Frequently asked questions about the 4-drug fixed-dose combination tablet recommended by the World Health Organization for treating tuberculosis

Prepared by the Secretariat managing the Global Partnership to Stop TB with contributions from various stakeholders belonging to the Global Partnership

Geneva, September 2002
Abbreviations

- **DOTS**: Directly observed treatment, short course (internationally recommended TB control strategy)
- **FDC**: Fixed-dose combination
- **2-drug FDC**: Two-drug fixed-dose combination
- **4-drug FDC**: Four-drug fixed-dose combination
- **HIV**: Human immunodeficiency virus
- **IUATLD**: International Union Against Tuberculosis and Lung Disease
- **MRC**: Medical Research Council, National Tuberculosis Research Programme, Pretoria, South Africa
- **NTP**: National tuberculosis programme
- **NIPER**: National Institute of Pharmaceutical Education and Research, Punjab, India (NIPER)
- **WHO**: World Health Organization

Drugs

- **E** = ethambutol
- **H** = isoniazid
- **R** = rifampicin
- **S** = streptomycin
- **T** = thioacetazone
- **Z** = pyrazinamide
The Stop TB Partnership Secretariat would like to thank the NTP managers and other NTP staff, representatives of the pharmaceutical industry, tuberculosis stakeholders met on Global Drug Facility country visits, and other WHO partners, who contributed to this document.
The majority of tuberculosis patients worldwide are still treated with single drugs, or with 2-drug fixed-dose combinations (FDCs) (1). To improve tuberculosis treatment, 2- and 3-drug FDCs were recommended by the World Health Organization (WHO) as part of the DOTS strategy (2; Table 1). Recently, however, a 4-drug FDC containing 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide, and 275 mg ethambutol was added to the WHO Model List of Essential Drugs (3, 4), which made possible an intensive-phase treatment for tuberculosis based fully on an FDC. This document is intended to answer frequently asked questions about the recently introduced 4-drug FDC, but many of the issues are also relevant to the 2- and 3-drug FDCs.
WHO RECOMMENDATIONS

Yes. WHO recommends the 4-drug FDC to treat tuberculosis, provided that the constituent drugs are of proven quality and are used at WHO-recommended strengths. Since 1994, WHO and the International Union against Tuberculosis and Lung Disease (IUATLD) have recommended the use of FDCs (5, 6), and in 1999 a 4-drug FDC was included in the WHO Model List of Essential Drugs (3, 4), based on the recommendations of a WHO Advisory Committee on FDCs which met in August 1998.

The rationale for recommending the 4-drug FDC is that it simplifies both treatment and management of drug supply, and may prevent the emergence of drug resistance (2).

Simplifying treatment. The 4-drug FDC may increase compliance with treatment because most tuberculosis patients need to take only 3–4 tablets per day during the intensive phase of treatment (Table 2), instead of the 15–16 tablets per day that is commonly the case with single-drug formulations. Also, the chance of taking an incomplete combination of drugs is eliminated, since the four essential drugs are combined in one tablet. Studies have shown that prescriptions for tuberculosis treatment are complex and that prescription errors are common (7). Clearly, the 4-drug FDC makes it easier to calculate the required dosage compared with single-drug formulations (2).

Simplifying management of drug supply. Using a 4-drug FDC means that there are fewer formulations to order and distribute, which simplifies the management of drug supply. However, countries will still need to maintain

Does WHO officially recommend the 4-drug FDC?

What are the advantages of the 4-drug FDC for treating tuberculosis?
small stocks of single-drug formulations at referral centres to deal with cases of adverse reactions to combined formulations (2).  

Preventing drug resistance. Multidrug-resistant tuberculosis is emerging throughout the world (8, 9). The causes include erratic drug intake (particularly interruptions of treatment) and treatment with a single tuberculosis drug (10, 11). A 4-drug FDC simplifies treatment and virtually eliminates the risk associated with monotherapy, i.e. the development of drug-resistant strains of Mycobacterium tuberculosis (2).  

Table 1. Recommended FDCs for antituberculosis drugs.  

<table>
<thead>
<tr>
<th>Drug</th>
<th>Form</th>
<th>Drug strengths for daily use</th>
</tr>
</thead>
<tbody>
<tr>
<td>RHZE</td>
<td>Tablet</td>
<td>R (150 mg) + H (75 mg) + Z (400 mg) + E (275 mg)</td>
</tr>
<tr>
<td>RHZ</td>
<td>Tablet</td>
<td>R (150 mg) + H (75 mg) + Z (400 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R (60 mg) + H (30 mg) + Z (150 mg) – for paediatric use</td>
</tr>
<tr>
<td>RH</td>
<td>Tablet</td>
<td>R (300 mg) + H (150 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R (150 mg) + H (75 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R (60 mg) + H (30 mg) – for paediatric use</td>
</tr>
<tr>
<td>EH</td>
<td>Tablet</td>
<td>H (150 mg) + E (400 mg)</td>
</tr>
<tr>
<td>TH</td>
<td>Tablet</td>
<td>T (50 mg) + H (100 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T (150 mg) + H (300 mg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Forms</th>
<th>Drug strengths for use 3 times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>RHZE</td>
<td>Tablet</td>
<td>R (150 mg) + H (150 mg) + Z (500 mg)</td>
</tr>
<tr>
<td>RH</td>
<td>Tablet</td>
<td>R (150 mg) + H (150 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R (60 mg) + H (60 mg) – for paediatric use</td>
</tr>
</tbody>
</table>

*From the WHO Model List of Essential Drugs, 1999 (4).  
*Drug symbols: E = ethambutol; H = isoniazid; R = rifampicin; S = streptomycin; T = thiacetazone; Z = pyrazinamide.  
*Dispersible form preferred.
Table 2. Dosage schedule for FDCs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Body weight (kg)</th>
<th>Intensive phase (2 months)</th>
<th>Continuation phase (4 months)</th>
<th>Continuation phase (6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RHZE(^b)</td>
<td>RHZ</td>
<td>RHZ 3/7(^c)</td>
</tr>
<tr>
<td>Children</td>
<td>≤ 7</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>8–9</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>10–14</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>15–19</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Adults</td>
<td>30–37</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>38–54(^g)</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>55–70</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>≥ 71</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

\(^a\) The schedules represent the daily number of tablets to be taken that contain the corresponding combinations of drugs at WHO-recommended strengths.

\(^b\) For programmes that use EH in the continuation phase of treatment for new cases, several new national guidelines for treatment, propose that the 4-drug FDC could be used in the continuation phase for retreatment cases (WHO treatment Category II), even though this has not yet been properly evaluated or agreed upon.

\(^c\) "3/7" means the formulation is used three times a week.

\(^d\) In the continuation phase for adults, the formulation R (150 mg) + H (75 mg) should be used for daily treatment, and R (150 mg) + H (150 mg) for intermittent treatment.

\(^e\) Numbers of tablets based on the TH formulation of T (50 mg) + H (100 mg). Thioacetazone-containing FDCs are used for daily treatment. Thioacetazone should not be used in intermittent regimens.

\(^f\) Ethambutol-containing FDCs (EH) are best avoided in children because of the risk of dose-dependent optic neuritis. However, RHZE can be used in the intensive phase for paediatric patients who are smear-positive for tuberculosis or who have miliary tuberculosis.

\(^g\) The composition of the 4-drug FDC ensures adequate doses of the drugs even when 50 kg is chosen as the cut-off point for changing between 3 and 4 tablets per day.
The WHO-recommended 4-drug FDC consists of 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide and 275 mg ethambutol. This is suitable for daily regimens.

Yes, absolutely. There are no new regimens for programmes using the 4-drug FDC. The 4-drug FDC is simply a vehicle for delivering short-course chemotherapy in a more reliable fashion. The only difference is that the 4-drug FDC is used during the intensive treatment phase, instead of single-drug formulations, or 2- or 3-drug FDCs. The previously-recommended regimens still apply, and in the continuation phase a 2-drug FDC should be used (rifampicin-isoniazid, ethambutol-isoniazid or thioacetazone-isoniazid).

Any one of the three combinations is acceptable, but rifampicin-isoniazid is the most potent. The dosage schedules for various FDCs are shown in Table 2. Rifampicin-isoniazid should be used only in a setting of directly-observed treatment: since rifampicin is the strongest and most valuable of current tuberculosis drugs, the risk of rifampicin-resistant \textit{M. tuberculosis} strains developing because of poor compliance with medication must be avoided at all costs. In addition, it has been proposed that the WHO-recommended 4-drug FDC could be used in the continuation phase for retreatment cases.

No. Although many countries use intermittent treatment (i.e. drugs are administered three times a week) to reduce the workload of health personnel and to relieve patients of the burden of attending clinics every day, the WHO-recommended 4-drug FDC is suitable only for daily treatment and therefore cannot be used in intermittent treatment. It is
Studies have shown that the short-course treatment for tuberculosis is highly effective under conditions of proper case management. For example, when drug-resistant mycobacteria are rare, short-course chemotherapy cures more than 90% of tuberculosis cases. Consequently, short-course treatment all smear-positive pulmonary tuberculosis cases is the backbone of any modern tuberculosis control programme, as recommended by IUATLD and WHO (12, 13). One advantage of the 4-drug FDC is the greater reliability with which tuberculosis programmes can deliver short-course chemotherapy (1). Because of the long duration of tuberculosis treatment and the large number of tablets that have to be taken every day, patients often default – use of 4-drug FDCs helps to overcome this problems.

WHO supports the use of the 4-drug FDC and has included the constituent drugs in the Model List of Essential Drugs on the basis of the solid evidence that short-course chemotherapy is effective and the assumption that, as long as the constituents of 4-drug FDCs provide the same bioavailability as the individual constituent drugs, the 4-drug FDCs will be as efficacious as single-drug formulations (14). Currently, 4-drug FDCs with proven rifampicin bioavailability are available, and clinical trials to establish their efficacy before their use in tuberculosis control can be recommended are unnecessary.

What is the evidence to support the use of 4-drug FDCs?

Not known whether 4-drug FDCs will be recommended for intermittent treatment in the future.
Informal consultation on 4-drug fixed-dose combinations compliant with the WHO model list of essential drugs, Geneva, Switzerland, 15–17 August 2001 (unpublished).

Circumstantial evidence of the benefits of FDC-based treatment comes from the low rates of multidrug-resistant tuberculosis in countries where good-quality FDCs have been used for some time, such as Brazil (8) and South Africa (15). Clinical trials in Algeria (16) and Hong Kong Special Administrative Region of China (17, 18) found that 3-drug FDCs were as efficacious as single-drug formulations, while a study in Singapore showed a higher relapse rate (compared with single-drug formulations) after 5 years in patients receiving 3-drug FDCs (19, 20). However, it is difficult to draw conclusions from one study and it is uncertain whether the Singapore study had any relevance for the 4-drug FDCs, particularly since the composition of the 3-drug FDC used was different from that of currently-recommended FDCs. A clinical trial comparing the WHO-recommended 4-drug FDC with conventional formulations has been planned by the IUATLD clinical trials network.1

QUALITY ISSUES

Treatment of tuberculosis with poor-quality drugs, will not only result in treatment failures but can also lead to the development of drug resistance. This will have a deleterious effect on the health of the wider population. Ensuring the quality of tuberculosis drugs, including the FDCs (locally manufactured and/or imported) used in a national tuberculosis programme (NTP) is therefore of utmost importance in combating the disease.

WHO experts have developed a protocol for testing the bioavailability of rifampicin in 4-drug FDCs\(^2\) \((21)\), but it has not yet been published as an official WHO document. It is recommended that not only rifampicin, but also all the other constituent drugs be tested for their bioavailability; in the future the protocol should be updated to describe the testing of all four components. To produce the documentation necessary for registering 4-drug FDCs, all standard procedures for testing the quality of pharmaceutical products should be followed \((22)\).

Quality problems with rifampicin, both as a single drug and in combination with other drugs, can result in unsatisfactory bioavailability. There are indications that poor-quality pharmaceutical products are common,

---

particularly in countries with limited resources to support regulatory institutions (23, 24, 25, 26, 27, 28, 29), and it is reasonable to assume that quality problems occur with both FDCs and single-drug formulations. The WHO-recommended laboratory network is one mechanism for ensuring the quality and bioavailability of FDCs, including 4-drug FDCs, but less attention has been paid to single-drug formulations. It may therefore be safer to opt for 4-drug FDCs that have been quality-tested in the laboratory network and found to have satisfactory bioavailability than to buy single-drug formulations whose quality may be suspect.

WHO has established a laboratory network that tests the quality of FDCs on the market and, on request from the pharmaceutical industry, can carry out bioavailability/bioequivalence studies (23, 28, 30, 31, 32). There are two laboratories in the network at present – the Medical Research Council, National Tuberculosis Research Programme (MRC), Pretoria, South Africa, and the National Institute of Pharmaceutical Education and Research (NIPER), Punjab, India.

While the bioavailability of rifampicin in some FDCs was satisfactory, this was not true of others (33, 34, 35, 36, 37, 38, 39, 40, 41). The differences appeared to be related to deficiencies in the manufacturing process. Unfortunately, an apparently satisfactory in vitro dissolution test does not guarantee adequate rifampicin bioavailability. WHO and IUATLD have therefore recommended using only FDCs with proven bioavailability (5). However, there was no consensus on procedures for ensuring the quality of FDC products; for the time being, WHO, IUATLD, and collaborating experts suggested a protocol for testing the bioavailability of FDC components (22, 23), and a laboratory network for FDC quality control.
How can NTP managers be sure that they get 4-drug FDCs of good quality?

NTP managers must insist that the product they buy meets all quality requirements (24), and manufacturers/suppliers should provide all required documentation, including documentation of satisfactory bioavailability as follows: proof of the bioavailability of the constituent drugs, particularly rifampicin (6); the dissolution profile of the same batch used for the bioavailability/bioequivalence study on all components (rifampicin, isoniazid, pyrazinamide, and ethambutol); and, at each delivery of FDCs, dissolution data for shipped batches. During the contracting process, the NTP manager or procurement officer should include the quality criteria in the contract; fulfillment of quality requirements and proof thereof, will be furnished at the expense of the manufacturer/supplier. Bioavailability testing can be performed by the WHO laboratory network for quality control of FDCs. NTPs may also obtain 4-drug FDCs through the Global Drug Facility (GDF), which supplies 4-drug FDCs of WHO-recommended strengths and proven quality. Under no circumstances should NTP managers accept 4-drug FDCs that do not meet the required quality standards.

Adverse side-effects serious enough to warrant withdrawal from tuberculosis drugs occur in 3–6% of patients (43, 44, 45, 46, 47). In the few cases when 4-drug FDCs cause sufficiently serious adverse effects for treatment to be modified, patients should be referred to a hospital.
The cost per patient of 4-drug FDCs is less than US$ 10 for a full daily treatment through the GDF, even when the tablets are provided in blister packages. This price was calculated for patients of body weight 38–54 kg (the most common weight range for tuberculosis patients), who would need 3 tablets per day. The price is the same as, or less than, that of treatment regimens using other products. Furthermore, the use of regimens based on 4-drug FDCs in an NTP is likely to reduce other programme costs (including procurement costs) by simplifying the management of drug supplies.

Several countries in most continents have registered 4-drug FDCs and are using them in their TB programmes.

At least six manufacturers produce high-quality 4-drug FDCs at WHO-recommended strengths. The GDF will make available on the web a list of products and of the manufacturers of all 4-drug FDCs of WHO-recommended strength and satisfactory bioavailability. The GDF team
Leading tuberculosis experts collaborated with WHO and agreed upon the composition of the WHO-recommended 4-drug FDC\(^3\) (1–3). The component drugs of the WHO 4-drug FDC are present in the recommended proportions per kilogram of body weight. WHO recommends that this 4-drug FDC alone be manufactured and used, since this will simplify and standardize treatment guidelines, and simplify the tendering and procurement processes. It may also lead to a price reduction, since manufacturers will produce tablets of only one strength. Currently, WHO does not recommend intermittent treatment with a 4-drug FDC.

All FDCs recommended by WHO are shown in Table 1, and dosage schedules are given in Table 2.

Why does WHO recommend only one 4-drug FDC?

What other FDCs are recommended by WHO, apart from the 4-drug FDC?

---

Yes. Although the most important issue is the bioavailability of the rifampicin component, the bioavailability of all constituent drugs must be tested to register the 4-drug FDC. Although proof that the constituent drugs of a 4-drug FDC have satisfactory bioavailability is an important part of the documentation for registration, it is not the only one. Registration of 4-drug FDCs should follow the standard registration procedures for any pharmaceutical product. The necessary documents are outlined in a WHO document (24) and should include the following information:

- Details of the product.
- Documentation of the product regulatory situation in other countries.
- Details of the properties of the active pharmaceutical ingredient(s).
- Details of the manufacturing sites of the active pharmaceutical ingredient(s).
- Details of the route(s) of synthesis of the active pharmaceutical ingredient(s).
- Specifications for the active pharmaceutical ingredient(s).
- Stability testing of the active pharmaceutical ingredient(s).
- Formulation details for the product.
- Site of manufacture of the finished product.
- Manufacturing procedure for the finished product.
- Specifications for excipients.
- Specifications for the finished product.
- Container/closure system(s) and other packaging details.
- Stability testing of the finished product.
- Container labelling information.
- Summary of pharmacology, toxicology, and efficacy of the product.
- Data on interchangeability of the product for quality, bioavailability/bioequivalence, therapeutic properties, and comparative *in vitro* dissolution tests with existing brands on the market, preferably with the reference product in the country.
- Patient information and package inserts.
- Justification for any differences in the product in the country or countries issuing the submitted WHO-type certificate(s).

For details, the source publication (24) should be consulted; Annex 6 is particularly relevant. The document is also available on the web (http://www.who.int/medicines/library/qsm/manual-on-marketing/multisource-contents.html).
GLOBAL DRUG FACILITY

INTRODUCING 4-DRUG FDCs IN NATIONAL TUBERCULOSIS PROGRAMMES

Are official guidelines on 4-drug FDC-based regimens provided by WHO, IUATLD, or Stop TB partners?

Guidelines for dosage schedules for the WHO-recommended 4-drug FDC have been published in the *Bulletin of the World Health Organization* (1) and in reports from WHO meetings on FDCs.4 WHO plans to publish guidelines for NTPs for the implementation and use of 4-drug FDCs, and the next version of the WHO treatment guidelines for national tuberculosis programmes (13) will be updated to include advice on treatment regimens based on 4-drug FDCs.

What does the national tuberculosis programme (NTP) need to do to prepare for the switch to 4-drug FDCs?

The change to a 4-drug FDC-based treatment has implications for the staff of the NTP, from the programme manager to the district coordinators and treatment assistants, and careful planning is necessary for the change to be successful. The most important issue would probably be to provide a coordinated training programme for the NTP staff. The NTP manual and all relevant NTP forms, such as treatment cards and drug-ordering forms, as well as training materials and modules need to be updated to reflect the

---

new treatment. The updated NTP manual, treatment guidelines, and forms then need to be distributed at all levels of the NTP. Finally, NTP staff at all levels need to be trained in the new treatment regimens and in using new forms and materials. WHO plans to publish guidelines to help NTP managers to implement 4-drug FDC-based treatment regimens.

**TREATMENT REGIMENS**

The dosage schedules for WHO-recommended FDCs are shown in Table 2. The compositions of WHO-recommended FDCs are designed to comply with the recommendations of WHO and IUATLD for dose (mg/kg body weight) for each of the essential tuberculosis drugs (Table 3).

### Table 3. Recommended doses of essential tuberculosis drugs

<table>
<thead>
<tr>
<th>Tuberculosis drug</th>
<th>Mode of action</th>
<th>Recommended dose (and range) (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>daily 3x per week</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Bactericidal</td>
<td>5 (4–6) 10 (8–12)</td>
</tr>
<tr>
<td><strong>Rifampicin</strong></td>
<td>Bactericidal</td>
<td>10 (8–12) 10 (8–12)</td>
</tr>
<tr>
<td><strong>Pyrazinamide</strong></td>
<td>Bactericidal</td>
<td>25 (20–30) 35 (30–40)</td>
</tr>
<tr>
<td><strong>Ethambutol</strong></td>
<td>Bacteriostatic</td>
<td>15 (15–20) 30 (25–35)</td>
</tr>
<tr>
<td><strong>Streptomycin</strong></td>
<td>Bactericidal</td>
<td>15 (12–18) 15 (12–18)</td>
</tr>
</tbody>
</table>

What is the dosage schedule for the WHO-recommended 4-drug FDC?
If our NTP starts using 4-drug FDCs, what should we do with Category III patients?

It is important for NTPs to differentiate between sputum smear-positive and sputum smear-negative patients, since the former are more contagious. In most programmes, the 4-drug FDC would be reserved for smear-positive patients (Category I); a separate regimen, probably based on a 3-drug FDC, would be used for smear-negative patients (Category III). However, using the 4-drug FDCs for both smear-positive and smear-negative patients (Categories I and III) is also an option and would reduce the number of formulations that need to be procured. Category II patients (retreatment cases) can be given 4-drug FDCs for the first 3 months of treatment, in addition to streptomycin injections for the first 2 months. Furthermore, as mentioned above, it has been proposed that the 4-drug FDC could be used in the continuation phase for retreatment cases (Category II) in programmes that use ethambutol–isoniazid in the continuation phase of treatment for new cases. However, it is emphasized that this is a proposal, which has yet to be properly evaluated or agreed.

What should we do with existing stocks of single-drug formulations?

This would depend on the size of the stock and the expiry dates. Most national tuberculosis programmes have limited resources for buying drugs, and if the NTP has a large stock, the bulk of these drugs should be used before switching to 4-drug FDCs. However, the switching could be made gradually by, for example, introducing 4-drug FDCs in pilot project areas while continuing to use single-drug tablets in other areas until the stock is
finished. If the NTP has a limited stock of single-drug formulations, the drugs could be directed to the few centralized referral institutions, where they will be needed for patients suffering severe side-effects, even after 4-drug FDCs have been routinely implemented in treatment.

Adverse side-effects serious enough to warrant withdrawal of treatment occur in 3–6% of patients (34–38), and the rates of adverse reactions to FDCs are not expected to be significantly different (16, 17). In areas with high rates of HIV infection, there may also be higher rates of adverse reactions. Some patients suffering adverse reactions could still be treated with 2-drug FDCs, depending on which drug provoked the reaction. Until more experience is gathered, it is suggested that NTPs order approximately 5% of their drug supplies in the form of single-drug formulations and 95% in the form of FDCs.

In case of unforeseen problems with drug supplies, a reserve stock should be kept at all levels of the system. The reserve stock for the whole NTP should be equivalent to the running requirement for one year, which can be calculated on the basis of the number of cases detected by the programme. The reserve stocks can be distributed as follows: a 6-month supply at central level; a 3-month supply at intermediate level(s); and a 3-month supply at tuberculosis management levels.
REFERENCES


For more information on the Global Drug Facility (GDF), please contact:
Stop TB Partnership Secretariat – 1211 Geneva 27 – Switzerland
Tel. +(41) 791 2385 – Fax +(41) 22 791 4886
http://www.stoptb.org/GDF

The Stop TB Partnership Secretariat is hosted by the World Health Organization