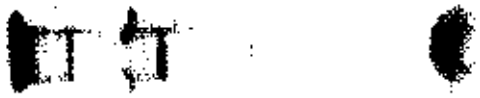
FINAL REPORT

THE INTRODUCTION OF THE *M.LEPRAE* LATERAL FLOW TEST FOR LEPROSY CONTROL:

A PILOT PROJECT



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1. Introduction

One of the core strategies for leprosy control is early diagnosis and effective treatment in order to prevent deformities and interrupt transmission. The diagnosis of leprosy is based on clinical, bacteriological and histopathological findings. However, facilities for bacteriological examination of slit-skin smears and histopathological examination of skin or nerve biopsy-specimens are often not available.

In an attempt to overcome the problem of the absence of diagnostic facilities WHO has adopted a simplified method of classification based on counting the number of lesions. Leprosy patients with less than 6 lesions will receive a PB treatment regimen and patients with 6 or more lesions will be treated as MB.

Several studies have shown that the presence of antibodies to the *M. leprae*-specific phenolic glycolipid-I (PGL-I) correlates with the bacterial load of a leprosy patient: 15-40% of PB patients are seropositive, compared to 80-100% of the MB patients. Detection of these antibodies may thus be a useful tool for confirming the diagnosis of MB disease.

Furthermore , it has long been known that contacts of leprosy patients run an increased risk of developing leprosy. It was found that seropositive contacts of leprosy patients have a higher risk to develop clinical leprosy (either PB or MB) compared to seronegative leprosy contacts. These findings indicate that serology can be used to identify people with an increased risk of developing clinical leprosy.

Until eight years ago there were no serological techniques available that could be used in the field: the most widely used technique, ELISA, requires expensive equipment, trained laboratory personnel and a cold chain and it takes about 24 hours before results are available. At the end of the 1990's KIT Biomedical Research had developed a simple and robust dipstick test that gave results in 3 hours in the absence of specialized equipment and a cold chain. As part of the current project this test was further improved and modified into a lateral flow test format. The resulting ML Flow test gives test results in 10 minutes and could in principle be used as part of routine leprosy control activities, but until the start of the implementation study described here the test had not been used for this purpose.

2. Objectives

With the introduction of the ML Flow test we aim at the following two applications:

1. As an additional tool for the correct classification of new leprosy patients.
2. As a tool to identify those contacts of leprosy patients that have an increased risk of developing leprosy in future.

The objective of this pilot introduction is to study the acceptability and feasibility of the use of the ML flow test in routine leprosy control.

3. Approach

During an initial workshop the purpose of the project and the intended approach was presented to and discussed with representatives from the three participating countries (Brazil, Nepal and Nigeria).

In the first year KIT Biomedical Research developed the ML Flow test and evaluated its performance on standard sets of serum and blood samples, also comparing the results with the results obtained with ELISA. In the meantime databases and forms for data collection

and evaluation were developed and health centres and -workers were selected in the participating endemic countries.

During 3-day workshops in the endemic countries the health workers were trained in the use of the ML Flow test, the interpretation of the results, the information that should be provided to patients and contacts and the data collection. After this training, the ML Flow tests were used for 18 months as part of the routine leprosy control activities, including both patients and controls after obtaining informed consent. Data were collected at the local level and sent at regular intervals to a central national data collection facility.

For assessing the feasibility and acceptability of the test, an anthropological study was formulated and discussed with three local social scientists during visits to the countries. Also a workshop was held in Amsterdam to facilitate the progress of these country studies. The anthropological study included focus group discussions, semi-structured and in-depth interviews with representative samples of health workers (both interviews and focus group discussions), patients, contacts (interviews) and leprosy experts.

During a final workshop held in Amsterdam in March 2005 the country reports (2 per country: one for the implementation and one for the anthropological study) were discussed and final conclusions were drawn. This final report is based on the country reports and the conclusions reached during this workshop.

The country reports are added as annexes to this final report.

4. Outcomes per country

Section 1 gives a short overview of the implementation results for patients and contacts (see implementation reports for further details), section 2 shows the main conclusions from the anthropological study (see feasibility and acceptability reports for more details) and section 3 gives the opinion on how one would like to proceed with the implementation of the ML Flow in the future.

4.1. Brazil

Between October 2002 and March 2004 1071 patients and 2840 contacts were tested with the ML Flow test in 13 health facilities in Minas Gerais State. In addition, 24 health workers, 171 patients, 210 contacts and 5 key informants participated in the anthropological study.

4.1.1. Implementation

Patients

Of the 1071 patients 544 (50.8%) were found positive with the ML Flow test. The ML Flow test results led to the reclassification of nearly a quarter of all leprosy patients.

Of the 498 patients who were initially classified as PB based on the WHO criteria, 114 were reclassified as MB. Three of these had a positive BI, the other 111 had a positive ML Flow result (97) or had both tests positive (14). This means that using the BI only 17/498 (3.4%) of the PB patients would be reclassified as MB, whereas with the ML Flow test 111/498 (22.3%) could be reclassified as MB, thus preventing under treatment.

Brazil is the only country in this study where MB patients were reclassified as PB if both the BI and the ML Flow results were negative. One hundred-thirty of the 573 patients (22.7%) that were initially classified as MB could be reclassified as PB, thus preventing over

treatment. If only the ML Flow would have been in use another 10 MB patients (1.7%) with a positive BI would have been (improperly) reclassified.

Contacts

Of the nearly 3000 contacts that were tested, 20.5% were found to be seropositive. Health education -and BCG vaccination, as is standard in Brazil for contacts of leprosy patients- were given to all contacts and seropositive contacts will be followed up for 4 years.

Impact on leprosy control activities

The ML Flow test "gave leprosy a face" and increased the status of leprosy in the health programmes.

The ML Flow test increased the confidence of the health workers that they had properly classified the patients. This led to less referrals, allowing the reference centre to concentrate on more difficult cases and on providing leprosy training for other teams from basic health programs. It was also felt that the ML Flow test helped in the organization of the teams in the health centres.

The availability of a tool for contact testing was felt as a very positive development. The implementation of the ML Flow test led to an increase in the contact examination, which assisted the early detection of new leprosy cases thus helping deformity prevention. It gave the opportunity to give health education to the contacts and it was felt that this would lower the stigma.

4.1.2. Acceptability and feasibility

Health workers
Health workers found the test easy to execute, read and interpret and it made them more confident in classifying patients.

Patients
All patients agreed to be tested. Patients understood the relationship between the test result and the treatment they received, leading to a demystification of the disease. They discussed the test results with their contacts and stimulated them to go for contact examination and testing.

Contacts
Nearly all contacts agreed to be tested. From the health education given to them, contacts understood that leprosy is a curable disease and that they should return in to the health facility in case they have any symptoms. No need for an intervention other then the one currently given was expressed.

Key informants
All key experts were positive about the ML Flow test, recognizing its merit for classification and thus proper treatment and mentioned its contribution to increasing the confidence of health workers, increasing the status of the Leprosy Control Program and demystification of the disease.

4.1.3. Future

The Leprosy Control State Coordinator is pressured by health workers from Minas Gerais state to implement the ML Flow test in the whole state. They want to use the test for both patient classification and for identification of high-risk contacts. They would like to implement the test gradually at all levels, but especially in the basic health programme, including family health programmes. If tests and support would be provided they would follow the pattern of this project, including (decentralized) training and supervision. A simplified guide should be made available and an informed consent form would be no longer needed. The analysis software of the current project could be used to perform quality control on patient classification.

The use of the ML Flow test should initially be supported by an NGO to sustain the use of the ML Flow test until the government policy makers have made a decision on the continued use of the ML Flow test. NGO support could be used to advocate the use of the ML Flow test with the Brazilian Government.

4.2. Nepal

Between April 2003 and December 2004 1375 patients and 1857 contacts were tested with the ML Flow test in 7 health facilities in Eastern Region. In addition, 18 health workers, 121 patients, 109 contacts and 5 key informants participated in the anthropological study.

4.2.1. Implementation

Patients

Of the 1375 patients 428 (31.1%) were found positive with the ML Flow test. Most analyses focused on the results obtained in the reference centre in Biratnagar, as they handled the majority of the patients (1066). It was the only facility where microscopy was available and ML Flow and BI results could thus be compared. The ML Flow test results led to the reclassification of 12% of all PB patients in Biratnagar.

Of the 602 patients who were initially classified as PB based on the WHO criteria, 78 were reclassified as MB. Of these 72 had a positive ML Flow result and 6 had both tests positive. This means that using the BI only 6/602 (1.0%) of the PB patients would be reclassified as MB, whereas with the ML Flow test 78/498 (12.6%) were reclassified as MB, thus preventing under treatment.

In Nepal MB patients were not reclassified as PB, even when both the BI and the ML Flow results were negative. If reclassification would have been possible, 189 of the 464 patients (40.7%) that were initially classified as MB could be reclassified as PB, thus preventing over treatment. If only the ML Flow would have been in use another 13 MB patients (2.8%) with a positive BI would have been (improperly) reclassified.

The high percentage of MB patients with a negative BI and ML Flow test in combination with the relatively low percentage of PB patients that were reclassified to MB is an indication that there may be extensive over-classification in Biratnagar. This is an example of how information generated by the data analysis can be used as a management information tool and as an indicator of quality of care.

Contacts

Of the nearly 1900 contacts that were tested, 9.7% were found to be seropositive. Health education was given to all contacts and seropositive contacts will be followed up for 4 years.

Impact on leprosy control activities

The ML Flow test increased the workload at the peripheral levels, but also the confidence in the classification. It was, like in Brazil, felt that the ML Flow test "gave leprosy a face" and increased the status of the health workers. The ML Flow test provided new knowledge and an independence from laboratory results, which were both seen as positive developments.

Contact tracing increased as part of the project, but remained lower than expected, because most patients only wanted to discuss the fact that they had leprosy with very close family members (like their spouses). Additional strategies were used to attract contacts, namely health volunteers and home visits. It was felt that information that there is a test that can identify high-risk contacts should be more widely disseminated to the general public and that the availability of an intervention (such as chemoprophylactic treatment) would also enhance the number of contacts that would be come for testing.

4.2.2. Acceptability and feasibility

Health workers
Health workers found the test easy to execute, read and interpret, but had some difficulties explaining "difficult results" (see 5.1). The forms and manual need to be simplified and there is a need for refresher training. Some health workers complained about the additional work and it was indicated to the anthropologist that health workers expect allowances for home visits, as this is a time-consuming activity.

Patients
Patients accepted being tested.

Contacts
Those contacts that came accepted to be tested. Seropositive contacts would like to have some kind of "medicine", meaning a (chemo)prophylactic intervention in addition to health education and follow-up. The main challenge is to find ways to convince the contacts to come for testing and to convince the patients to discuss their leprosy with their contacts and ask them to report to the health centre for testing.

Key informants
Most key experts found the ML Flow test impressive, feasible and acceptable and helpful for tracing contacts. At the beginning one expert was not quite sure of the capability of the health workers at the (Sub)Health Post level to carry out the test (this opinion was contradicted by the results obtained during this project).

4.2.3. Future

It was felt that it would be possible to use the ML Flow test in the future. However, this would require sufficient political commitment and permission from the government, and provision of the test free of charge, similar to MDT. The test could be used for classification of patients, screening of contacts and –at the peripheral level- could replace microscopy.

For political commitment/government permission it would be essential to convince the people at policy making level the value of the test and the feasibility to have the ML Flow test

performed by health workers. For this, a local workshop to disseminate the results from the study will be organized.

The test could be gradually introduced, starting from the referral level and expanding first into higher endemic areas. Local senior staff can provide training to new users, but training of trainers like the training sessions used in this project would be helpful. Training could also be included as one additional day in the general leprosy-training module. Training of at least two staff members of each facility would better ensure the continued use of the ML Flow test.

Supervision, refresher training and cross checking (and other quality control aspects) can be provided by the referral centre.

4.3. Nigeria

Between November 2002 and April 2004 186 patients and 529 contacts were tested with the ML Flow test in 28 health facilities in Jigawa State. In addition, 34 health workers, 39 patients, 118 contacts and 5 key informants participated in the anthropological study.

4.3.1. Implementation

Patients

Of the 186 patients 117 (62.9%) were found positive with the ML Flow test. Microscopy to determine the BI was not done in the leprosy control programme in Jigawa State. During the data analysis we found out that health workers in Nigeria defined MB leprosy as "5 or more lesions" instead of the WHO definition "6 or more lesions".

The Nigerian health workers initially classified only 8 patients as PB; all of these patients were ML Flow negative, meaning no reclassification. If the WHO definition had been used 43 patients would initially have been classified as PB. Of these 24 (56%) had a positive ML Flow result and could be reclassified as MB, thus preventing under treatment.

In Nigeria MB patients were not reclassified as PB if the ML Flow result was negative. If reclassification would have been possible, about a third of the patients that were initially classified as MB (regardless of whether the Nigerian or WHO definition was used) could be reclassified as PB, thus preventing over treatment.

The high percentage of seropositivity among the newly diagnosed patients is an indication that there is a diagnostic delay in the study area. This is another example of how information generated by the data analysis can be used as a performance indicator and management information tool.

Contacts

Of the 540 contacts that were tested, 22.9% were found to be seropositive. Seropositive contacts received a single dose of ROM (rifampicin-ofloxacin-minocycline). The high percentage of seropositivity among contacts (the highest of the three study areas) indicates that there is active transmission.

Impact on leprosy control activities

During the project, the ML Flow test had no impact on the classification of patients: the 8 patients that were classified as PB were all seronegative. If the definition of MB leprosy would be adjusted, the use of the ML Flow test would lead to some reclassification of PB

patients to MB. However, the impact of the ML Flow test on classification could only be maximized if it would also be used to reclassify MB patients as PB.

The ML Flow test increased the confidence of the health workers in the classification, and gave a new impulse to the leprosy control activities, especially the contact tracing. The implementation of test and the subsequent data analysis also contributed to a better insight into the quality of the Leprosy Control Programme in Jigawa State.

4.3.2. Acceptability and feasibility

Health workers
Almost all health workers thought the test was feasible and more than half of them felt that carrying out the test during the service routine was easy. The training they had received was perceived as very good, but revised, locally adapted training modules should be developed. The health workers indicated that they needed motorcycles and/or petrol in order to perform the contact tracing and testing.

Patients
All patients accepted to be tested, but some thought that the test led to treatment, and had apparently not understood that the test result determined the type of treatment they would receive. They understood the test, but some indicated that they needed more explanations about the test.

Contacts
All contacts interviewed accepted to be tested; the provision of ROM to seropositive contacts may have influenced this acceptability. More than half had a clear understanding of the test, but others definitely needed more information and clarification. A sizeable number of contacts felt that the test gave them the opportunity to check if they can fall ill.

Key informants
All key experts were positive about the ML Flow test, mentioning that it was useful for leprosy control, feasible to be implemented and that the training for the health workers was well conducted.

4.3.3. Future

Despite the fact that the ML Flow test currently makes no sizeable contribution to the classification of leprosy patients in Nigeria (see 4.3.1.) it was still felt that the test could make a contribution in contact tracing and in classification if the WHO definition of MB would be followed. It could be used at all service levels where leprosy diagnosis and treatment takes place, except in those services where they directly refer suspected leprosy cases.

The country study supervisor from Jigawa State held the opinion that extensive training of staff is needed with revised modules and training of trainers. ML Flow tests should be widely available for free, subsidized by NLR and/or state government. NLR vehicles could be used for contact examination and supervision. A strategy for quality control needs to be designed and put in place.

In the opinion of the Dutch experts it is mandatory to first enhance the basic leprosy control of the Jigawa control programme, since this study showed that there are some very basic problems. After this, the next step (as suggested above by the country study supervisor) can be made.

5. Similarities and differences

During the final workshop results from the three countries were summarized and compared. This was particularly facilitated by identifying and discussing the similarities and differences between the three study settings (Brazil, Nepal and Nigeria). The main similarities and differences are listed below.

5.1. Similarities

- In all three settings health workers, patients and contacts readily accepted the ML Flow test and the implementation of the test was feasible.
- Collection of the small amount of blood required was painless and no problem
- Test execution, reading and interpretation was found to be easy, except for the explanation of "difficult results", such as:
    a. Positive results for contacts
    b. Positive result for a contact from a seronegative patients
    c. Negative result for patients classified as MB according to the WHO rules.
    d. Positive BI and negative ML Flow
    e. Negative BI and positive ML Flow

  These points will need further attention in future training and in manuals.
- Seropositive PB patients were reclassified as MB because there was confidence in the test results and it was perceived as very important to prevent under treatment. Patients liked to be tested because it made them feel more comfortable with the diagnosis and classification.
- The use of the ML Flow test boosted the contact tracing, but this depends also on the enthusiasm of the health worker.
- The test "gave leprosy a face" and made it a more "normal" disease, leading to demystification of the disease.
- The following needs were identified:
    a. Need for counselling, especially of seropositive contacts, because the emotional impact.
    b. Need for a simplified manual and/or a 1-page leaflet for referral during routine work.
    c. Need for refresher/ongoing training and supervision.
    d. Need for quality control.
- The test increased the status of the health system and (in combination with political commitment) may motivate health workers.
- The information generated from the data analysis could be used as management information tool, quality of care measurement and/or performance indicator.

5.2. Differences

- Context, partners and organization of work differed between countries and influenced the use of the ML Flow test. This was actually exactly what we wanted to study and thus the reason for choosing study areas in three different countries.
- Only Brazil was prepared to reclassify seronegative and BI negative MB patients as PB. This may have been due to the fact that the BI result was available for all patients in Brazil and that all patients are seen by a doctor, who also uses his/her clinical judgment to decide whether reclassification is appropriate. In Nepal and Nigeria the government was not (yet) willing to change the classification.
- The opinions of the key informants/experts differed between countries. The more critical opinion of one of the key experts in Nepal was probably also due to the fact that this person was not present at the initial project workshop. It emphasizes the need to involve

people holding key positions from the beginning in the implementation of a new tool like the ML Flow test.

- The information provided to and understanding by the patients and contacts varied between countries, probably due to the educational levels of both health workers and patients/contacts, the social stigma involved, the quality of the information provided and the time available for explanation.
- The increase in contact tracing was lower in Nepal than in Nigeria and Brazil, probably due to the social stigma involved and cultural differences: in Nepal people who are not ill feel that there is no need to be checked, whereas Brazilian people like to be checked. Also, due to differences in stigma, family structure, gender issues etc. people in Nepal felt less free to discuss their disease with their family and other contacts, leading to less contacts coming for examination. This lowers the impact of the ML Flow test.
- The availability of a (chemo)prophylactic intervention would help strengthen contact tracing in Nepal, where seropositive contacts wanted a "medicine" to prevent them from getting leprosy. In Brazil this need was not felt.
- In Brazil and Nigeria the ML Flow test increased the motivation and the status of the health workers, whereas this was less the case in Nepal. This may be due to the fact that almost all health workers have a private practice on the side: more activities means less time to spend on their private practice.
- Sustainability of the implementation may vary between countries due to differences in available funds, logistics, political commitment and permission. All of these factors need to be in place for a successful and sustainable implementation.
- The impact of ML Flow testing on classification and treatment differed:
    a. In Nepal it reduced under treatment.
    b. In Nigeria it had more or less no impact, but it would make a difference if the WHO criteria would be followed.
    c. In Brazil the exchange between PB and MB resulted in a better classification and more appropriate treatment.

6. Outcomes SWOT analysis

During the final workshop a SWOT analysis for the ML Flow test was performed and major elements within each category were prioritised. The analysis was based on the results of the study and the experiences of the workshop-participants when conducting the study. The SWOT analysis was particularly relevant because the necessary condition that the test was feasible and acceptable was met by the study.

6.1. Strengths

1. The ML Flow test can be used for the proper classification of leprosy patients. In Brazil this lead to re-classification of both PB patients into MB and MB patients into PB, in Nepal and Nigeria the test was only used for reclassification of PB patients into MB and thus for the prevention of under treatment.
2. It assists in early contact tracing and the identification of high-risk contacts.
3. The availability of a touchable (ML Flow) test helped in demystifying leprosy: it provided people with an opportunity to discuss leprosy, it gives leprosy a face and it makes leprosy a more "normal", mainstream disease.
4. The test is simple, robust, easy to perform and practical for the field and there is no need for a laboratory technician like for microscopy.
5. It enhances the motivation of the individual health worker and may give increased status to the control program.
6. Additional information can be used as a management information tool to measure quality of care.

Other points raised were:

- Increased confidence in classification at lower levels of the health care system diminishes referral to and thus workload at the referral centre. This means less time and costs for the patients and the opportunity for the referral centre to concentrate on more complicated cases.
- Training leads to capacity building.
- Better coverage.

6.2. Weaknesses

1. As serology cannot be used for diagnosis (the majority of the PB patients are seronegative), the ML Flow test has a limited applicability, namely only for the proper classification of leprosy patients and for the identification of high-risk contacts
2. Serology is (currently) not well accepted for reclassification of MB patients to PB, and in some situations, like the Nigerian situation in our study where extremely high percentages of MB leprosy were found, reclassification from PB to MB may have no profound effects on the control program.
3. The cost of the test (currently about 2 euro/test), the needs for investments (training, counselling and an intervention for seropositive contacts) and the incentives that are in some settings expected by the health workers are all potential financial constraints.
4. It may be difficult and time-consuming to trace contacts and if there is no intervention (such as chemoprophylaxis) available for seropositive contacts this may limit the value of the ML Flow test for contacts.

Other points raised were:

- Additional administration and the current, very extensive project manual, but these are part of the project and not weaknesses of the ML Flow test as such.
- The ML Flow test misses some MB patients.
- In some instances it was felt that the workload increased, but complaints diminished over time. Also, other groups claimed that the workload diminished due to proper classification at a lower level in the health system.

6.3. Opportunities

1. Clinically, the ML Flow can be used in those facilities where no microscopy services are available. It may even replace BI determination, as it seems to be more sensitive in detecting MB leprosy.
   Anthropologically, the ML Flow test for the first time "gives leprosy a face" with visible results, making it easier to discuss leprosy. This makes working on leprosy more attractive to health workers.
2. The additional information gathered can also be used as a management tool for the program manager
3. When leprosy control is integrated into the general health services the ML Flow provides an easy tool for inexperienced health workers to help classify leprosy.
4. Early detection of high-risk contacts in combination with prophylactic treatment may help to bring down transmission.
5. The ML Flow test may provide a tangible tool for advocacy towards leprosy decision makers
6. Health workers can use the format of the test and the training for similar tests aimed at other diseases.

6.4. Threats

1. If WHO decides to implement uniform MDT (6 months treatment for all patients), classification is no longer necessary and ML Flow testing for patients becomes superfluous. However, the ML Flow test could be used to identify the (limited) group of patients with high bacterial loads that will need more than 6 months treatment.
2. The ML Flow test is NOT a diagnostic tool, but can be used for classification and contact tracing as described above. Improper use of the ML Flow test as a diagnostic tool may lead to a bad reputation if wider dissemination is not guided properly.
3. The implementation of the ML Flow test depends on political commitment and on the commitment of the persons involved at the implementation, management and decision-making levels.
4. The diminishing government commitment to leprosy and the increased difficulties to raise funding for leprosy control may hamper the implementation of the ML Flow test and the sustainability of its use.

Other points raised were:

- Reclassification decision depends on national policy (see Weaknesses point 2)
- Weakness of certain leprosy control programs
- Availability requires good planning at the level of the individual health care facilities
- Too high expectations of what the test may achieve
- This project was carried out in a field research setting. Implementation on a wider scale may lead to unforeseen problems.

7. Conclusions and recommendations for future use

The main conclusion from the final workshop is that the implementation of the ML Flow test is acceptable and feasible from the perspective of health workers, patients and contacts and the key informants. The implementation had an impact on classification in Brazil and Nepal and led to an increase in contact tracing.

The first step needs to be the dissemination of the results of this project to ILEP, WHO, policy makers, control officers and leprosy experts and scientists all over the world and to advocate the use of the ML Flow test for classification of patients and testing of contacts.

A cost-effectiveness study, preferably using different scenarios, would shed light on the cost-benefit aspects of the use of the ML Flow test. Different scenarios could include one or more of the following elements for analysis:

1. Use for reclassification PB into MB
2. Use of reclassification MB into PB
3. Contact tracing with health education for all contacts
4. Contact tracing with follow-up for seropositive contacts
5. Contact tracing with chemoprophylaxis for seropositive contacts
6. Use at different levels of the health care system

From the discussions it became clear that sustainability would depend on commitment by a funding agency as well as political commitment. If NLR (or another funding agency) decides to proceed with the ML Flow test, the following steps need to be taken into account for implementation. It should be noted that involvement of experts and policy makers should be ensured from the beginning.

1. Determine for which application(s) the ML Flow test is going to be used. This may differ per country.

   a. Reclassification of PB patients to MB
   b. Reclassification of MB patients to PB
   c. Identification of high-risk persons through contact testing. If this latter application is used, one also needs to determine which intervention is going to be used for seropositive contacts (health education, follow-up, prophylactic treatment)
2. Determine whether the expected impact would merit the introduction of the ML Flow test.
3. Set up the logistic system for the provision, importation and dissemination of the tests. An interesting suggestion was made that this could be done in parallel to the MDT provision system.
4. Set up a system of counselling, especially for seropositive contacts.
5. Discuss the needs for appropriate facilities and/or incentives, especially for contact tracing.
6. Preparation of a simplified manual, adapted to local needs.
7. Decide which data need to be collected and analysed and adapt the current forms and databases accordingly. We showed in the project that the collection and analysis of additional data may provide valuable information for program managers, but this has to be balanced against the extra burden for the health workers.
8. Training (of trainers). This can be done in regional and/or national workshop; the local trainers can then train any new users in their country or state.
9. Provide information for the general public, to ensure that the availability and merits of the test are widely known
10. After training of the users: introduce a system of quality control, supervision (and if needed refresher courses) to ensure the continued quality of test performance, reading and interpretation

It seems to be advisable to introduce the test in a "stone-in-the-pond" like way, starting at the reference/referral level and expanding from there to the lower levels of the health care system, first into higher endemic areas and then into lower endemic areas. Training in the use of the ML Flow test could also be included in the curriculum of the leprosy training received by general health workers.

At the moment two of the three countries used the ML Flow test only for reclassification of PB patients to MB to prevent under treatment. If countries/programs would be prepared to use the ML Flow test also for reclassification of MB patients to PB, this would maximize the impact of the ML Flow test.
Follow-up of all patients of the Brazilian part of the study may shed light on the question whether the risk of relapse did not increase in MB patients reclassified as PB compared to MB patients who remained MB. If the risk of relapse did not increase, this would be a good argument to use the ML Flow test also for reclassification of MB to PB.

8. Acknowledgements

An implementation study like this requires the input and dedication from a large number of people, without whom it would have been impossible to carry out this project:

This project was funded by the Netherlands Leprosy Relief and we gratefully acknowledge their active input, especially of Mr. Jan Willem Dogger. In Amsterdam the technicians Jannet van Leeuwen en George Gussenhoven were involved in the development and quality control of the ML Flow test and in the three endemic countries the work would not have been possible without the active input and enthusiasm of the health workers, the people responsible for the databases and all the students involved in the anthropology study.

Finally we want to thank all the patients and their contacts for participating in the feasibility/acceptability and/or implementation parts of the study.