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COMPUTER PROGRAM

The program starts with a database file. The database file includes fields:

* Year
* population
* incidence
* interest rate
* variable
* fixedcost
* benefit

The number of records should be taken on the number of years within the timeframe defined for estimation of benefit, eg 10 years for a long run analysis population is the population in the control area. This population grows annually. Population projection of the control area should be calculated on the population growth rate and on actual population.

Incidence or annual incidence is the number of new parasite positive cases per 1,000 population in the control area in the year. This incidence decreases annually according to the efficacy of malaria surveillance activities. The annual decrease rate of the coming years can be estimated from the decrease rate of the past years if there are no major changes being expected to occur.

Annual interest rate should be taken into consideration since present value of future benefit against present value of future annual recurrent cost have to be calculated. Annual interest rate can be estimated from estimations of the national bank of each country.

All future cost and benefit should be estimated with consideration of the annual interest rate, except the capital cost. Variable cost and outcome values (benefit) depend on annual population size and annual incidence.

On records and fields of the database file, a program file is developed on inputs and calculation mentioned in paragraph 3.1.3. as follows:

```
set talk off
set score off
```

```
clos all
clear all
?
* define information
* population in control area
      p    =
* population per service point
      ppp =
* population per quality control point
      ppcp=
* trainees per service point
      tpp =
* trainees per quality control point
      tppq=
* training days per service person
      tdp =
* training days per quality control person
      tdpq=
* trainees per trainer for service
      tpt =
* trainees per trainers for quality control
      tptq=
* perdiem for service persons
      pdj =
* perdiem for quality control persons
      pdjq=
* perdiem for trainers for service
      pds =
* perdiem for trainers for quality control
      pdsq=
* transport for trainees for service
      tpj =
* transport for trainees for quality control
      tpjq=
* transport for trainers for service
      tps =
* transport for trainer for quality control
```

```
      tpsq=
* administration cost rate for training for service
      adm =
* administration cost rate for training for quality
control
      admq=
* equipment cost per service point
      epp =
* equipment cost per quality control point
      eppq=
* space cost per service point
      scp =
* space cost per quality control point
      scpq=
* monthly salary of service person
      ms  =
* space maintenance cost of service point
      sm  =
* test specificity
      spc =
* cost of unit test
      cut =
* cost of unit quality control test
      qcuc=
* labor cost quality control
      lqc =
* space maintenance cost per quality control point
      sqc =
* supervision times per service point
      stp =
* supervision days per time
      sds =
* quality control rate
      tcr =
* waiting days per case
      wdp =
* rate of waiting cases among diagnostic cases
```

```
      rwt =
* accompanying rate
      apr =
* income day
      ind =
* distance house service point
      dhs =
* transport cost per 10 kim
      cpk =
* rate of presumptive treatment among waiting cases
      prw =
* cost per presumptive treatment case
      cpc =
* rate of self treatment among hospital and malaria
clinic cases
      rost=
* cost of self treatment case
      cstc=
* cost per radical treatment case
      crt =
* working proportion of service persons
      psp =
* working proportion of quality control persons
      pcs =
* calculations
* number of service points (nsp)
      nsp = p/ppp
* number of trainees for service points (not)
      not = nsp * tpp
* cost trainees/trainers for service points (ctt)
      ctt = tdp*pdj*not + tpj * not+pds *
      tdp*not/tpt+tps*not/tpt
* administration cost for training of service persons (adc)
      adc = adm * ctt
* training cost for service persons
      tco = ctt + adc
* space cost for service points (sco)
```

```
            sco = nsp * scp
        * equipment cost for service points(eco)
            eco = nsp * epp
        * administration cost of upper level for establishing the
        new test (adc)
            adc = 0.05 * (eco + tco)
        * number of quality control points (ncp)
            ncp = p/ppcp
        * number of trainees for quality control (notq)
            notq= ncp * tppq
        * cost for trainees/trainers foi quality control (tqc):
        tqc = notq * tdpq * pdjq + notq * tpjq + notq/tptp      *
pdsq * tdpq
        * administration cost for training for quality control
        (adcq)
            adcq= admq * tqc
        * equipment cost for quality control (eqc)
            eqc = ncp * scpq
        * establishing cost for quality control (esqc)
            esqc=tqc + eqc + sqc
        * salary for service persons (ssp)
            ssp = ms * not * 12 * psp
        * annual retraining cost for service persons (art)
            art = ctt * 0.1
        * space maintenance cost for service points (smc)
            smc = nsp * sm
        * annual supervision cost (mfc)
            mfc = nsp * stp * sds * pds * nsp * stp * tps
        * space maintenance cost for quality control (tsqc)
            tsqc= sqc * ncp * 12
        * salary for quality control
            tlqc= lqc * ncp * tppq * 12 * pcs
        * inverse specificity
            ispc= 1 - spc
        * capital cost field level (cof)
            cof = tco + sco + eco
        * capital cost upper level (coqc)
```

```
        coqc= adc + esqc
    * total capital cost (tcc)
        tcc = cof + coqc
    * fixcost field level (ffc)
        ffc = ssp + art + smc
    * fixcost upper level (fcqc)
        fcqc = mfc + tsqc + tlqc
    * total fixcost
        tfc = ffc + tcqc

use (database file)
    * data base file has fields
    * incidence (annual)
    * population (annual)
    * interest (annual change on defined rate)
    * fixcost (present value)
    * variable (cost present value)
    * benefit (present value)
    * equation for tpi (number of tests per positive case) on
    incidence

do while !eof()
    * number of positive cases
        npca = incidence * population/1000
    * number of test per positive case tpi = f (incidence) e.g:
        tpi = 43 - 3 * incidence
    * number of tests
        ncr = npca * tpi
    * test cost field level
        scf = ncr * cut
    * cost of false positive cases
        cfc = ispc * (ncr - npca) * crt
    * total test cost field level
        cfl = scf + cfc
    * consumable cost for quality control
        cct = npca * tpi * rwt
```

```
        * number of accompanying persons
              nap = nwt * apr
        * travel cost by users
              trc = cpk * dhs/10 * (nwt + nap) * 2
        * total waiting days
              ttwt = nwt * wdp
        * opportunity or time cost
              ops = ttwt * inc
        * saving external cost
              B1 = ops + trc
        * value of prevented presumptive treatment
              B2 = nwt * prw * cpc
        * value of prevented self treatment
              B3 = (ncr - nwt) * rost * cstc
        * benefit (B)
              B = B1 + B2 + B3
        * total variable cost (tvc)
              tvc = cfl + cct
replace benefit with B * interest for recno()< number of required
years;
replace variable with tvc * interest for recno()< number of
required years;
replace fixcost with tfc * interest for recno()< number of
required years;
enddo
use (datafile)
sum benefit, variable, fixcost to tben, tvar, tfix
      ratio= tben/(tcc + tvar + tfix)
      ?
      ?ratio
      ?tben
      ?tvar
      ?tfix
      ?
```

*Para*Sight TM F

RAPID TEST FOR *P.FALCIPARUM* MALARIA

BECTON DICKINSON TROPICAL DISEASE DIAGNOSTICS
SPARKS, MD 21152

PERFORMANCE CHARACTERISTICS

The performance of *Para*Sight™ F to detect *P. falciparum* from whole blood samples was determined by correlation to standard thick and thin blood smear examination. 491 whole blood samples collected at 3 clinical sites worldwide from individuals with symptoms of malaria were evaluated with *Para*Sight™ F.

*Para*Sight™ F demonstrated 95.6% sensitivity, 86.8% specificity, 83.7% positive predictive value, and 96.5% negative predictive value compared to blood smear. The sensitivity of *Para*Sight™ F compared to blood smears with > 10 parasites/uL was 95.6%.

Table 1
Sensitivity and Specificity of the *Para*Sight™ F Test

Site	No. Patients	No. Blood Film Positive	That are *Para*Sight™ F Positive (Sens.)	No. Blood Film Negative	That are *Para*Sight™ F Negative (Spec.)
Brazil	113	49	46 (93.9%)	64	57(89.1%)
Indonesia	105	33	32 (97.0%)	72	56 (77.8%)
Tanzania	273	122	11795.9%)	151	136(90.1%)
Total	491	204	195(95.6%)	287	249 (86.8%)

Table 2
Time to Clearance of *Para*Sight™ F Antigenemia vs. Parasitemia

No. Patients Studied	No. Days Antigenemia After Parasitemia	Parasitemia Prior to Treatment Mean (Range) Parasites/uL
34 (85%)	0 - 7	2250 (200 -40,000)
6 (15%)	8 - 17	18,500 (400 - 40,000)

The cross reactivity of *Para*Sight™ F was evaluated by testing parasites other than *P. falciparum*. None of the organisms (listed below) reacted positively in the test. *P. malariae, P. ovale, S. mansoni, E. histolytica, D. perstans, Babesia, Loa Loa.* In 9 out of 47 (19%) of patients diagnosed with *P. vivax*, *Para*Sight™ F test was also positive for HRP II antigen.

AVAILABILITY

Reorder Numbers:
*Para*Sight™ F, 20 Test Kit Cat. No.5353061
*Para*Sight™ F, 100 Test Kit Cat. No. 5353060
*Para*Sight™ F, Positive and Negative Control Set Cat. No. 5353064

INTENDED USE

ParaSight^{TM} F is a rapid test for the qualitative detection of the histidine rich protein II (HRPII) antigen of *Plasmodium falciparum* directly from whole blood without any instrumentation.

PRINCIPLES OF PROCEDURE

HRPII is a water-soluble protein released from parasitized erythrocytes(1). It has been found in all natural isolates of *P. falciparum* tested (2) and has been detected in plasma and urine (3,4) as well as whole blood (5).

Antibodies specific for *Plasmodium falciparum* HRPII are immobilized on a Test Strip. *P. falciparum* antigen in lysed whole blood binds to the antibody as the blood absorbs into the Test Strip. Detector particles containing a dye and coated with antibodies specific for *P. falciparum* absorb to the Test Strip and bind if antigen is present. A solid pink line indicates a positive test. A dashed pink control line and a white to light pink background will always be present if the test has been performed properly.

REAGENTS

Test Strips (20 or 100)	membrane coated with mouse anti- *P. falciparum* antibody and *P. falciparum* antigen
Reagent 1 (9.0 mL)	Lysing, 0.25% detergent, with 0.2% sodium azide (preservative)
Reagent 2 (5.0 mL)	Detection, rabbit anti-HRPII, liposome, with 0.2% sodium azide (preservative)
Reagent 3 (9.0 mL)	Wash, 0.2% detergent, with 0.2% sodium azide (preservative)

Precautions

Reagents: Once opened, reagents may be used until the expiration date. Do not use beyond the expiration date. Do NOT mix reagents from different kit lot numbers.

To assure proper drop delivery the DispensTube^{R} and reagent bottles must be held vertically when dispensing one free-falling drop at a time.

Observe established precautions against microbiological and serological hazards in specimen handling, disposal and throughou all procedures.

Warning: Reagents contain sodium azide which may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.

Test Strip: Remove from pouch just prior to use. Discard desiccant. Do not eat.

Storage: Store kit at 2 - 37 C, away from direct sunlight. DO NOT FREEZE.

SPECIMEN COLLECTION AND HANDLING

Use blood from a finger or heel puncture or a freshly collected venous specimen. Observe the general precautions:

Clean the skin area thoroughly with antiseptic agent and dry with a sterile wipe.

For capillary blood, puncture the skin with a sterile lancet. Collect blood directly into the *Para*Sight™ F capillary tube as described under PROCEDURE.

For venous blood, draw the specimen with a sterile syringe or evacuated collection device with heparin or EDTA anti-coagulant. See PROCEDURE for filling the *Para*Sight™ F capillary tube.

Anticoagulants: *Para*Sight™ F capillary tubes are coated internally with sodium heparin.

PROCEDURE

Materials Provided:

20 or 100 Test Strips
20 or 100 Capillary Tubes and 3 Rubber Bulbs
20 or 100 DispensTube® Devices (Tubes and Tips)
Reaction Stand
2 or 10 10-well Cards

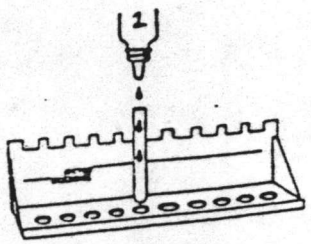
Reagent 1	9.0 mL
Reagent 2	5.0 mL
Reagent 3	9.0 mL

Materials Required But Not Provided:

Lancets
Sterile Wipes

SPECIMEN PREPARATION

Place one 10-well card in Reaction Stand. Discard card after all 10 wells have been used.



1. Squeeze three (3) drops of Reagent 1 (lysing agent) into a DispensTube®. Stand DispensTube® in Reaction Stand.

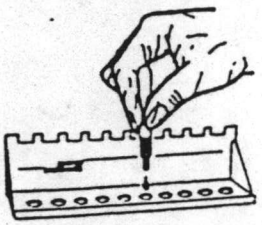
2. Fill the *Para*Sight™ F capillary tube, from the end farthest from the line, directly from a finger or heel puncture or a collection tube of well mixed venous blood. Fill the tube by capillary action to the line.

3. Keep the tube nearly horizontal and roll between the fingers several times to mix the blood with the anticoagulant coating.

4. Drain the blood from the capillary tube into the DispensTube®. If necessary, use a rubber bulb to force the blood from the capillary tube. Do not mouth pipette. Insert the empty end of the capillary tube into the small opening of the bulb. Hold the large opening of the bulb closed with index finger, then squeeze the bulb.

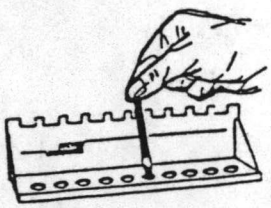
5. Place a DispensTube^{R} tip onto the DispensTube^{R}. DO NOT INVERT TUBE UNTIL READY TO DISPENSE.

TEST DEVELOPMENT

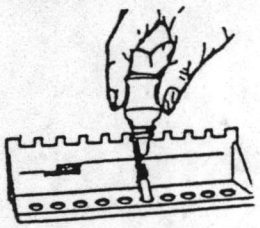


Remove Test Strip from pouch just prior to use. Label Test Strip with patient identification.

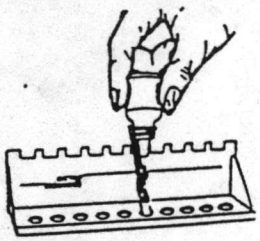
1. Squeeze one (1) drop of lysed whole blood from the DispensTube^{R} into one disposable well in the Reaction Stand.



2. Stand Test Strip in the drop of lysed blood with patient identification facing forward. Wait until all the blood is absorbed into the Test Strip and the well is empty before proceeding to Step 3.



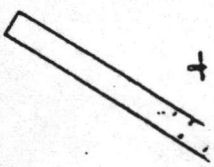
3. Squeeze one (1) drop of Reagent 2 (detection agent) into the same well. Wait until all of Reagent 2 is absorbed into the Test Strip and the well is empty before proceeding to Step 4.



4. Squeeze two (2) drops of Reagent 3 (wash agent) into the same well. Wait until all of Reagent 3 is absorbed into the Test Strip and the well is empty.

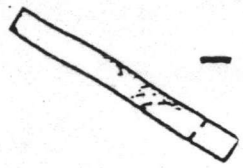
RESULTS

Immediately read the results in a well-lighted area.

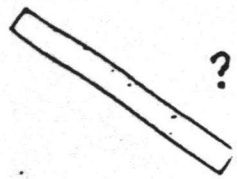


1. Positive Test (*P. falciparum* malaria antigen is present in the specimen) - A solid pink line appears on the Test Strip.

   A pink procedural control dash should also be visible above the solid line. In cases of very strong positives, the control dash may be very faint. The background should be white to light pink.



2. Negative Test (*P. falciparum* malaria antigen is absent) - A pink dash only is visible. The background should be white to light pink.



3. Uninterpretable Test - The test is uninterpretable if neither a pink line nor dash is visible or the background is dark pink. The test should be repeated.

USER QUALITY CONTROL

- A positive procedural control is provided by the Control Dash on the Test Strip.
- A negative procedural control is provided by the non-reactive (white to light pink) background area of the Test Strip.

If the test is performing properly and the reagents are added correctly, a distinct result (solid line, dash, or both) will appear on the Test Strip and the background will be white to light pink. If the procedural controls are not present as described, the result is invalid, must not be reported, and the test must be repeated. External liquid positive and negative controls (Cat. No. 5353064) are available as a means of additional quality control testing. Contact your distributor or local Becton Dickinson office.

LIMITATIONS OF PROCEDURE

*Para*Sight™ F is a qualitative method which depends on the amount of *P. falciparum* antigen present. It may not correlate with blood films or other malaria tests performed at the same time which detect presence of parasites. Antigen may appear earlier and/or persist longer than presence of parasites. Other species of *Plasmodia* will not be detected by *Para*Sight™ F. Test results must always be interpreted in conjunction with other clinical and laboratory data available to the physician.

EXPECTED VALUES

Prevalence of *P. falciparum* was 42% in the population tested in the clinical studies.

BIOGRAPHY

Mrs NGUYEN THI KIM CHUC is Pharmacist. She was born on 02, February, 1954 in Thanh hoa Province, Viet nam. At the time she is lecturer of Pharmacology at Hanoi Medical School and works for the Center for Human Resources in Health, Ministry of Health as a researcher. Any correspondences concerning this thesis please send to Mrs Chuc at the following address:

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