

Disease Specific Documents for XII Plan

Lymphatic Filariasis

High Power Committee to Evaluate the Performance of ICMR, 2012-13



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Lymphatic Filariasis

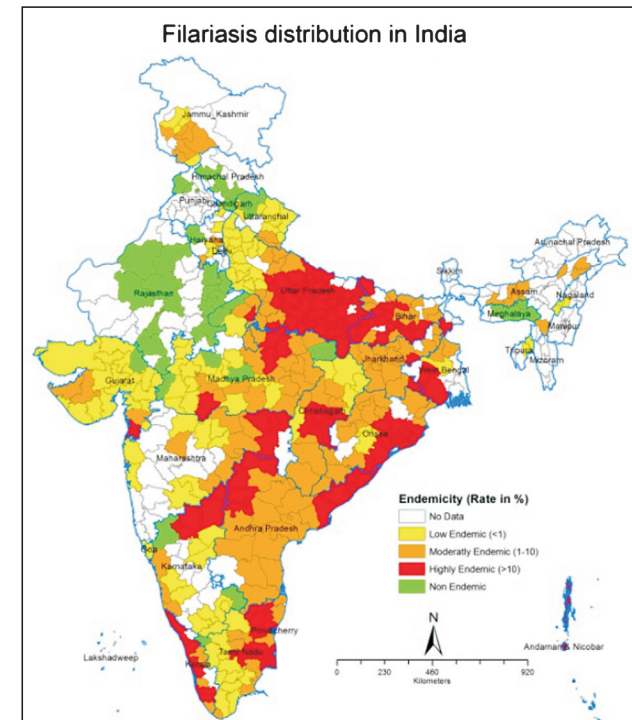
1. ICMR Institutes involved in Filariasis research

1. Vector Control Research Centre, Puducherry
2. Regional Medical Research Centre, Bhubaneswar
3. Centre for Research in Medical Entomology, Madurai
4. Regional Medical Research Centre, Port Blair
5. Regional Medical Research Centre, Dibrugarh
6. Regional Medical Research Centre for Tribals, Jabalpur
7. Division of Epidemiology and Communicable Diseases, ICMR Hqrs

2. Current situation of the disease/disease burden with contribution of ICMR

Lymphatic filariasis (LF) is endemic in 250 districts distributed in 20 States and Union Territories of India (Map). Nocturnally periodic form of *Wuchereria bancrofti* is widely distributed while nocturnally period *Brugia malayi* is restricted to small pockets in six States. Diurnally sub periodic *W. Bancrofti* is confined to the Nancowry group of islands in Nicobar district. The people at risk of infection are estimated to be 614 million. *B. malayi* infection recorded originally in 13 districts has shown natural decline due to environmental changes and contributes to only about 0.6% of the problem due to lymphatic filariasis in India.

National Programme to eliminate lymphatic filariasis (ELF) was launched in 2004 in India covering all the districts, endemic for *W. Bancrofti* and/or *B. malayi* to achieve filariasis elimination by 2015, one of the goals of our National Health Policy. The strategies are (a) to treat all the eligible (<2 years of age) population with annual single dose of DEC and albendazole (co-administration) for 5-6 years and (b) morbidity management for diseased individuals to alleviate disability. By the end of XI five year plan period, more than five rounds of MDA have been completed in all the endemic districts (implementation units. The overall human infection (mf rate) reported has been reduced from 1.24% in 2004 to 0.35% in 2011. Line listing of cases with filarial disease has been completed by 2010 for up scaling morbidity management. A total of 11.38 lakh cases with chronic manifestations have been



recorded. Based on this data, Vector Control Research Centre (VCRC) re-estimated the disease burden as 95 thousand Disability Adjusted Life Years.

Before launching of Filariasis elimination programme village level demonstration of annual/semi-annual rounds of mass administration of DEC by the VCRC led to implementation of pilot scale trials by the National Vector Borne Disease Control Programme (NVBDCP) in collaboration with the VCRC.

Operational Research on Lymphatic Filariasis (LF) by ICMR

The research activities of the ICMR institutes during the XI plan period were mainly focused on solving operational issues relating to implementation of LF elimination programme in India. Studies on the efficacy and operational feasibility of co-administration of DEC with albendazole, development of strategies for drug delivery, advocacy and social mobilization strategies, independent assessment of programme performance, and estimation of disease burden for implementation of morbidity management were the main activities during this period. A filaria map was also developed to assess the risk of transmission in unsurveyed areas (districts) and which are not included in the elimination programme.

By the end of XI plan period, many of the endemic districts completed at least five rounds of MDA and ready for impact assessment before verification of elimination of filarial transmission, which requires robust evaluation tools and protocols. Accordingly, the research activities, initiated and continued during XII plan period are: development and evaluation of newer diagnostic tools, sampling strategies for impact assessment, formulation and demonstration of supplementary strategies to enhance the effect of MDA in areas with persistent infection despite repeated rounds of MDA, improved morbidity management strategies, development of potential macrofilaricidal compounds and evaluation methods for morbidity management.

The research priorities during XII plan period will be the development of post MDA surveillance strategies for areas where the Mf rates are reduced to threshold level of <1% and MDA could be stopped. This includes application of more sensitive impact indicators to monitor and prevent resurgence, implementation of supplementary strategies in confined and persistent transmission areas to eliminate LF, assessment of the current status of unsurveyed areas for inclusion in the programme.

The time frame of all these activities is in line with the target year of LF elimination (2015) in our country. Capacity building is crucial as new methods and protocols are recommended/ used for evaluation of MDA programme and therefore ICMR institutes are also involved in supporting the National LF elimination programme by imparting training to the programme personnel.

3. Major achievements

1. VCRC and CRME demonstrated that co-administration of DEC with albendazole was more efficacious in clearing filarial infection, operationally feasible, safe and acceptable to the community. CRME also demonstrated reduction in the intestinal worm load among school children due to MDA with the combination. These facilitated formulation of National policy on co-administration of DEC and albendazole for elimination of LF in India.
2. The VCRC demonstrated that mass distribution of DEC salt for one year as a supplement to five rounds of MDA in persistent transmission areas reduced the mf rate below 1% leading to interruption of transmission without resurgence. This strategy will be validated by RMRC, Port Blair in an operational setting to eliminate the lone foci of sub periodic bancroftian filariasis in Nicobar Islands.
3. A Geo-Environmental Risk Model (GERM) developed by VCRC in collaboration with NVBDCP, on GIS platform was used to create a transmission risk map for the entire country which identified risk of transmission in 113 of the 190 hitherto unsurveyed districts.
4. A cluster design based LQAS was developed and validated by VCRC to evaluate the filariasis elimination programme and to make decision on stopping MDA. This cluster based LQAS strategy has been a major input for the revised WHO guidelines for Transmission Assessment Surveys (TAS), which is used for verification of absence of transmission in LF elimination programme. This protocol is now being followed to assess the LF elimination programme in India.
5. Identified spatially clustered transmission hotspots in an evaluation unit which has undergone 8 rounds of MDA. The results indicate that the TAS for stopping MDA should be at a level (block/ PHC) lower than that of a district. The results of this study carried out by VCRC have implications in post MDA surveillance of our National programme.
6. A study conducted by CRME showed that annual rounds of MDA (DEC) alone and in combination with vector control indicated that combination was more effective but cost prohibitive. However this strategy can be supplemented in hotspots during post MDA surveillance in our country.
7. In a study carried out by RMRC, Bhubaneswar, 100mg of DEC given uniformly to all age groups was found to be better tolerable and as effective as 200mg and 300mg dose in reducing Mf rate in the community and infection/infectivity rate in mosquitoes. The results of this study indicated an alternate option to improve community compliance for MDA.
8. Double dose of albendazole (800mg) with DEC (300mg) administered biannually was found to be superior to the existing regimen (400 mg Albendazole + 300 mg DEC annual) in adult worm clearance in a study conducted by the RMRC, Bhubaneswar.
9. A methodology to assess quality of life of LF patients was developed by VCRC which could be used as a tool to assess the impact of morbidity management on disability alleviation in national LF elimination programme.

10. At VCRC (a) four monoterpenes from *Trachyspermum ammi* and (d) 14 substituted naphthoquinone analogues that exhibit macrofilaricidal activity against *Setaria digitata* have been identified.
11. A marker has been developed to differentiate primary lymphoedema from secondary lymphoedema cases. This finding of VCRC will be useful in morbidity management.
12. Infective stage specific molecular tool was developed at VCRC, which could be used as a xenomonitoring tool for *Wuchereria bancrofti* in the LF elimination programme, particularly during post-MDA period.
13. Association of endothelin1 gene polymorphism with lymphoedema and TNF receptor-II with hydrocele was observed by RMRC, Bhubaneswar, indicating the pathway for differential mechanism of these clinical forms.
14. Molecular markers have been identified by the VCRC to differentiate genotypes of *W. Bancrofti*, which will be useful to identify the genotype causing persistent infection following MDA.
15. The role of endosymbiont *Wolbachia* in mediating reactions after administration of Diethylcarbamazine in infected human subject Identified pre-treatment TNF- α levels significantly more in Mf carriers (AS) and patients with chronic filarial disease (free of detectable infection) in comparison to subjects with cryptic infection (amicrofilaraemic with filarial antigenemia only).

4. No. of Research publications: 165

Vector Control Research Centre, Puducherry : 117

Centre for Research in Medical Entomology, Madurai : 8

Regional Medical Research Centre, Bhubaneswar : 23

Regional Medical research Centre, Port Blair: 5

Extramural projects, ICMR Hqrs : 12

5. List of patents: (VCRC)

Patents filed

- a. A cyclic lipopeptide of *Bacillus subtilis* subsp. *subtilis* with potential to kill mosquito stages
Indian Patent Application No. 544/DEL/2008.

- b. New bacterial culture media for the production of mosquito pathogenic Bacilli using industrial wastes
Indian Patent Application No. 1106/DEL/2007
- c. *Wuchereria bancrofti* infective stage – specific RT-PCR assay
Indian Patent Application No. 2793/DEL/2006

Patents granted

- d. A process for the *production* of mosquito oviposition attractant
199635 dated 25.06.2007
- e. Controlled release *formulation* (CRF) of an indigenous IGR DPE-28
191820 dated 25.6.2007

Patent process initiated

- f. A process for the preparation of an eco-friendly dehairing protease enzyme from *Bacillus* sp. for leather processing
- g. Fly ash based *mosquito* larvicidal formulations of *Bacillus thuringiensis* var. *israelensis* (serotype H14)
- h. Improved process *for* the production of Cyclosporin-A using the fungus *Tolypocladium* sp. strain NRRL No: 18950

6. Technologies developed/technologies transferred to the Industry

A process for production of mosquitocidal formulations of *Bacillus* var. *thuringiensis* was transferred to four commercial firms.

7. Technologies used by WHO/others

- a. The results of the project on development of sampling strategies to decide stopping/continuing Mass Drug Administration towards filariasis elimination was used as input for the WHO protocol for Transmission Assessment Survey which has been adapted to evaluate LF elimination programme in India (VCRC)
- b. Filariasis risk map based on Geo-environmental risk model (GERM) developed for delimitation of lymphatic filariasis transmission is used for conducting microfilaria surveys in unsurveyed areas by the programme (VCRC).

8. Man power trained (VCRC)

Formal:

Regional Training Course on Integrated Vector Management (IVM): 22 participants from 10 countries (Bangladesh, Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand & Timor Leste) - VCRC

WHO Fellows (16) from SEARO countries

Regional Training Course on Transmission Assessment survey for Filariasis elimination: 23 candidates from nine countries

Informal:

Public Health Officials (38), Scientists/Researchers (25) and administrators (12)

9. New human resources generated (VCRC)

- Ph.D. Programme: 17 candidates - Microbiology (5), Zoology (10) and Chemistry (2)
- Post Graduate Diploma in Medical Entomology: 12 candidates
- M. Sc., Public Health Entomology: 24 candidates
- Post Doctoral Fellowship: 1 candidate (Chemistry)

Table 1. Status of Completed Research Studies undertaken during XI plan – Lymphatic filariasis

Sr. No	Thematic area	Title of the Study	Objectives	Completed/any offshoot during XII th plan	If Off-Shoot, Refer To XII th Plan Study	Institution
Basic Research						
1		Genetic polymorphism of <i>Wuchereria bancrofti</i>	To study the genetic polymorphism of <i>Wuchereria bancrofti</i> parasites from different regions.	Completed. Identified three genetic markers. The markers will be used for genotyping the parasite in persistent foci of transmission in a National Network mode during XII plan	Sl. No. 1, Annexure III	VCRC, Puducherry
2		Role of VEGFR – 3 and FOXC2 genes as risk factors in the pathogenesis of lymphatic filariasis in filarial lymphedema	To study the role of VEGFR-3 and FOXC2 genes and develop an AS-PCR assay to differentiate primary lymphoedema from secondary lymphoedema cases.	Completed. A marker has been developed to differentiate primary lymphoedema from secondary lymphoedema cases. The marker will be evaluated in a hospital based study during XII plan	Sl. No. 2, Annexure III	VCRC, Puducherry
3		Pharmacogenomics approach to unravel the variation in response to Diethylcarbamazine (DEC).	To identify biomarkers for the detection of non-responsiveness to DEC.	Completed. Three single nucleotide polymorphisms (SNPs) in the genes of arachidonic acid metabolic pathway have been identified as biomarkers for the detection of non-responsiveness to DEC.	No	VCRC, Puducherry
4		Immune mechanisms and diagnostic markers of infection and disease	To identify immune markers for morbidity in hydrocele and elephantiasis	Association of endothelin1 gene polymorphism with lymphoedema and TNF receptor-II with hydrocele was seen indicating the pathway for differential mechanism of these clinical forms.	No	RMRC Bhubaneswar
5		Studies on Regulatory T cells in human <i>Bancroftian</i> filariasis	To identify a marker for the absence of active infection	Completed. T-regulatory cells were found to down regulate the inflammatory responses and facilitate parasite survival. Anti-sheath antibody marked absence of active infection. <u>Offshoot</u> - A new study is proposed to identify the stage of infection/disease, which may be useful for MDA monitoring.	Sl. No. 3 Annexure III	RMRC Bhubaneswar

6.		Genetic polymorphism of <i>Wuchereria bancrofti</i> parasitic genes"	To study Genetic polymorphic of functional genes for typing <i>Wuchereria bancrofti</i> strains isolated from different geographical areas towards the development of genetic markers.	WbALT2 & WbGST genes were amplified with gene-specific primers and were cloned directly into sequencing vector. Both these antigens can very well be used as potent immunoprophylatics,	No	Extramural grant, ICMR Hqrs
7		Genetic polymorphism of host molecules involved in immunity and immunoregulation in human filariasis	To type polymorphism of human genes that plays a role in innate and/or adaptive immunity in human <i>bancroftian</i> filariasis	No significant association was found in distribution of MBL (XY & HL), CD14 (-159), IL-10 (-819 & -592), TNF- α (-308) and IFN- γ R1 (-56) polymorphisms in different clinical categories suggesting that these polymorphisms may have no role in human filariasis.	No	Extramural grant, ICMR Hqrs
8		Post-DEC reactions in human bancroftian filariasis: An immunobiological study in Orissa, India	The project addressed the issue of reactions observed in human communities after administration of Diethylcarbamazine citrate, the anti-filarial drug being currently used for control of lymphatic filariasis.	Post-DEC reactions are not dependent on presence or density of circulating Mf nor are related to plasma <i>Wolbachia</i> density.	No	Extramural grant, ICMR Hqrs
Clinical Research						
1		Alternate chemotherapy regimen for clearance of <i>Wuchereria bancrofti</i>	To develop alternate chemotherapy for treatment of filariasis	Completed. A clinical trial showed that 12 days treatment with DEC followed by a single dose albendazole was more efficacious than conventional DEC treatment for microfilaria carriers.	No	VCRC, Puducherry
2		Alternate MDA regimen with superior efficacy or better tolerability - Clinical trial with anti filarial drugs for adulticidal effect.	To conduct a clinical trial (hospital based) with alternate drug regimen having anti-adult effect.	Completed. Double dose of albendazole (800mg) with DEC (300mg) administered biannually was found to be superior to the existing regimen (400 mg Albendazole + 300 mg DEC annual) in adult worm clearance. This regimen has the potential to reduce the period of MDA required for elimination.	No	RMRC Bhubaneswar

3		Studies of cohort of children below 5 years in areas endemic for <i>Bancroftian</i> filariasis	To demonstrate subclinical lymphatic pathology in children.	Completed. Lymphoscintigraphy and ultrasonography conducted in young children with <i>W. bancrofti</i> infection established presence of lymphatic pathology that reverses with annual dosage of MDA. This information can be used as an advocacy tool in MDA programme for improving drug compliance in children. <u>Offshoot</u> - Proposed to study the impact of MDA on reduction/reversal of morbidity in early disease condition.	Sl. No. 5, Annexure III	RMRC, Bhubaneswar
Epidemiological/Operational Research						
1		Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	To assess the feasibility, safety, acceptability and effect of co-administration of albendazole and DEC.	Completed. Co-administration of DEC with albendazole was more efficacious in clearing filarial infection. It was operationally feasible, safe and acceptable to the community. This facilitated formulation of National policy on co-administration of DEC and albendazole for elimination of LF in India.	No	VCRC, Puducherry (ICMR TF)
2		Evaluation of mf and disease after MDA in Assam and Chhattisgarh.	To assess the impact of MDA on infection and disease,	Completed. Prevalence of infection remained high even after several rounds of DEC. In Assam, Tea Gardens are identified as the foci of infection. Feedback provided to the programme.	No	RMRC Dibrugarh, RMRCT, Jabalpur
3		Situation analysis of sub-periodic <i>Wuchereria bancrofti</i> in Andaman and Nicobar districts	To assess the current situation of diurnally subperiodic bancroftian filariasis	Completed. The overall mf prevalence in seven islands was 3.8%. <u>Offshoot</u> – this information is used as base line for the proposed trial to test the effect of supplementary strategy with DEC salt on elimination of the foci.	Sl. No. 7, Annexure III	RMRC, Port Blair

4		Feasibility of elimination of persistent foci of transmission of filariasis by supplementing DEC fortified salt	To assess the technical and operational feasibility of DEC fortified salt as supplementary to MDA	Completed. Mass distribution of DEC salt for one year as a supplement to five rounds of MDA in persistent transmission areas reduced the mf rate below 1% leading to interruption of transmission without resurgence. <u>Offshoot</u> - This strategy will be validated by RMRC, Port Blair (during XII Plan) in an operational setting to eliminate the lone foci of sub periodic bancroftian filariasis in Nicobar Islands and its scope in eliminating filariasis in Tea Gardens in Assam will be explored.	Sl. No. 7, Annexure III	VCRC, Puducherry (WHO/ Intramural)
5		Evaluation of the impact of MDAs on filarial infection variables both in the community and in vector population in two revenue blocks of Tirukoilur and Mugaiyur in Villupuram district, Tamil Nadu, India.	To evaluate the impact of MDA alone and in combination with vector control on filarial infection variables.	Completed. Annual rounds of MDA (DEC) alone and in combination with vector control indicated that combination was more effective but cost prohibitive.	No	CRME, Madurai
6		Efficacy and adverse reactions of single dose DEC of 100mg, 200mg and 300mg strength against filarial infection	To assess the efficacy of DEC at different doses	Completed. 100mg of DEC given uniformly to all age groups was found to be better tolerated and as effective as 200mg and 300mg dose in reducing Mf rate in the community and infection/infectivity rate in mosquitoes. <u>Offshoot</u> - Proposed to assess the level of community compliance and feasibility of administration of low dose DEC (100 mg) with 400 mg of Albendazole.	Sl. No.9, Annexure III	RMRC Bhubaneswar
7		Assessment of health related quality of life (HRQoL) among lymphatic filariasis (LF) patients using disease specific instrument	To develop an instrument to assess Health Related Quality of Life of filariasis patients and field test	Completed- A methodology for assessing quality of life of LF patients as a tool to assess the impact of disability alleviation through morbidity management is developed <u>Offshoot</u> - Study proposed on application of this method to assess the impact of morbidity management of LF patients in operational settings.	Sl. No. 11, Annexure III	VCRC, Puducherry (Intramural)

8		Delimitation of Lymphatic Filariasis in India, based on Geo-environmental risk model (GERM)	To develop a GIS based geo-environmental filariasis transmission risk map for India and validate.	Completed. A Geo-Environmental Risk Model (GERM) developed in collaboration with NVBDCP, on GIS platform was used to create a transmission risk map for the entire country which identified risk of transmission in 113 of the 190 hitherto unsurveyed districts. These districts are to be brought under the MDA programme after ascertaining that they merit consideration (i.e. $\geq 1\%$ human infection prevalence) for intervention. The GERM model will be used as a tool to assess the current situation in the un-surveyed area but not covered under MDA	Sl. No. 12, Annexure III	VCRC, Puducherry (ICMR- TF)
9		Spatial pattern of infection and risk of filariasis transmission: impact of filariasis elimination programme	To identify the determinants of persistence of transmission 'hotspots' in the MDA implementation units.	Identified heterogeneity in vector breeding habitats as the risk factor for persistence of transmission 'hotspots'. The findings are useful for targeted approach of supplementary intervention measures.	No	VCRC, Puducherry

Table 2. Important and essential activities which needs to be continued to XII plan

Sr.No	Type and title of Research Study	Justification	Time Frame	Deliverable Outcome with Public Impact	Institution	Funding
Basic Research						
1	Development and evaluation of filarial immunodiagnostics (assays for human exposure and infection)	LF elimination programmes currently depend upon two diagnostics (ICT and Brugia Rapid) which are cost prohibitive. There is a need to develop / identify cost-effective diagnostic for large scale use in the evaluation of MDA programme. Two filarial specific peptides identified and anti-body assays developed by VCRC through an extramural project need to be evaluated.	2012-2014	Additional tool to evaluate the impact of MDA for LF elimination	VCRC, Puducherry	ICMR, Hqrs.
2	Synthesis and evaluation of mosquito attractants for vector surveillance and control	A total of 24 compounds and combinations were tested, of which six and 16 compounds show significant attraction and repellence respectively. Characterization, synthesis and evaluation of these leads are to be continued during the XII plan period.	2012-2015	Tool for vector surveillance: Agents to be used in the ovitraps or adult mosquito capturing devices.	VCRC, Puducherry	ICMR, Hqrs.
Clinical Research						
1	Effect of yogic exercise and Electrotherapy induced muscular contraction in reduction of filarial Lymphoedema grade-II and grade-III a hospital base study.	Management of lymphedema is still a challenge and reversal of oedematous limb to normalcy is not always attainable with the available treatment modalities. This is an interventional study to reduce lymphedema by yoga manoeuvres combined with electrical induced muscle contraction	2012-2014	Improved lymphedema management in filariasis (a physiotherapeutic tool).	RMRC Bhubaneshwar	ICMR, Hqrs.
2	Identification of the causative organism (bacterial/fungal) and their drug sensitivity in management of filarial Lymphoedema with complications.	Skin scraping and wound secretion from patients attending OPD, revealed bacterial growth in 82 % cases of which <i>S.aureus</i> was dominant followed by <i>S. epidermatitis</i> , <i>Streptococcus</i> spp. and <i>E.coli</i> . During 12 th plan it is planned to continue the study by enrolling more subjects from community setting to look for any associated fungal infection besides drug sensitivity pattern, which can give recommendation to physicians of this region for more effective treatment of ADLA (Acute inflammation episodes with fever and increase limb swelling) by proper selection of antibiotics /antifungals in patients with chronic filarial morbidity.	2012-2015	Guidelines for effective management of clinical cases	RMRC Bhubaneshwar	ICMR, Hqrs.

Translational Research						
1	Multicentric evaluation of L3 specific RT-PCR assay for xenomonitoring	An infective stage (L3) specific RT-PCR assay developed by VCRC for xenomonitoring is being validated in multicentric mode by other ICMR institutes before recommending for operational use.	2012-2014	A diagnostic tool for xenomonitoring of LF elimination, particularly during post-MDA period for verification of elimination.	VCRC, CRME, RMRC Bhubaneshwar, Dibrugarh & Port Blair	ICMR, Hqrs.
2	Development of Macrofilaricidal drugs	(a) Four monoterpenes from <i>Trachyspermum ammi</i> and (b) 14 substituted naphthoquinone analogues that exhibit macrofilaricidal activity against <i>Setaria digitata</i> under <i>in vitro</i> conditions have been identified from two extramurally supported studies. These lead compounds need to be evaluated under <i>in vivo</i> condition.	2012-2014	Macrofilaricidal compound(s) for clinical trial.	VCRC, Puducherry	ICMR, Hqrs.
Epidemiological Research						
1	Lymphatic Filariasis endemicity mapping in states of north-east India	To determine the prevalence of <i>Wucheria bancrofti</i> in the northeastern state of India, to find the risk factors associated with its prevalence and to estimate the transmission potential of the vector involved. The study area is north eastern state of Tripura	2012-2015	Prevalance of LF in Tripura, risk factors associated transmission of the disease and mapping the endemicity of the disease in Tripura will be elucidated	RMRC, Dibrugarh	Supported in extramural research mode (ICMR)

Table 3. XII plan proposals with link with past achievements and clear cut goals as well as relevance to national programme

Sr.No	Thematic area and Title of the study	Justification		Time Line	Deliverables	Institution
		Off-Shoot of an earlier completed programme	De Novo idea which is either nationally relevant or it is likely to lead to a new scientific breakthrough.			
Basic Research						
1	National network for genotyping of human lymphatic filarial parasite, <i>Wuchereria bancrofti</i> for different endemic areas	Molecular tools to differentiate genotypes of <i>W. bancrofti</i> have been developed in an earlier study. Using these markers it is necessary to study the possible parasite polymorphism and its relation to persistent infection following MDA.	Not applicable	2012-2013	A marker to identify parasite population "non-responsive" to MDA in LF elimination programme	VCRC, Puducherry
2	Evaluation (screening and validation) of biomarkers developed for lymphatic filariasis	This is an offshoot of earlier study in which an AS-PCR assay based on VEGFR-3 gene (Vascular Endothelial Growth Factor-3) was developed, which will be helpful to differentiate primary lymphoedema from secondary lymphoedema cases. Evaluation of this marker will be taken up during the XII plan period as it could lead to a new biomarker for management of lymphatic filariasis which is a component of national filariasis elimination programme	Not applicable	2013-2015	Diagnostic tool for management of lymphoedema	VCRC, Puducherry
3	Assessment of anti sheath antibodies as an alternate tool to detect immune status in human filariasis	An earlier study has demonstrated the inverse association between anti-sheath antibodies and active filarial infection. The relationship of anti-sheath antibodies with various immunological parameters will be studied to develop a marker to differentiate the clinical stages of filarial infection and disease.	Not applicable	2013-2016	A marker for the immune status of the filarial patients.	RMRC, Bhubaneswar

4	Characterization of host and parasite factors among residual microfilaraemic individuals following MDA programme in filariasis		Even after six rounds of MDA, it has been observed that some individuals retain microfilaria who may act as the source of transmission and resurgence. Characterization of residual microfilaria and host factors will help to develop specific intervention tool for Mf clearance.	2013-2015	Identification of such individuals/ risk areas will help in applying an intensive MDA program with a more effective regimen like DEC 300 mg + Alb 800 mg (biannual) for achieving elimination and reduce risk of resurgence.	RMRC Bhubaneswar
Clinical Research						
1	Impact of MDA on reduction / reversal of Morbidity in early disease condition	Offshoot of an earlier study. Planned to assess the impact of MDA on possible reversal of lymphatic pathology or reduction in the degree of clinical manifestation, by prospective follow up of patients using lymphoscintigraphy and ultrasound (non-invasive) techniques. This will provide information on additional benefit of MDA in morbidity control, which can be used as an advocacy tool as well as early treatment tool for lymphoedema	Not applicable	2014-2016	Advocacy tool for lymphoedema management and MDA programme.	RMRC Bhubaneswar
Epidemiological/Operational Research						
1	Field evaluation of sampling strategies for xenomonitoring of infection in <i>Culex</i> vector by PCR as a surveillance tool for lymphatic filariasis elimination programme	Offshoot of an earlier study (extra-mural). The objective is to provide an alternate/additional method for assessing transmission in LFE programme. Currently, Transmission Assessment Survey is recommended for making decision on stopping MDA and Post-MDA surveillance until certification. This is mainly based on detecting antigen in children to verify absence of transmission. Monitoring infection in vectors is appropriate when human infection levels are very low following MDA.	Not applicable	2014-2016	An alternate method to human sampling for monitoring/evaluation of LF elimination programme.	VCRC, Puducherry

2	Elimination of sub-periodic filariasis from Nancowry group of islands	Offshoot - Studies by RMRC, Port Blair showed evidence of persistence of infection and acquisition of new infections even after six rounds of MDA in Nancowry islands, the lone foci of sub periodic bancroftian filariasis in India. Mass distribution of DEC salt for one year as a supplement to five rounds of MDA in persistent transmission areas was shown to reduce the mf rate of nocturnally periodic form of bancroftian filariasis below 1% leading to interruption of transmission without resurgence (VCRC). Since the feasibility of implementing mass distribution of DEC salt is more in island situations, the strategy will be tested for eliminating the LF from these islands.	Not applicable	2013-2016	Elimination of lone foci of subperiodic bancroftian filariasis in India	RMRC Port Blair, VCRC and state Health Department
3	Simulation model to predict and prevent resurgence		A tool to prospectively assess the various post-MDA scenarios that can aid the national programme to take appropriate action in time is necessary. The LYMFASIM model will be improved and adapted to post-MDA situation.	2014-2016	A decision making tool (simulation model) to the National Programme for managing the Post-MDA period/risk of resurgence	VCRC, Puducherry
4	Alternate regimen with uniform low dose (100mg) of DEC with Albendazole (400mg) to enhance compliance in MDA	It is an offshoot of earlier clinical trial, which showed that a low dose, 100mg is as effective as 200 and 300mg of DEC. This study needs to be validated in the field so that the lower dosage can be recommended to the programme	Not applicable	2012-2016	An alternative approach to enhance compliance in low compliance areas for LF elimination.	RMRC Bhubaneswar

5	Detection of transmission hot spots/high risk pockets in MDA units and interventions to prevent resurgence (in <i>W. bancrofti</i> and <i>B. malayi</i> areas)	Earlier studies (extra-mural) have shown the presence of transmission hotspots in the endemic districts, which are qualified for stopping MDA. Detection of such hotspots is necessary to prevent resurgence through targeted interventions.	Not applicable	2014-2016	Targeted intervention to clear persisting infections or hotspots	VCRC Puducherry RMRC, Bhubaneswar
6	Application of lymphatic filariasis quality of life (HRQoL) instrument to assess the impact of morbidity management in filariasis patients in operational settings	Offshoot - While indicators and strategies to assess the impact of MDA are available, no such protocols are available to assess the impact of morbidity management. The method developed at VCRC to assess the quality of life of patients can be used to develop the guidelines to evaluate morbidity management after validation in operational setting	Not applicable	2014-2016	Evaluation tool to assess the impact of morbidity management under LF elimination programme	VCRC, Puducherry
7	Studies on transmission dynamics in unsurveyed areas	Offshoot - Predictions based on GERM (VCRC) and other studies (RMRCT) have shown existence of foci of infection/transmission in some of the hitherto unsurveyed districts and not covered under MDA. Therefore, it is necessary to assess the current situation in these districts for their inclusion under MDA programme	Not applicable	2014-2016	Assessment of filariasis transmission in areas at risk for inclusion in the LF elimination programme	VCRC, Puducherry RMRC, Dibrugarh, RMRCT, Jabalpur

Table 4. Research and development – extramural projects – Lymphatic filariasis

Sr.No	Thematic area	Title of the Study	Objectives	Completed/any offshoot during XII th plan	If Off-Shoot, Refer to XII th Plan Study	Institution (Funding Agency)
Basic Research						
1		Development of Macrofilaricidal drugs: <i>In vivo</i> screening of macrofilaricidal compounds	To identify potential macrofilaricidal compound among six substituted benzoyl/ phenyl acetyl piperazides, that exhibit macrofilaricidal activity against <i>Setaria digitata</i> under <i>in vitro</i>	Ongoing (2012-2015)	No	VCRC, Puducherry (DST)
Epidemiological/Operational Research						
1		Development and validation of sampling strategies for stopping/continuing programme to eliminate lymphatic filariasis	To validate a cluster design based LQAS to revise the guidelines to assess the impact of MDA and to decide on stopping MDA and for post-MDA surveillance	Completed- The achievements are: 1) A cluster design based LQAS was developed and validated to evaluate the filariasis elimination programme and to make decision on stopping MDA. This cluster based LQAS has been recommended and incorporated in the revised WHO guidelines for Transmission Assessment Surveys (TAS). 2) Identified spatially clustered transmission hotspots in an evaluation unit which has undergone 8 rounds of MDA. The results indicate that the TAS for stopping MDA should be at a level (block/ PHC) lower than that of a district.	Sl. No. 10, Annexure III	VCRC, Puducherry (LF Support Centre, Gates Foundation)
2		Development and validation of sampling strategies for xenomonitoring of infection in <i>Culex</i> vector by PCR as a surveillance tool for assessing post-MDA situation of lymphatic filariasis elimination programme	To develop xenomonitoring tool and strategy to evaluate MDA programme	Developed and tested a cluster design based sampling strategy for collecting vector mosquitoes and monitoring vector infection by PCR assay. Demonstrated that monitoring infection in vector can be a potential alternative to antigen based transmission assessment survey (TAS) in human. This will be tested in an operational setting during XII Plan.	Sl. No.6, Annexure III	VCRC, Puducherry (LF Support Centre, Gates Foundation)

3		Evaluation of the impact of MDAs on filarial infection variables both in the community and in vector population in two revenue blocks of Tirukoilur and Muagiyur in Villupuram district, Tamil Nadu, India.	To evaluate the impact of MDA alone and in combination with vector control on filarial infection variables.	Completed - Annual rounds of MDA (DEC) alone and in combination with vector control indicated that combination was more effective but cost prohibitive.	No	CRME, Madurai (LF Support Centre – Gates Foundation)
4		Reassessment of disease burden due to lymphatic filariasis in India using DALY as a summary measure	To estimate the current disease burden due to filariasis in India using Disability Adjusted Life Years (DALY)	Completed –assessed the burden in India which was 6.6% of global burden of 2.86 Million DALY	No	VCRC, Puducherry (WHO- SEARO)
5		In-depth review of the National Programme for Elimination of Lymphatic Filariasis in India	To Identify the gaps in programme implementation and provide suggestions for improved performance	Completed – Identified advocacy and community preparation as the major determinants of programme performance (success and failure).	No	VCRC, Puducherry NVBDCP, Delhi
6		Assessment of MDA coverage and compliance in implementation units	To carry out independent assessment of MDA coverage and compliance in selected endemic districts	Completed- Levels of drug coverage and compliance ranged from 30 to 90 % in different implementation units. Feedback to the LF elimination programme for improved coverage/compliance.	No	VCRC, Puducherry RMRC, Bhubaneswar, RMRC, Portblair RMRC, Dibrugarh, RMRCT, Jabalpur NVBDCP, Delhi
7		Inclusive partnership strategy for improved coverage of MDA in urban setting	To develop a specific strategy is required for improved coverage in urban settings that lack an organized community and health structure.	Completed – the study in a municipal area of Odisha has shown that involvement of community groups coordinated with the health system improved the coverage (79%) of DEC distribution during MDA.	No	RMRC, Bhubaneswar (WHO-TDR)

8		Assessment of active filarial infection through ICT and to evaluate the impact of Mass Drug Administration in selected districts for decision making on the continuation or stopping of MDA.	To evaluate the impact of MDA and to recommend for stopping/continuation of MDA.	Completed -Persistence of infection and transmission observed in seven districts from 3 States (VCRC) necessitated the continuation of MDA.	No	VCRC, Puducherry (NVBDCP)
Translational Research						
1		Fly ash based biopesticidal formulations of <i>Bacillus thuringiensis</i> var. <i>israelensis</i>	To develop fly ash based biopesticidal formulations and assess their efficacy in controlling <i>Culex quinquefasciatus</i> and other mosquito species	Completed- Potential formulations to control mosquito larvae developed. Patent filed.	No	VCRC, Puducherry (Coal India Limited)

