NOTE: Please read these "Instructions" and "List of definitions of TB diagnosis and treatment outcomes" carefully before you complete the forms. Please use black ink when filling out the form.

6 Month Follow-up form should be completed for all HIV-infected patients diagnosed with TB at your clinic at least 6 months ago and who are enrolled in the prospective TB:HIV Study (had completed Enrolment forms). Please notice that information on HIV infection should be collected on a separate form (HIV infection form).
In case you already have data on HIV infection electronically in your database, please contact us at hivtb@cphiv.dk for electronic data-exchange.

1. In general:

- **Please cross-check the information provided on the form and complete where missing.**
- Complete these forms either by writing "*X*", by filling out a numeric field, or by completing the information regarding the day, month, and year for time-variables. If the month is unknown, write only the year. If the month and year are both unknown, write "02/79".
- If information is incorrect, please draw a single line through the incorrect information, write correct information, circle the correction, and write your initials and date.

2. Section A: Background demographics:

- All questions should be completed. Please cross-check all pre-printed information. Please provide information, if missing.
- For IDUs please provide updated information on whether the patient is currently (i.e. at 6 Months follow-up) an active IDU or receiving substitution therapy. Please complete on all follow-up forms.
- The most recently measured weight should be entered. Please try to collect this parameter on as many patients as possible. Please complete on all follow-up forms.
- Height should also be entered for all patients. If this information was missing at enrolment, please provide it on the 6 months follow-up.

3. Section B: Previous TB diagnosis (should only be filled out if a patient has had TB in the past)

- Please cross-check information provided at Enrolment and update, if necessary (according to Instruction for the Enrolment forms).

4. Section C: Current TB diagnosis

- Please cross-check information provided at Enrolment and update, if necessary (according to Instruction for the Enrolment forms).
- The date of the current TB diagnosis is either the date when a specimen positive for *Mycobacterium tuberculosis* was obtained, or the date when anti-TB treatment was initiated, **whichever comes first**.
- For all patients please answer **update information on question 5**. Should be completed on all follow-up forms. If the patient has initiated / restarted / changed cART regimen for other reasons than toxicity AND experienced worsening of TB disease diagnosed prior to initiation of cART, please fill out a separate IRIS form.
- Section C2: Diagnostic procedures for TB: Please cross-check and update information provided at Enrolment. Indicate **all** tests which were performed **since last reported** by indicating a number for the type of test (left column) and a letter for the type of specimen used (right column). If biopsy was taken (specimen ID E), please specify the tissue. Please

indicate all tests that were performed, irrespectively of results available. **Insert the date when the specimen was obtained** from the patient (not the date of result).

- If a culture was not taken at baseline please indicate why in section C2, question 2, if not already reported.
- Section C3: Clinical presentation of current TB disease: **Please update this section. If additional locations of TB process have been identified, please tick "x" respective boxes.** Several answers are possible, if patients e.g. have both pulmonary and extrapulmonary locations.

5. Section D: Drugs used for TB disease and resistance test:

- All drugs used for the current TB disease should be filled out, including vitamin B6 and steroids. **Please cross-check information provided at Enrolment and add all drugs** that have been used since last reported. Please remember that it is essential for the study to provide start and stop dates, as well as reasons for discontinuation for all drugs used. Please also complete stop date if a patient dies.
- Information on resistance testing is required. If the resistance test was done for a drug, but this drug was not used for treatment, please write drug name in the left column "Drugs used for current TB disease" and then provide date of resistance test and result in the right columns "Resistance Test Results"
- For drug names please use abbreviations provided on the top of the page
- Please indicate daily doses and frequency of drugs intake. Please see codes for frequency on the top of the page.
- Please indicate reasons of discontinuation by using codes on the top of the page. If patient has completed the full course of TB treatment as prescribed, please indicate the reason for discontinuation as *93.1 "Completed recommended duration of therapy".*
- If resistance test was not performed, please indicate reasons for that in **question 3**
- If standard RHZ-based treatment has not been given as initial therapy, please make sure that the **question 4 is answered**
-

6. Section E: Clinical outcome for the current TB case:

- Clinical outcome of current TB diagnosis should be filled out. Definitions of clinical outcome are listed below (page 3) (please use these definitions for correct outcome). **Please note that outcomes "cure" and "treatment completed" should only be indicated if patient had completed the course of TB therapy of min 6 months duration. Please read carefully definitions of outcome below (page 3) before ticking "x"**
- **If patient is still receiving anti-TB treatment, please tick "x" the respective box**

7. Section F: For patients who died:

- For patients who have died, please provide the date of death. **A "Cause of Death" (=CoDe) form should be filled out for all patients who died.**

List of definitions of TB diagnoses and treatment outcomes 1,2

TB diagnoses

A ***"definite"*** case of tuberculosis is a case with culture confirmed infection with *M. tuberculosis* complex (if routine culturing of specimens from all cases is not performed, a patient with sputum smear examinations positive for acid-fast bacilli (AFB) is also considered to be a "definite" case).

Pulmonary: Pulmonary is defined as tuberculosis of the lung parenchyma and the tracheobronchial tree only. Extrapulmonary tuberculosis is then defined as tuberculosis affecting any site other than pulmonary as defined.

Pleural: Pleural tuberculosis is defined here as extrapulmonary tuberculosis and is tuberculous pleurisy only, with or without effusion.

Lymphatic: Lymphatic tuberculosis includes tuberculosis involving the lymphatic system. Because of the intrathoracic manifestations of tuberculosis in patients with human immunodeficiency virus (HIV) infection, lymphatic tuberculosis is preferably further differentiated into intrathoracic and extrathoracic lymphatic tuberculosis: 1) Intrathoracic - intrathoracic lymphatic tuberculosis; and 2) Extrathoracic - lymphatic tuberculosis other than intrathoracic lymphatic tuberculosis.

Bone joint: Tuberculosis of the bones and/or joints should be subdivided into: 1) tuberculosis of the spine; and 2) tuberculosis of bones/joints other than spine.

Central nervous system (CNS): Tuberculosis of the central nervous system should be subdivided into: 1) tuberculousmeningitis; and 2) tuberculosis of the CNS other than meningitis.

Genitourinary: Tuberculosis of the genitourinary system, including tuberculosis of kidney, ureter, bladder, and male and female genital tract.

Peritoneal/digestive tract: Peritoneal/digestive tract tuberculosis includes tuberculosis of the peritoneum with or without ascites and tuberculosis of the digestive tract.

Disseminated: Disseminated tuberculosis includes tuberculosis of more than two organ systems or miliary tuberculosis. If one of the affected sites is the lung parenchyma, the case should be classified as having both pulmonary and disseminated tuberculosis. Miliary tuberculosis, *e.g.* is thus classified as pulmonary and disseminated.
Where *M. tuberculosis* complex has been isolated from blood, the disease site should be designated "disseminated".

Treatment outcomes

Cure: A patient is considered cured if he or she has completed a full course of anti-TB therapy and a) if the diagnosis was confirmed by culture, and conversion (culture negative) has been documented (at least on one occasion) during the continuation phase; or b) if the diagnosis was based on microscopy, there is documented evidence of two negative sputum smears during the continuation phase, one of which must be at the end of treatment. Applicable only for **pulmonary** TB.

Treatment completed: A patient who was notified as a definite case is defined as having completed treatment if the course of treatment prescribed was completed and if the patient was officially discharged by the attending physician, but in whom a) when the diagnosis was confirmed by culture, no bacteriological conversion has been documented, or b) when the diagnosis was based on microscopy, no smear result is available at the end of treatment.

Treatment failure: A patient, who fails to achieve bacteriological conversion within 5 months after the start of treatment or, after previous conversion, becomes sputum smear or culture positive again, and in whom the first-line treatment is replaced by second-line treatment, should be considered a failure case.

Death: A patient who died of any cause during the course of treatment is recorded under death.

Treatment interrupted: If the patient interrupts treatment for any reason, this is recorded as treatment interrupted. To be classified as such, interruption of treatment should be for >2 months, noncompletion of treatment within 9 months if placed on a 6 month regimen or within 12 months for an 8 or 9 month regimen, or if the drug intake was <80% of the prescribed dose. Prolonged interruption of treatment, caused by serious adverse effects to the drugs, is also recorded under this heading.

Transfer out: Some patients may continue treatment at another treatment centre during the course of treatment. Where it is known that the patient moved, but no additional information is available, this should be recorded as transfer out.

Immune Reconstitution Inflammatory Syndrome (IRIS)

For details, please see instructions for specific IRIS form

IRIS induced by antiretroviral therapy in case of adequately treated case of tuberculosis

1. The patient had a diagnosis of tuberculosis prior to cART initiation. This case has been (or is still) adequately treated, and
2. Symptoms consistent with an infectious/inflammatory condition appearing within three months of a new antiretroviral therapy (initiation/ reintroduction/ change of cART regimen), and
3. These symptoms cannot be explained by a newly acquired infection, nor by the expected clinical course of a previously recognized infectious agent, nor by side effects of therapy.

   The date of IRIS is greater than the date of TB diagnosis (NEW-date).

Other disease of interest

1. Symptoms consistent with an infectious/inflammatory condition appear within three months of a newly started antiretroviral therapy (initiation/ reintroduction/ change of cART regimen), and
2. Symptoms can be attributed to a new opportunistic disease and, according to the treating physician, can not be explained by a newly acquired infection but by unmasking of a subclinical opportunistic disease and can not be explained by side effects of therapy.

   The date of IRIS is equal to the date of TB diagnosis (NEW-date).

Copenhagen HIV Programme,
December 2011

Reference List

1. Rieder, H. L. *et al.* Surveillance of tuberculosis in Europe. Working Group of the World Health Organization (WHO) and the European Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) for uniform reporting on tuberculosis cases. *Eur Respir J* **9**, 1097-1104 (1996).

2. Veen, J. *et al.* Standardized tuberculosis treatment outcome monitoring in Europe. Recommendations of a Working Group of the World Health Organization (WHO) and the European Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) for uniform reporting by cohort analysis of treatment outcome in tuberculosis patients. *Eur Respir J* **12**, 505-510 (1998).