KALADRUG-R: management SOP I-A

SOP for the data collection, data selection and data entry for KA patients in BPKIHS, Dharan

March 1st 2010

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The clinical database was created initially by Mr. Santosh, and adapted by B.Ostyn, M.Vanaerschot and S. Decuypere after consensus meeting with Prof. S.Rijal and clinical coordinator(s) in February 2010.

All KA patients enrolled in KalaDrug-R are registered in the KalaDrug database. Clinical, epidemiological and laboratory data are collected either immediately in the Case Report Form (CRF), either from the hospital file (in which case the doctor filling the CRF selects the relevant data from the hospital file).

A. Opening a new CRF

(as said, may be at discharge of the patient, and from the hospital file, may be during hospitalization, after confirmation of the diagnosis, or may be at admission, as informed consent is requested anyhow).

*In case a patient with **suspected KA is found not to have KA** (negative smear, other cause of fever detected) then this **patient does not need to be registered** in the KalaDrug database.*

1. **A new CRF** is opened by filling in the cover sheet of a CRF booklet. Relevant data are Name; Occupation; Age; Sex; District; Ward Nbr; VDC Municipality; Pt ID nbr.

2. **Study nbr** is a unique KalaDrug-R number composed of BPK and a 3 digit number (consecutive).

> Ex.   BPK476, BPK477, BPK478, etc....

The number refers to a patient. Should this patient have a second treatment episode (= a new treatment course e.g. after treatment failure, SAE, default or relapse), then a new CRF booklet needs to be started with the same patient number but followed by a number corresponding with the number of months since the start of the previous treatment.

> Ex.   BPK476/1, BPK477/3, BPK478/48, etc....

This system allows us, in case of relapse, to trace the first sample as well as the consecutive samples of biological material collected in the same patient.

Note that a patient who is already a relapse at enrolment in the KalaDrug-R project should be registered with a patient number only, without a reference to the time since his first treatment.

Once you open a second file for a KalaDrug patient, you may choose to append a **/O** to the initial code on the file: this way everyone can see that there are more files (i.e. treatment episodes) to follow on this patient.

3. Write **date of admission** and **date of discharge**.

4. Fill in **Height** and **Weight** at admission (Important baseline data on nutritional status, allows to calculate W/H in children and BMI in adults. Weight gain is one of the most relevant clinical parameters for clinical improvement.)

5. At discharge, fill in **F/U Dates expected** with the appointment date for the follow up visits:

> For Miltefosine treated patients:

- at day 14 (2nd week) to pick up the remaining MIL tablets for the coming 14 days of oral treatment
- at day 28 = at end of treatment to do the end-of-treatment evaluation (**essential** = early outcome)

    (1st week and 3rd week, as mentioned on the CRF, are no appointments)
    (As Amphotericin-B treated patients stay in the hospital until the 14th dose, they don't need an appointment for the early outcome evaluation.)

> For all patients (MIL and AMPHO-B):

- At 2nd month: 2nd month from end of treatment, or 3rd month after start of treatment
- At 6th month: **essential** for final outcome
- At 12th month = 1 year evaluation

Next to the **F/U Dates expected**, add a column to write the **actual visit date**: this way follow-up status can be checked without opening the file, and the files of all patients that are expected for a follow-up visit in one month can be put together.

6. **Location Map to reach the patients** is meant to draw a map (or write a telephone number) in order to trace the patient in case he/she does not show up for his follow-up appointment(s).

All these data are to be entered in the database, except for the location map.

- If data are missing, write **NA** (not available).
- For the F/U Dates expected: fill in **NR** if not relevant (no appointment)
- For the actual follow-up dates: if patient came but date is not found in the CRF, write **DNR** (date not recorded)

B. Opening the database and creating a new patient file

1. Open the file by clicking on the filename: you obtain the welcome screen:

<div align="center">

Click "**click here to continue**"

</div>

2. A "**choose action**" screen appears with the following choices:

       ☐ Add new record

       ☐ Update record

       ☐ Close program

    Click on "**Add new record**"

3. You obtain the Cover page: a blue sheet with all the data corresponding with the cover page of the CRF. Fill in as described above.

4. After filling in all fields, mark ***yes/no*** in the right upper case (form completed) and eventually look for missing data in the hospital file.

5. To fill in one of the other 6 pages of the database record, click the specific "**Go to…**" button. By choosing another sheet of the same patient (6 different choices "Go to…), the information is automatically saved.

6. **Start** by entering **"Study no."** (should be <u>exactly the same</u> as on the cover page) on each page.

7. Subsequently fill in the other fields as specified in point D (see below).

C. Updating an existing patient file

1. Similar as above. Click on "Update record" and find the patient record you wish to update by:

- clicking the arrows at the bottom of the record screen which allow you to browse between different patient records.
- click the button '**Find Study No.**'. A classic Microsoft 'Find' window appears, type the patient no. in the field '**Find What**', change the fields underneath as follows:

<div align="center">

Look in: **Cover page: Form**

Match: **Any part of the field**

Press Enter. The requested record should appear.

</div>

2. By choosing another sheet of the same patient (6 different choices "Go to…), the information is automatically saved and you switch to a different section of the same patient file.

D. Guidelines to fill in the different sections of the CRF and matching fields in database

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PAGE 1: CLINICAL EVALUATION (CRF and database)

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1. in CRF

HISTORY

1. Make note of all relevant data with regards to the duration of the **symptoms** (in weeks), as well as appetite, weight loss, abdominal fullness, skin darkening etc.

2. If there is a **history of treatment** for KA, collect as much details as possible, including adherence (number of days taken, interruptions, etc.) and place of treatment.

3. **Lactating/pregnant**: relevant for contra-indication for MIL

4. **Family history** (KA cases in family)

5. **Co-existing chronic disease** (TB, HIV, pneumonia, etc...): contra-indication for MIL and relevant for co-administration of other drugs.

ON EXAM

1. Fill in all requested data from CRS (except for vision and fundoscopy). If afebrile, write "**no**" or "**98**".

2. in database: open relevant patient file, open sheet (go to:) "p1. clinical evaluation"

1. Fill in number for the **weeks (approx.) of symptoms** before admission:

(Note: 2 months = 8 weeks, 3 months = 13 weeks, 6 months = 26 weeks)

2. **History of KA treatment**: fill in yes/no. If yes, fill in number of episodes.

In table below, start with first episode and calculate the time (in months, approx.) between the first diagnosis and the current relapse.

3. **Lactating/pregnant**:

       For male, elderly and children: choose "**NR**" (not relevant)

!!! If data absent in CRF: check in hospital file, and only if not available there as well, write "**NA**".

Crucial data for CRF and database: **spleen size**, **liver size & weight** MUST be recorded at baseline AND at each clinical visit, as these are the essential clinical outcome parameters. The same for the laboratory parameters **hgb** and **protein/albumin**, and the **parasitological smear** at end of treatment.

Timing of evaluations:

in the CRF there are 5 columns on p.2 CRF:

day 1 of treatment - 1st week date – 2nd week date – 3rd week date - and 4th week date

Apart from the baseline evaluation, there needs to be AT LEAST 1 second evaluation recorded at the end of treatment.

To avoid confusion, clearly **record the date of evaluation in CRF**. 2nd week for AMPHO treatment corresponds with end of treatment, but for MIL treatment, the 2nd week is only halfway.

Columns on p.3 CRF:

These must be filled in at every return visit. Fill in the relevant column and always **record the date of evaluation in CRF.** (Note that a patient may present himself spontaneously before the planned follow up visit at 3 or 6 months. This is crucial information, if at these visits clinical evaluation shows relapse.)

Write at the bottom of the column the **conclusion of the clinical evaluation** e.g. improved/not improved (relapsed, re-emergence of symptoms).

Crucial data: laboratory parameters at baseline AND at the end of treatment to evaluate treatment outcome. Laboratory parameters during treatment are important to document adverse events.

For MIL treated patients: baseline and end of treatment (EoT) should always be recorded in CRF and database (baseline to exclude contra-indications, EoT to evaluate improvement). If intermediate laboratory tests are done (recorded in CRF) and are abnormal, then they should be entered in the database (with the data of occurrence).

For AMPH treated patients, middle of treatment (MoT) lab results should be reported in database. As there are often many recorded in the CRF, **systematically only record the most abnormal value in the database** (these are not necessarily the lab results of day 7 or 8).

Example: MoT may contain Creatinine highest value at 4th AmphB dose, as well as highest Potassium value measured at 12th AmphB dose.

1. Choose **drug of choice** (including dosage formulation) and **daily dosage** (e.g. MIL-50 DB = 100mg). If a combination of MIL 10 and MIL 50 tablets is used to attain daily dosage, then choose MIL 50/10.

2. **Reason use Amphotericin B**:

Only fill out in case of Amphotericin B treatment. Relapse to Miltefosine is considered as "contraindication for MIL use".

3. **Treatment interruption**:

Ideally obtained by consulting <u>patient's treatment card</u> and important to evaluate adherence.

Treatment interruption is defined as having 2 consecutive days without any treatment taken.

Examples:

> Amphotericin taking on alternate days: *interruption* = no
> Missing one day of MIL treatment: *interruption* = no
> Amphotericin delay of 2 days (e.g. waiting for side effects to reside):
>
>> *interruption* =yes
>>
>> *duration* = 2
>>
>> *reason* = RF impairment

4. **Other medication**:

Only for other medication that is taken on a chronic basis, such as anti-TB drugs and antiretroviral treatment, but also anti-depressive medication (which could interfere with the anti-leishmanial drugs metabolism).

> Antibiotics can also be mentioned
> No need to mention anti-pyretic drugs

5. **Discontinuity**:

Refers to whether or not treatment duration has been shortened.

Write reason, but also mention number of doses taken if not clear (e.g. in case of Amphotericin B).

6. **Remarks on treatment**:

Anything you want to add with regards to treatment and adherence.

Special cases:

1. **PKDL** requires another CRF for data collection and a new set of forms for the database, these are currently being designed.

2. **Cases that have started their treatment in another health structure and who were referred to BPKIHS because of complication**:

1 - The treatment that was installed initially is **continued** in BPKIHS after the subsiding of the adverse events:

Register under Clinical Evaluation:

Patient type:	new case
VL history:	No
Number of previous KA episodes:	0

Register under Diagnosis and treatment:

Fill in drug of choice, daily does etc. (same as started in other health str.)

Start of treatment: use the date of start of treatment, in the health institution where it was started.

End of treatment: date of completion of treatment in BPKIHS

Treatment interruption: Yes

Duration: number of days

Reason: AE (specify adverse events)

More details can be mentioned under "Remarks on treatment"

2 - The treatment that was installed initially is **not continued** at BPKIHS after the subsiding of the adverse events, but another treatment is started:

Register under Clinical Evaluation:

Patient type:	treatment after SAE
VL history:	Yes
Number of previous KA episodes:	0 (= still the same episode)
Time since end of earlier ttmt:	e.g. 4 days
Drug used then; Daily dose;	
Duration:	e.g. 8 days,
	or for Amph B: 5 doses

Register under Diagnosis and treatment:

Fill in new drug of choice, daily dose etc.

Start of treatment: = start of the new treatment

End of treatment: = date of completion of treatment

Treatment interruption: Yes/No

Duration: number of days

Reason: (specify)

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The last page in the database record is to report important adverse events. Try to be as detailed as possible: date of occurrence (or number of dose), type of side effect and CTC grading. If no severe adverse events were reported, then simply choose "no" in the upper box "SAE present", as a sign that the sheet has been completed and there were no AE to report.

Note that the reporting should not be limited to severe adverse effects. Even if treatment was not interrupted or changed, any mention in the patient's written file on side effects should be noted here (with the CTC grade).

Common abbreviations used in the database:

NA	result **N**ot **A**vailable
NR	**N**ot **R**elevant
DNR	**D**ate (of follow up visit) **N**ot **R**ecorded

SOP written on Feb 10-14, 2010, bo