for methodologies on research and evaluation of traditional medicine
- Guidelines for assessment of herbal medicines
- WHO monographs on selected medicinal plants

4.1.2 Conforming to general requirements for foods, including:

- *Codex Alimentarius* code of practice, general principles of food hygiene
- *Codex Alimentarius* guidelines for the production, processing, labeling and marketing of organically produced foods
- *Codex Alimentarius* code of practice for spices and dried aromatic plants

4.1.3 Packaging instructions for DLA tablets or capsules. Information should normally include, or make reference to:

- The name of the product;
- A description of its pharmaceutical form, strength and, where applicable, method of application;
- The pack size expressed in terms of the number, weight or volume of the product in the final container;
- A complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types, with the code or reference number relating to the specifications for each packaging material;
- Where appropriate, an example or reproduction of the relevant printed packaging materials and specimens, indicating where the batch number and expiry date of the product have been marked;
- Special precautions to be observed, including a careful examination of the packaging area and equipment in order to ascertain the line clearance before and after packaging operations;
- A description of the packaging operation, including any significant subsidiary operations, and equipment to be used;
- Details of in-process controls with instructions for sampling and acceptance limits.

4.1.4 While the above listed items are not applicable to natural extracts (e.g. tea infusions) made at home, they do apply to DLA tablets and capsules. Potential fully African-owned and operated supply chains for DLA tablet production of *A. annua* have been identified. They include cooperatives or individual producers following GACP growing, drying and threshing operations (following GTDP), a GMP tablet manufacturer and packager, and pharmacy outlets for tablet distribution. QC testing procedures, although not yet validated, are also already technically established. Details provided on request.

4.2. The application of these norms should be entrusted to the African Regional Office of WHO.

5. Conclusions

5.1. The WHO Executive Council is asked to include in the Agenda of the WHO General Assembly of May 2017 the lifting of its reservations against the use of natural extracts or DLA tablets or capsules

of *Artemisia annua* against malaria in Africa under conditions to be controlled by the African Regional Office of WHO.

5.2. The Ministry of Health of Burkina-Faso is planning a colloquium on the use of *A. annua* against infectious diseases in Africa that will bring together representatives of the Regional Office of WHO, international and African researchers, practitioners of the plant and other interested parties to discuss the way forward. Timing will depend on the decision of WHO's Executive Committee.

Annex: Bibliography