RARE DISEASES INITIATIVE MEET

on 20th – 22nd January, 2016

at

National Institute of Pharmaceutical Education and Research (NIPER)
Kolkata – 700 032 (West Bengal)
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4, Raja S. C. Mullick Road, Jadavpur

Kolkata – 700 032 (West Bengal)
FOREWORD

Rare diseases initiative was taken up on the advice of Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Govt of India, to prepare a course curriculum of rare diseases for all the NIPERS by NIPER-Kolkata. Accordingly a concept paper has been made and discussed in-house including the students to understand their requirements. Following the same two multi-disciplinary expert committees consisting of clinicians from diverse speciality like medicine, Paediatric endocrinology, cardiology, and oncology including onco-surgery, pathology, neurology, molecular biology, tropical medicine, microbiology, biotechnology, public health, paediatrics and communicable diseases. Scientists and researchers from chemical biology, medical record specialty, health policy experts and administrators from Kolkata and also from the different parts of the country constituted the expert group. One expert from Minnesota University, USA, was also involved in the exercise. Clinical pharmacologists, pharmacologists, and experts from regulatory body were also in the group.

The NIPER-Kolkata hopes that the proceedings and the recommendations will go a long way in raising awareness of rare diseases among professionals and health administrators. We are hopeful that if this novel initiative is taken to its logical conclusion it will raise hope to the millions of rare disorder patients for appropriate support from the health care providers.

Dr. V. Ravichandiran
Director
National Institute of Pharmaceutical Education and Research (NIPER), Kolkata – 700 032
Acknowledgement

NIPER-Kolkata acknowledges with deep appreciation to all who helped in conducting the experts’ meeting successfully. We are particularly grateful to Prof. (Dr.) Bhabatosh Biswas, Hon. Vice-Chancellor, West Bengal University of Health Sciences, Kolkata, for sparing his valuable time and inaugurate the Meeting of Experts at Calcutta School of Tropical Medicine. We are thankful to Dr. Nandita Basu, Director, CSTM and her colleagues for providing the Venue of the inaugural session of the seminar. Special thanks are due to all the experts and the organizations namely National Institute of Biologicals, Noida, Tamilnadu Dr. MGR Medical University, Chennai, AIIMS, New Delhi, CSTM Kolkata, Calcutta Medical College, Institute of Post Graduate Medical Education and Research, IICB-CSIR, Kolkata, NICED-ICMR, Kolkata, AIHH&PH-DGHS, Kolkata, Apollo Hospitals, Medica Superspeciality Hospital, TATA Medical Centre and ARMA Medical Foundation for sparing their services to share their valuable clinical experiences with us and enrich the deliberations.

Sincere thanks are due to Drug Regulatory Authority of Bengal (Drug Controller and Assistant Drug Controller) for enriching the deliberations.

Special thanks are due to Dr Surinder Singh, Director National Institute of Biologicals, Noida for agreeing to provide IT support to Rare Disease Registry.

Sincere thanks are also due to all the support staff of Calcutta School of Tropical Medicine, Apollo Hospitals, IICB-CSIR, and CGCRI–CSIR for the very successful expert meeting.

Last but not the least thanks are also due to the officials, faculty and the students of NIPER–Kolkata for working very hard during the last three months for making the meet a success.

Dr. V. Ravichandiran
Director
National Institute of Pharmaceutical Education and Research (NIPER), Kolkata – 700 032
## Chapter-I: Name of the participants and institutions

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Name &amp; Designation</th>
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</table>
| 1.      | **Prof. Bhabatosh Biswas**  
Vice Chancellor  
West Bengal University of Health Sciences, Kolkata, West Bengal |
| 2.      | **Dr. Surinder Singh**  
Director  
National Institute of Biologicals (NIB), Noida, Uttar Pradesh |
| 3.      | **Prof. Ramaiah Muthyala**  
Associated Professor  
Invited Expert  
Minnesota University, USA & President/CEO, IORD |
| 4.      | **Prof. V. Nagarajan**  
Emeritus Professor, Neurology  
The TN Dr. MGR Medical University, Chennai, Tamil Nadu |
| 5.      | **Prof. Nandita Basu**  
Director  
Calcutta School of Tropical Medicine, Kolkata, West Bengal |
| 6.      | **Dr. (Prof.) Santanu Tripathy**  
Professor, Experimental Medicine  
Calcutta School of Tropical Medicine, Kolkata, West Bengal |
| 7.      | **Prof. Samit Chattopadhyay**  
Director, CSIR-IICB, Kolkata |
| 8.      | **Dr. Shymal Roy**  
Sr. Principal Scientist, CSIR-IICB, Kolkata |
| 9.      | **Dr. P. Jaisankar**  
Sr. Principal Scientist, CSIR-IICB, Kolkata |
| 10.     | **Prof. Manoj Singh**  
Professor, Dept. of Pathology  
All India Institute of Medical Sciences (AIIMS), New Delhi |
| 11.     | **Dr. Sameer Bakhshi**  
Professor, Dept. of Oncology  
All India Institute of Medical Sciences (AIIMS), New Delhi |
| 12.     | **Dr. Chinthamoni Ghosh**  
Drugs Controller  
Drugs Control Department, Kolkata, West Bengal |
| 13.     | **Dr. R. N. Chaudhury**  
Director  
All India Institute of Hygiene and Public Health (AIH&PH), Kolkata West Bengal |
| 14.     | **Dr. Madhumita Dobe**  
Professor  
All India Institute of Hygiene and Public Health (AIH&PH), Kolkata West Bengal |
| 15.     | **Dr. Shanta Dutta**  
Director  
National Institute of Cholera and Enteric Diseases (NICED)-ICMR, Kolkata, West Bengal |
| 16.     | **Dr. Samiran Panda**  
Senior Medical Scientist  
National Institute of Cholera and Enteric Diseases (NICED)-ICMR, Kolkata, West Bengal |
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<tr>
<th></th>
<th>Name</th>
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<th>Institution / Details</th>
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<td>17</td>
<td>Prof. Siddhartha Roy</td>
<td>Dean</td>
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<td>18</td>
<td>Dr. Subrata Dey</td>
<td>Paediatric Endocrinologist</td>
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<td>Dr. D. P. Sinha</td>
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NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION & RESEARCH – KOLKATA

PROGRAMME

Expert core group panel of NIPER-Kolkata on Rare Diseases initiative

20-22 January 2016

20.01.2016
10.00 A.M. – 11.00 A.M.
Courtesy meeting with the Director and his colleagues in NIPER-Kolkata – Optional
Venue: IICB Conference Hall First floor

11.30 – 2.00 P.M. Symposium (Venue: Calcutta School of Tropical Medicine)
11.30 to 12 noon Exchange of pleasantries

12.00 hr - 12.30 hr:
• Welcome the Dignitaries and Felicitating with Floral Bouquet
• Lighting the Sacred Lamp
• Address by Prof. Nandita Basu, Director, Calcutta School of Tropical Medicine, Kolkata.
• Address by Prof. R. N. Chaudhury, Director, All India Institute of Hygiene and Public Health, Kolkata
• Address by the Chief Guest – Prof Bhabatosh Biswas, Hon’ble Vice Chancellor, West Bengal University of Health Sciences, Kolkata
• Vote of Thanks by Dr. V. Ravichandiran, Director, NIPER-Kolkata

12.30 hr - 14.00 hr:
• Rare Diseases Initiative in India – A Priority Agenda - Dr K K Datta (5 mins)
• Calling Attention of All Stakeholders Prof Santanu K Tripathi (7 mins)
- The Public Health Perspectives in Rare Diseases
  **Prof Madhumita Dobe** (8 mins) – AIIH&PH - Kolkata
- Diagnosis and Management of Rare Diseases – The Clinician’s Perspective
  **Dr Subrata Dey** (15 mins) – Apollo Hospitals - Kolkata
- The Problem Statement and the Way Forward (Key Lecture)
  **Dr Ramaiah Muthyala** (35 mins), Minnesota University, USA
- Floor Discussion (15 mins)
- Closing Remarks (5 mins)

**Working Lunch**

**PANEL DISCUSSION** – At Hotel GATEWAY

5-30 – 6.00 P.M.  Exchange of pleasantries

6.00 P.M.- 7.00 P.M.  1st Panel discussion
Moderator: Prof. Samit Chattopadhyay
Director, IICB-Kolkata

Panelists: Dr. Surinder Singh, Director,NIB, Noida  Dr. Subrata Dey,( Apollo)
Prof. V. Nagarajan (The TN Dr. MGR Medical University)
Dr. Samir Bukshi (AIIMS)
Dr. V. R. Ramanan (TMC- Kolkata )
Prof Manoj Singh (AIIMS)
Dr. D.P. Sinha (PG –Kolkata )
Medical/clinical perspective

Discussants: Dr Shanta Dutta, Director,
NICED. Dr Samiran Panda (NICED)
Dr. Madhumita Dobe (AIIH&PH)
Special mention: Health Policy viz. Rare
Disease Initiative – Dr. Arul Pitchai
Narayanan

7.00 P.M.- 8.00 P.M.  2nd Panel discussion
Moderator: Dr Ramaiah Muthyala, Minnesota University, USA

Panelists : Dr. Prof. Santanu Tripathy ( STM)
Dr Siddhartha Roy (Bose Institute)
Discussants: Dr.V.Ravichandiran, Director (NIPER-Kolkata), Dr. P.Jaisankar (IICB), Rep. from Roche Diagnostics and Dr.C.M.Ghosh (Drug controller, West Bengal)
Pharmaceutical and Biomedical perspective

8PM  Dinner hosted by Director NIPER -Kolkata

Venue  Hotel Gateway

21.01.2016

08.30 A.M.– 10.00 A.M.  Seminar at Apollo Glen Eagles Hospital

Prof. Ramaiah Muthyala, Minnesota University, USA and Dr. Subrata Dey, Paediatric Endocrinologist, will address a Group of Doctors at Apollo Glen Eagles Hospitals on Rare Disease Initiative followed by breakfast (Courtesy Apollo Hospital).

12.00 Noon – 1.15 P.M.  LUNCH at Hotel Gateway

2.00 P.M. – 6.00 P.M.  Round Table Discussions on Rare Disease Initiative: Future direction, Course Curriculum Development for Post-Graduate Students of NIPERS including indicative course content.
Moderator:
Dr Mahammed Ariz Ahammed, IAS, JS (DoP) and Prof. Ramaiah Muthyala (Minnesota University, USA)

Venue: IICB Conference Hall (First Floor)
22-01-2016

Venue: CSIR Guest House, 59 Lake Road

10.00 A.M. – 12.00 noon  Technical session

Moderator:
Dr. V. Ravichandiran. Director
NIPER-Kolkata

Registry, Data Format including data generation indicating source and review of medical record of Rare Disease.

Lead speakers:

Prof. Ramaiah Muthyala, Minnesota University, USA
Dr. Kuntal Biswas (Kolkata Medical College)

12 noon to 12-30 PM  Concluding session and thanks giving followed by working lunch

Transport arrangements

Airport picks up and drops

For those who are coming from outside Kolkata and staying at Hotel Gateway: Transport at Hotel Gateway will be available for going to the venue and back

For others transport will be available at NIPER-KOLKATA (IICB campus)
The expert meet was inaugurated at the Calcutta School of Tropical Medicine by Hon’ble Prof. (Dr.) Bhabatosh Biswas, Vice-Chancellor of West Bengal University of Health Sciences, Kolkata, who lauded this novel initiative of NIPER- Kolkata and thanked Dr. V. Ravichandiran and his team for initiating RDI in the country

Dr Nandita Basu, Director, CSTM and Dr.R.N.Chaudhuri, Director, AIH&PH made some initial remarks before the inauguration congratulating Director, NIPER for initiating such program and assured NIPER for their full technical support.

Dr. V. Ravichandiran proposed a vote of thanks. CSTM was particularly appreciated for their support in organizing the first seminar at CSTM.

- Dr. K. K. Datta while initiating made a small presentation on Rare Diseases Initiative in India – A Priority Agenda explained the background of the initiative and strongly advocated its public health importance.
- Rational epidemiological data on rare diseases globally are poor.
- Rare Diseases Institute estimates over 30 million people in the US suffer from rare.
- Despite the combined large number of people affected by rare and genetic diseases, only about 15% of rare diseases have organizations providing support or advocating for them.
  For too many patients with those diseases live their lives undiagnosed or with no potential treatments. They live without hope. There are approximately 7,500 rare disorders, several of them are life-threatening.
  Diagnosis is usually problematic and costly investigations are needed.
  Therapies are available only for a few Drugs available for treatment are nick named orphan drugs.
- Before the passage of the Orphan Drug Act in 1983 in USA, neither the pharmaceutical industry nor universities devoted much effort to research on rare diseases.
Important changes have occurred since then within and outside universities that position them to play a significant role in developing orphan drug.

Several approaches are in practice to promote drug-related research: disease-focused, discovery-focused, development-focused, and industry-partnership-focused approaches. However, several barriers challenge universities' ability to fully contribute to orphan drug development.

In India, 72 million people are estimated to be suffering from rare diseases, and only 6,000–8,000 rare diseases could be diagnosed, including Alzheimer, Norrie Disease, Arthrogryposis, Cystic Fibrosis, Wilson Disease, Phenyl ketone uria (PKU), acute intermittent porphyria etc., many of which still do not have any cure and are mostly genetic in nature.

Now India has developed an enviable network of great academic and research institutions with availability of large number of globally recognized scientists. Therefore academic and research institutions, along with industry, government, and not-for-profit organizations, should come forward to a common platform to address these issues around rare diseases.

Dr Subrata Dey, Senior Paediatric Endocrinologist and HOD Academics Paediatrics, Apollo Hospitals, Kolkata, presented a dazzling array of case cameos of rare disorders from his clinical practice and shared the challenges involved in the diagnosis and management of these cases. He gave a face to the concept of rare diseases with images of congenital hyperinsulinism, neonatal diabetes mellitus, osteogenesis imperfecta, hypophosphatemic rickets to name a few. The principal message was that rare disorders are not a single disease entity. There are over 7000 rare diseases described in global literature. One rare disease could be rare but all rare diseases together become a significant public health problem. “Alone we are rare. Together we are strong.”

Globally rare disorders have enjoyed advocacy in developed countries for the past three decades. NORD (National Organization of Rare Disorders) was founded in 1983 in USA to support
Dr. V. Ravichandiran, Director, NIPER-Kolkata, Dr. Ramaiah Muthyala, Minnesota University, USA & Prof. Samit Chattopadhyay, Director, CSIR-IICB, Kolkata

Round Table Conference of Rare Diseases Initiative at CSIR-IICB, Kolkata
individuals with rare diseases by advocating and funding research, education and networking among service providers. Indian Organization of Rare Diseases (I-ORD) was founded in 2005 to harness the strengths of various service providers and advocacy groups in India and advise the Government of India on the way forward.

Apollo Gleneagles being a very a large corporate super speciality hospital gets cases referred to a Paediatric Endocrinologist from a wide catchment area including North Eastern States. Most of the rare diseases he sees are of genetic origin with significant challenges in diagnosis and management. As a clinician his approach is to arrive at a clinical diagnosis obtain laboratory confirmation if available and administer treatment subject to availability and affordability of drugs. Laboratory confirmation of genetic diagnosis and drug management is exorbitantly costly. Therefore, without appropriate government support the issue of taking on rare diseases as a priority agenda will remain on paper and he is extremely happy and hopeful as well that Govt has come forward to offer some support to those who needs the same most. At this juncture the critical areas are laboratory confirmation and availability of drugs.

His prescriptions to the way forward are:

- Formation of a National Multidisciplinary Panel of Experts (Panel already constituted should function on a term basis)
- Diagnostic Support from National Research laboratories Genetic, Molecular, Biochemical & Microbiological is made available to confirm diagnosis. (He is happy to see that several important laboratories attended the meeting),
- NIPER should stream line drug availability & Orphan drug research and govt should take necessary steps to provide affordable treatment.

In conclusion only the government in partnership with relevant stake holders can provide relief to hundreds of thousands of
individuals 80% of whom are infants and children. The problem is of a staggering magnitude and deserves immediate attention and advocacy.

- Prof. Santanu Tripathy in his address drew attention of all stakeholders to come forward to put their efforts to support the program to move the govt to reach out to the patients of rare disorders with some support and indicated that he and CSTM will provide full technical support for the initiative.

In his address, he said that the Universal Declaration of Human Rights by the United Nations in 1948 acknowledged everyone’s ‘right to health and well being by means of medical care and social services, and the right to security in the event of sickness and disability’. Yet, millions of people worldwide are denied of such rights, just because the diseases they suffer are rare. It is the infrequency of their occurrence that the caregivers cannot easily recognise these diseases – and they keep on posing a diagnostic challenge. Again, since diagnosis is a problem, many patients tend to remain undiagnosed. This makes it difficult to correctly gauge the magnitude of the problem. More ironically, people afflicted with such diseases are not too many – just not enough to encourage the industry investing in research for developing their treatment. The patients are helpless and the governments seem clueless, unwitting accomplice to their woes and suffering. Rare diseases, therefore, are a problem not only to the patients and physicians, but to the health administrators, the policy makers, and the government, as well. Unfortunate that the issue has yet not received adequate attention in India; it is time we at least start talking about it. The objectives are to understand the problem of rare diseases in India and to explore the ways towards mitigating it.

Prof. Madhumita Dobe in her address detailed out public health perspectives of rare diseases disorders and explain how crucial to understand how the people view the problem and how do they view to address the issue and how to handle the stigma associated with the diseases apart from complexity in management of the
Prof. Santanu Tripathy, Professor, Experimental Medicine, CSTM, Kolkata
case from home and large cost involved. She talked about policy, Development of registers and databases to find out the magnitude of the problem, Organizational mandates, Diagnosis & record keeping, Mainstreaming into existing regulations, Awareness, finding the patients, General Practice, Community Practice, People. She talked about challenges to supportive environment. She talked about Rastrioya Bal Swasthaya Katakram early identification and early intervention for children from birth to 18 years to cover 4 ‘D’s viz. Defects at birth, Deficiencies, Diseases, Development delays including disability.

**District Early Intervention Centre (DEIC) level.**

First level of screening is done at all delivery points through existing Medical Officers, Staff Nurses and ANMs. After 48 hours till 6 weeks the screening of newborns will be done by ASHA at home as a part of Home Based New-born Care (HBNC) package.

Outreach screening will be done by dedicated Mobile Health teams for 6 weeks to 6 years at anganwadis centres and 6-18 years children at school.

30 selected health conditions for Screening, early detection and free management. States may also include diseases namely hypothyroidism, Sickle cell anaemia and Beta Thalassemia based on epidemiological situation and availability of testing and specialized support facilities within State and UTs. She suggested to screen selected Health Conditions for Child Health Screening & Early Intervention Services Defects at Birth Deficiencies

1. Neural tube defect
2. Anaemia especially severe anaemia
3. Down's Syndrome
4. Vitamin A deficiency (Bitot spot)
5. Cleft Lip & Palate / Cleft palate alone.
6. Vitamin D Deficiency, (Rickets)
7. Talipes (club foot)
8. Severe 8 acute Malnutrition.
9. Developmental dysplasia of the hip 10 Goiter
10. Congenital cataract
11. Congenital deafness
12. Congenital heart diseases
13. Retinopathy of Prematurity Diseases of Childhood Developmental delays and Disabilities
14. Skin conditions (Scabies, fungal infection)
15. Vision Impairment and Eczema)
16. Hearing Impairment
17. Otitis Media
18. Neuro-motor Impairment
19. Rheumatic heart disease
20. Motor delay
21. Reactive airway disease
22. Cognitive delay
23. Dental conditions
24. Language delay. She also mentioned about available data bases. She talked about adreno leuco dystrophy and its consequent on family life.


In fact rare disorders are not uniformly distributed. Silckle cell disease gene was first found in India at Nilgiris and thereafter extensive population survey found sickle cell disease gene is well
Prof. Ramaiah Muthyala, Associate Professor & Invited Expert, Minnesota University, USA
distributed in most parts of central India like Orissa, Madhya Pradesh, Maharashtra, Gujrat, North-east etc. particularly in tribal population. Quoting from online data base on Amyotrophic Lateral Sclerosis (ALS) mutations he provided data on onset and range, he said ALS is a rapidly progressive, invariably fatal neurological disease that attacks the nerve cells (neurons) responsible for controlling voluntary muscles (muscle action we are able to control, such as those in the arms, legs, and face). The disease belongs to a group of disorders known as motor neuron diseases, which are characterized by the gradual degeneration and death of motor neurons.

He specifically mentioned about Bubble Boy Disease a severe combined immunodeficiency syndrome 1 in 100,000 births in USA; 1 in 65000 in Australia, 1 in 2500 Navsjo; similar genetic pattern in Apache People.

Explaining the difference between rare and common diseases he said rare diseases typically occur in a young population, they usually occur with a Mendelian pattern of inheritance, often occur as syndromes, involving several organs or physiologic systems, often in surprising ways, environmental factors play no or little role in the inherited rare diseases, there are many rare diseases and rates of occurrence of the rare diseases—high; whereas common diseases typically occur in adults, increasing in frequency with age, the most common diseases may sometimes cluster in families, but they are without exception, non-Mendelian, most common diseases are non-syndromic, environmental factors play a major role in the cause of common diseases, there are few common diseases and rate of occurrence of common diseases - low.

Following the rare disease initiative in USA some good things happened:

Encourages the development of drug therapies for diseases that affect fewer than 200,000 people in the USA (6.6/10,000).

or

Diseases for which sales in the USA are unlikely to recoup R&D costs.

Office of Rare Diseases Research execute Research Activities related to Phase II and Phase III administer grants.

He further stated that there are about 7000 rare diseases in the USA affecting 25-30 million people at any given point of time. Movement in USA was followed by other countries: 2000 in the EU; 1997 in Australia; 1993 in Japan; 1991 in Singapore.

**Most of the Rare Diseases have Genetic Origin**

He then detailed out the magnitude and some epidemiological details concerning rare disease:

- 18 – 25 Million People in the USA with one of > 6500 Genetic and Acquired Rare Diseases;
- 30 Million People in European Union
- 6%-8% of Population have a Rare Disease

While stating what constitutes a rare disease he said:

- Prevalence < 200,000 people in the USA and Prevalence < 5 in 10,000 people in the EU are considered as a rare disease

He then further outlined the problems around rare diseases:

- Obtaining the Diagnosis –
  - <1 year - 51% Diagnosed
  - >1 year but <5 Years – 31% Diagnosed
  - >5 years – 15% Diagnosed
  - 6% of Requests to GARD for Undiagnosed Diseases
Panel Discussion on Rare Diseases Initiative meet at Hotel Gateway, Kolkata

Dr. V. Ravichandiran, Director, NIPER-Kolkata, Dr. V. Nagarajan, Professor, The TN Dr. MGR Medical university & Dr. P. Jaisankar, Sr. Principal Scientist, CSIR-IICB
Against the backdrop of very few people who are suffering, availability of scanty information, poor research support, non-availability of treatment, limited access to of rare disease focused clinicians and little or no hope for the future we need to act and outlined the way forward:

- Expand Newborn Screening Programs in States ~ 29 Diseases.
- Increase Development of Genetic and Diagnostic Tests with Appropriate Counselling and Sequencing Programs.
- Require Phenotype and Genotype Correlations.
- Need Better Diagnostic Criteria for Rare Diseases
- Perceptions Surrounding Rare Diseases
- Meeting Patient and Family Needs.
- Expand Informational and Educational Training Programs on Living and Coping with Rare and Genetic Diseases.
- Gain Acceptance for Disabilities and Improving Educational Opportunities for Patients.
- Maximize Access to Rehabilitation Therapies – Physical, Hearing, Speech, Vocational, Occupational, and others.
- Assure Worldwide Access to Safe and Effective Products for the Prevention, Diagnosis, and Treatment of Rare Diseases.
- Gaining Access To Knowledgeable Physicians And Other Health Care Providers.
- Knowing There Are Other Families Living With The Disease – Avoiding Stigmatization.
- Understanding the Process. Going From Life As We Knew It To Life As It's Going To Be.
- Meeting Patients And Families Where They Are And Not Try To Rush Them.

Prof Ramaiah also mentioned about frequently asked questions on Rare Diseases.

- Where Can I Find Information On Symptoms, Cause, Diagnostic Testing, Treatment, Heritability?
- Are There Support Groups Available?
- How Can I Get Financial Assistance?
- Are There Research Or Clinical Trials Available?
- How Can I Find An Expert?
- How Many People Have This Disease?

While explaining his vision to where we want to be he talked about Priority Review Voucher (PRV) to

- Encourage Research and Development for the World’s Neglected Tropical diseases (17 of them).
- PRVs as low cost solution to inspire drug companies to create new drugs that address the unmet needs of developing nations without additional cost to tax payers.
- The FDA will award a priority review voucher (PRV) to the sponsor of a newly approved drug or vaccine that targets a neglected disease or rare disease

Panel Discussions

Dr. Shaymal Roy, Principal Senior Scientist from IICB moderated the first panel discussion and the panellists were -

Prof. Nagarajan, Neurologist (TN Dr. MGR Medical University), Dr Sameer Bakhshi, Pediatric Oncologist (AIIMS), Dr. V. R. Ramanan, Surgical Oncologist (TMC, Kolkata), Prof. Manoj Singh, Pathologist (AIIMS), Dr. D. P. Sinha, Cardiologist (PG.Kolkata), Dr. Surinder Singh, Microbiologist (NIB), raised issues from clinical perspectives

Initiating the panel discussion. Prof. Bakhshi said that every case of pediatric cancer should be under the category of Rare Disease. However there is no definition available in the context of India.

The issue of categorizing rare disease was taken up. Existing definition of rare disease in different countries was discussed. Prof. Nagarajan intervened and asked whether we need categorization. Prof. Ramaiah stated that definition in USA follows primarily what could be the number that will take care that drug industry do not run into loss. He reiterated US definition less than 2000000 at any given point of time on the entire country of USA. However majority opined India should have its own definition. In this regard WHO definition could be adopted. Dr.K.K.Datta in a brief intervention said any disease which is less than 1 per thousand is considered to have ceased to be a public health problem. We may consider I
case for less 2,000 population may be considered. We may put up the definition in website for wider acceptance.

Dr. Ramanan in his intervention said that from oncology perspective no clinical data is available under the category of rare diseases. About 1300 rare cancers are known but no drugs. Clinicians can hardly do anything. He informed TMC has a good laboratory set up and could perhaps help.

Dr Manoj Singh lauded the efforts of NIPER-Kolkata and assured that all assistance from his will be available and AIIMS may provide significant input to the data registry.

Dr Dey in his intervention suggested that NORD data base could be used till Indian data base is fully established. 90 % of cases are of genetic origin. Focus of the initiative should be that people know that in case of such diseases where they should go. Treatment with growth hormone is costly. Good photos of the case may be used for initial diagnostic tool.

Dr Surinder Singh in his intervention stressed on policy and strategy issues if the initiative is to meet its logical end. If NIPER wants to establish a registry NIB will be able to support its IT requirements. The initiative should have some visibility in public domain to enhance awareness amongst general population.

NIPER with the help of pharmaceutical industry should move forward to take on the issue of orphan drug act in India so that pharmaceutical industry can get some extra facility like relaxation of duties and licensing requirements and exclusive marketing rights. NIPER Kolkata may identify the molecules and motivate pharmaceutical companies for R& D. Drugs are required to be produced in the country to make available the drugs at an affordable cost. We may take up preparation of essential drugs for rare diseases in the country. Such meetings are to be held in different locations of the country and NIPER- Kolkata should take a lead in this.

Dr. D. P. Sinha in his intervention said that he sees a lot of rare cases. NIPER should take up R&D work for drug development on
a small scale and once the technology is available transfer to the industry.

Ds should be remembered: Definition of diagnosis, Drugs, Data, Defects at birth, Deficiencies, Diseases, Development delays including disability.

Dr. Arul Narayanan in his intervention said importance of documentation and R&D to bring it to the notice of the Govt for policy inclusion. The Group could consider including Rare Disease Initiative in its upcoming policy document. Issues like tax exemption, CSR, mediclaim insurance provision, Students and clinicians for case detection and diagnosis, inclusion in medical curriculum, NIPER Kolkata be given the responsibility of coordinating Rare Disease registry like ICMR doing it for cancer.

Dr. Sameer Bakhshi said Rare Disease could be broadly categorised commoner rare disease and very rare diseases. He also said definition should not address the industry requirements it should address the needs of clinicians.

Dr. Shanta Datta brought to the notice of the house the criticality of diagnostic issues.

Andrew from CSTM said issues like definition, catalogue / classification, drug availability are important including R&D. NIPER could act as a focal point of surveillance.

2nd Panel

2nd panel discussions was moderated by Dr. Ramaiah Muthyala and panellists were Dr. Prof. Santanu Tripathy (CSTM), Dr. Siddharta Ray (Bose Institute) and discussants were Dr. Rravichandiran, (NIPER-Kolkata), Dr. Jaisankar (IICB) and Dr. C. M. Ghosh (Drug Controller,West Bengal) – Pharmaceutical and Biomedical perspective.

Dr. Shanta Datta said most of the Rare Diseases are of genetic origin - 2nd requires 2\textsuperscript{nd} generation sequencing. Use available facilities forth diagnostic support needed and look for higher diagnostic
Panel Discussion on Rare Diseases Initiative meet at Hotel Gateway, Kolkata
support where needed, Dr. Dey said that he gets so many types of autism and drugs are so difficult to procure.

Dr. P. Jaisankar pointed out the need for documentation. Dr. V. Ravichadiran in his intervention said challenges in documentation is charting out relevant epidemiological data region wise 7500 rare disorders. We may take up to do so for West Bengal and North-East to start with. Diagnostic support available and needed for each disorder to be worked out and thereafter rare disorders are to be short listed for interventions that are available and also could be possible and thereafter identify priority research and development inputs which NIPER could take up or the industry could be approached.

Prof. Nagarajan said approach the physicians for the data. R&D component may have to think of genetic engineering. Regulatory authority may address the needed issues with regard to Orphan drug act. Stem cell bank could be established and it may open up meeting the challenges of treatment. Dr. Subhra Basu talked about the need of data, advocacy and needed diagnostic support.

Dr. Surinder Singh talked about the self-sufficiency in ASV production which is now available at an affordable price. CRI Kasauli led the foundation in this direction. He also said that the available data should be opened up to facilitate the understanding of the problem.

Round table discussion

Moderator – Dr. Ramaiah Muthyala, Minnesota University, USA

The members, after careful and elaborate discussions and exchange of views amongst themselves prepared the tentative Course Curriculum including indicative course content for Post-Graduate students of NIPER-Kolkata.

Course Contents:

(a) Rare Diseases History:
(b) Challenging Management
(c) Strategies to address Challenges.
(d) Research Gaps.
(e) Access to Treatment
(f) Reaching out to the Patients.
(g) Assignments.

Chapter I

Rare Disease History

Introduction
Global History of the Rare diseases.
Indian Perspectives
Genesis of Rare Diseases Movement
Geographical Distribution of rare Diseases
Definition, how they are different from common diseases.

Classification and causes - genetic, non-genetic and acquired.
Diagnosis - Current Status, Clinical diagnosis and Laboratory Diagnosis
Communication, Misconceptions.

Chapter – II

Challenging Management
Diagnosis – Clinical, Laboratory, Family, Policy (Review and India scenario)
Community – Myths and misconception, stigma/dis-communication
Support groups – Rehabilitation
Pharmaceutical Challenges
Logistics

Chapter – III

Strategies to address the challenges
Drug discovery
Theranostis
Biomarkers
Companion Diagnostics
Information, Education, Communication
Dr. V. Ravichandiran, Director, NIPER-Kolkata & Dr. Sameer Bakhshi, Professor, AIIMS, New Delhi

Dr. Santanu Tripathy, Professor, CSTM, Kolkata, Dr. Ramaiah Muthyala, Minnesota University, USA & Prof. Siddhartha Roy, Dean, Bose Institute, Kolkata
Management – Family and Community based management, Clinical and Drug based management, Technology based management, Genetic counselling.
Policies – Advocacy

Chapter – IV

Research Gaps
Review of current status
Identification of the gaps
Non-availability of data
Current Research Priorities
Epidemiological
Biomarker development
Screening, strategy development
Drug discovery targets
Psychosocial and behavioural

Chapter – V

Access to Treatment
Current Status
Availability
Strategies for facilitating access

Chapter – VI

Reaching out to the patient community
Engaging the community
Awareness and sensitisation
Building Patient groups
Patient Rights and Responsibility

Chapter – VII

Assignments

Khan Academy

Dr Kuntal Biswas talking about definition
• There is no Universal definition.
• It varies from country to country.
• A disease or disorder is defined as rare in Europe when it affects fewer than 1 in 2000.
• A disease or disorder is defined as rare in USA when it affects fewer than 200,000 Americans at any given time.
• WHO considers it as a Rare Disease when it affects at-least 1 in 1000.
• Over 8000 rare diseases are characterized by a broad diversity of disorders and symptoms that vary not only from disease to disease but also from patient to patient suffering from the same disease.
• 80% of rare diseases have identified genetic origins whilst others are the result of infections (bacterial or viral), allergies and environmental causes, or are degenerative and proliferative.
• 50% of rare diseases touch children.
• Rare diseases are characterized by a broad diversity of disorders and symptoms that vary not only from disease to disease but also from patient to patient suffering from the same disease.

• Codification means a disease is assigned an individual code so that it can be easily recognized within a health information system.
• A health information system is a group of IT tools; databases and procedures related to patient cases and diseases and are used to make decisions to improve treatment, research, care and healthcare management.
• Codification allows healthcare professionals to store, aggregate and search for disease information in a faster and easier way.

While talking about guiding action
• Rare Diseases should be traceable in mortality and morbidity information systems
• There are two categories of RD
  – The récurrent RD (1,500 to 2,000)
    • should have a specific code in ICD11
  – The ultra rare (around 4,000)
    • should be coded as «other specific RD » within relevant subcategory but indexed

While talking about benefits for codification
Dr. V. Ravichandiran, Director, NIPER-Kolkata, Dr. P. Jaisankar, Sr. Principal Scientist, CSIR-IICB, Kolkata, Dr. S.B. Mandal, Dean, NIPER-Kolkata & Dr. T.K. Dhar, Dy. Registrar, NIPER-Kolkata

Dr. Ramaiah Muthyala, Minnesota University, USA
• The 2009 Council Recommendation on an Action in the field of Rare Diseases refers to improved codification of rare diseases as a priority.
• Effective codification can make it easier to identify and diagnose a patient's disease.
• Effective codification of each individual rare disease can help to ensure that no rare disease, and as a result no rare disease patient, is lost within a healthcare system.
• The data retrieved through codification can also be used in much-needed rare disease clinical research and also for national healthcare services to better perform epidemiological studies and to better plan their services.

There are several existing codification systems. Among them the most important are:
• The World Health Organization’s International Classification of Diseases (ICD) came into use as a morbidity classification system in 1949.
• **Nearly 500 rare diseases have a specific code in the ICD10.**
• The Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) is run by the International Health Terminology Standards Development Organization and is available in over 50 countries.
• **Nearly 3000 rare diseases have a specific SNOMED CT code.**

ICD -10 are being revised and ICD 0ii is coming up.

1. **Definition of the classification entity:**
   • *medical disease, disorder (syndrome), injury, sign, symptom, …*
   1. Clustering of signs, symptoms, & operational features
   2. Link to underlying pathophysiology & genetic markers
   3. Clinical utility of the classification entity
   4. Reliability of the classification entity
   5. Validity of the classification entity
   6. Separation of disease and disability elements
   7. Cultural elements that need to be attended
   8. Threshold considerations
   9. Other nosological issues relevant to this disorder
While talking about ORPHANET

- It is the most comprehensive online database of rare diseases.
- The Orpha codes system is designed based on Orphanet data.
- Each of the nearly 7000 rare diseases listed on the Orphanet website has an Orpha code, meaning a larger number than those rare diseases that have either an ICD or SNOMED CT code.
- Collaboration between the organizations behind these three systems is continuously underway to ensure that they contain comparable data. The European Commission is also supporting the revision process of the ICD to ensure that more rare diseases will have a code in ICD11, possibly all of those already coded within Orphanet.

Recent progress made in this regard:

In November 2014 a recommendation on ways to improve Codification for Rare Diseases in Health Information Systems was adopted by the EU Commission Expert Group on Rare Diseases.

- The document includes a recommendation to further promote Orpha codes within the development of ICD11, in order to allow a seamless transition of rare disease classification from Orpha codes to ICD11 when the latter is released.

While concluding

- Possibility to propose a profound evolution of the organisation of chapters II to XVIII
  - With a possible migration of almost all existing codes
  - With a common logics applied to all chapters
  - Putting rare diseases where they should be
    - Everywhere as a lower node
- Cross- mapping data sets allows
  - To identify mistakes and improve coding
  - To identify ICD-10 problems, i.e.
    - Need for categories rearrangement
    - Need for more specific categories, better reflecting homogeneous groups of rare diseases
Dr. Ramaiah Muthyala then presented some important requirement of the registry from his US experience

<table>
<thead>
<tr>
<th>Item</th>
<th>Common Data elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>First Name</td>
</tr>
<tr>
<td>2</td>
<td>Last Name</td>
</tr>
<tr>
<td>3</td>
<td>Middle Name</td>
</tr>
<tr>
<td>4</td>
<td>Street Address</td>
</tr>
<tr>
<td>5</td>
<td>City</td>
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<tr>
<td>6</td>
<td>State</td>
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<tr>
<td>7</td>
<td>Zip code</td>
</tr>
<tr>
<td>8</td>
<td>Email</td>
</tr>
<tr>
<td>9</td>
<td>Phone</td>
</tr>
<tr>
<td>10</td>
<td>Registrar (person entering the data)</td>
</tr>
<tr>
<td>11</td>
<td>Registrar - Relationship to patient</td>
</tr>
<tr>
<td>12</td>
<td>Consent</td>
</tr>
<tr>
<td>13</td>
<td>Date of Birth</td>
</tr>
<tr>
<td>14</td>
<td>Vital status (Dead or alive)</td>
</tr>
<tr>
<td>15</td>
<td>If dead when</td>
</tr>
<tr>
<td>16</td>
<td>Sex</td>
</tr>
<tr>
<td>17</td>
<td>Religion</td>
</tr>
<tr>
<td>18</td>
<td>Caste</td>
</tr>
<tr>
<td>19</td>
<td>Health insurance coverage</td>
</tr>
<tr>
<td>20</td>
<td>Patient education level</td>
</tr>
<tr>
<td>21</td>
<td>Family income</td>
</tr>
<tr>
<td>22</td>
<td>Disease (rare) diagnosis</td>
</tr>
<tr>
<td>23</td>
<td>Age at diagnosis</td>
</tr>
<tr>
<td>24</td>
<td>Diagnosis testing</td>
</tr>
<tr>
<td></td>
<td>Description</td>
</tr>
<tr>
<td>---</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>25</td>
<td>Age of Symptom onset</td>
</tr>
<tr>
<td>26</td>
<td>Rare Disease Family history (which family member has)</td>
</tr>
<tr>
<td>27</td>
<td>Birth weight</td>
</tr>
<tr>
<td>28</td>
<td>Term Delivery</td>
</tr>
<tr>
<td>29</td>
<td>Premature Gestational Age at birth</td>
</tr>
<tr>
<td>30</td>
<td>Number of pregnancies</td>
</tr>
<tr>
<td>31</td>
<td>Number of live births</td>
</tr>
<tr>
<td>32</td>
<td>Number of Living children</td>
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<tr>
<td>33</td>
<td>Participant weight</td>
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<tr>
<td>34</td>
<td>Age for weight (at what age this weight is)</td>
</tr>
<tr>
<td>35</td>
<td>Height</td>
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<tr>
<td>36</td>
<td>General health</td>
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<tr>
<td>37</td>
<td>Physical functioning</td>
</tr>
<tr>
<td>38</td>
<td>Pain</td>
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<tr>
<td>39</td>
<td>Depression</td>
</tr>
<tr>
<td>40</td>
<td>Fatigue</td>
</tr>
<tr>
<td>41</td>
<td>Medical foods</td>
</tr>
<tr>
<td>42</td>
<td>Special diet</td>
</tr>
<tr>
<td>43</td>
<td>Previous surgeries</td>
</tr>
<tr>
<td>44</td>
<td>Hospitalization (recent, or how many times in a year)</td>
</tr>
<tr>
<td>45</td>
<td>Assistive device</td>
</tr>
<tr>
<td>46</td>
<td>Source of record (which hospital)</td>
</tr>
</tbody>
</table>
Dr. Subhash Mandal, Assistant Director, Drugs Control Department, Govt. of West Bengal

Dr. Andrew Zurde, an Expert of Rare Diseases Initiative
RECOMMENDATIONS

Based on the above deliberations and interactive intense discussions the recommendations of the meeting and carrying RDI forward are:

The initiative is laudable, timely and every one complimented Department of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India and NIPER-Kolkata for the same. The New health policy of the country is under finalization. Perhaps it is appropriate to include a small paragraph on rare diseases in the new health policy. NIPER-Kolkata may draft a paragraph based on the deliberations and send it to Department of Pharmaceuticals for onward transmission to the Union Ministry of Health for its inclusion.

Considering Rational epidemiological data on rare diseases globally are poor and In India, 72 million people are estimated to be suffering from rare diseases, where as only 6,000–8,000 rare diseases could be diagnosed leaving far too many patients with those diseases live their lives undiagnosed or with no potential treatments, living without hope. Rare Diseases victims require some attention.

There are approximately 7,500 rare disorders, several of them being life-threatening and diagnostic support being not widely available and un-affordable, therapies being available for few, rare diseases victims need some organised support from the Govt.

- Before the passage of the Orphan Drug Act in 1983 in USA, neither the pharmaceutical industry nor universities devoted much effort to research on rare diseases.

- Important changes have occurred since then within and outside universities that position them to play a significant role in developing orphan drug
Several approaches are in practice to promote drug-related research: disease-focused, discovery-focused, development-focused, and industry-partnership-focused approaches. However, several barriers challenge universities' ability to fully contribute to orphan drug development.

Now India has developed an enviable network of great academic and research institutions with availability of large number of globally recognized scientists. Therefore academic and research institutions, along with industry, government, and not-for-profit organizations, should come forward to a common platform to address these issues around rare diseases.

The principal message was that rare disorders are not a single disease entity. There are over 7500 rare diseases described in global literature. One rare disease could be rare but all rare diseases together become a significant public health problem. “Alone we are rare. Together we are a large number.” And therefore left uncared for.

Globally rare disorders have enjoyed advocacy in developed countries for the past three decades. NORD (National Organization of Rare Disorders) was founded in 1983 in USA to support individuals with rare diseases by advocating and funding research, education and networking among service providers.

Indian Organization of Rare Diseases (I-ORD) was founded in 2005 to harness the strengths of various service providers and advocacy groups in India. However, we are way behind in our efforts compared to advanced countries.

Clinicians in big corporate and govt hospital see many rare diseases and most are of genetic origin with significant challenges in diagnosis and management. As a clinician his approach is to arrive at a clinical diagnosis obtain laboratory confirmation if available and administer treatment subject to availability and affordability of drugs. Laboratory confirmation of genetic diagnosis and drug management is exorbitantly costly. Therefore without
appropriate government support the issue of taking on rare diseases as a priority agenda will remain on paper until Government comes forward:

- Formation of a National Multidisciplinary Panel of Experts (Panel already constituted should function on a term basis)

- Diagnostic Support from National Research laboratories Genetic, Molecular, Biochemical & Microbiological be made available to confirm diagnosis. (he is happy to see that several important laboratories attended the meeting)

- NIPER should streamline drug availability & Orphan drug research and govt should take necessary steps to provide affordable treatment

Only the government in partnership with relevant stake holders can provide relief to hundreds of thousands of individuals 80% of whom are infants and children. The problem is of a staggering magnitude and deserves immediate attention and advocacy.

Dr. Ramaiah said that following the rare disease initiative in USA some good things happened. He expects similar things will happen in India as well. Drug controller may bring Orphan drug act which is a potent al instrument for enhancing R&D and drug development.

- Expand Newborn Screening Programs in States ~ 29 Diseases
- Increase Development of Genetic and Diagnostic Tests with Appropriate Counselling and Sequencing Programs
- Require Phenotype and Genotype Correlations
- Need Better Diagnostic Criteria for Rare Diseases
- Perceptions Surrounding Rare Diseases
- Meeting Patient and Family Needs
- Expand Informational and Educational Training Programs on Living and Coping with Rare and Genetic Diseases
- Gain Acceptance for Disabilities and Improving Educational Opportunities for Patients
- Maximize Access to Rehabilitation Therapies – Physical, Hearing, Speech, Vocational, Occupational and others.
- Assure Worldwide Access to Safe and Effective Products for the Prevention, Diagnosis, and Treatment of Rare Diseases
- Gaining Access To Knowledgeable Physicians And Other Health Care Providers
- Knowing There Are Other Families Living With The Disease – Avoiding Stigmatization
- Finding Useful Information On A Gradual Basis – The Building Blocks For Decision Making
- Understanding the Process. Going From Life As We Knew It To Life As It's Going To Be
- Meeting Patients And Families Where They Are And Not Try To Rush Them

Prof. Ramaiah also mentioned about frequently asked questions on rare diseases

- Where Can I Find Information on Symptoms, Cause, Diagnostic Testing, Treatment, Heritability?
- Are There Support Groups Available?
- How Can I Get Financial Assistance?
- Are There Research Or Clinical Trials Available?
- How Can I Find An Expert?
- How Many People Have This Disease?

While explaining his vision to where we want to be he talked about priority review voucher (PRV) to

- Encourage Research and Development for the World’s Neglected Tropical diseases (17 of them).
- PRVs as low cost solution to inspire drug companies to create new drugs that address the unmet needs of developing nations without additional cost to tax payers.
- The FDA will award a priority review voucher (PRV) to the sponsor of a newly approved drug or vaccine that targets a neglected disease or rare disease.

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The FDA will award a priority review voucher (PRV) to the sponsor of a newly approved drug or vaccine that targets a neglected disease or rare disease.

Universal Declaration of Human Rights by the United Nations in 1948 acknowledged everyone’s ‘right to health and well being by means of medical care and social services, and the right to security in the event of sickness and disability’. Yet, millions of people worldwide are denied of such rights, just because the diseases they suffer are rare. It is the infrequency of their occurrence that the caregivers cannot easily recognise these diseases – and they keep on posing a diagnostic challenge. Again, since diagnosis is a problem, many patients tend to remain undiagnosed. Rare diseases, therefore, are a problem not only to the patients and physicians, but to the health administrators, the policy makers, and the government, as well. The issue has yet not received adequate attention in India; it is time we at least start talking about it. The objectives are to understand the problem of rare diseases in India and to explore the ways towards mitigating it.

Health policy: Development of registers and databases to find out the magnitude of the problem, Organizational mandates, Diagnosis & record keeping, Mainstreaming into existing regulations, Awareness, finding the patients, General Practice, Community Practice, People’s perception need to be understood. Challenges to supportive environment are very crucial to be examined and taken care of. Rastrioya Bal Swasthaya Karyakram to early identify and early intervene for children from birth to 18 years to cover 4 ‘D’s viz. Defects at birth, Deficiencies, Diseases,
Development delays including disability at District Early Intervention Centre (DEIC) level.

First level of screening is done at all delivery points through existing Medical Officers, Staff Nurses and ANMs. After 48 hours till 6 weeks the screening of newborns will be done by ASHA at home as a part of Home Based New-born Care (HBNC) package.

Outreach screening will be done by dedicated Mobile Health teams for 6 weeks to 6 years at anganwadis centres and 6-18 years children at school. Rare diseases should be considered in the package.

30 selected health conditions for Screening, early detection and free management. States may also include diseases namely hypothyroidism, Sickle cell anaemia and Beta Thalassemia based on epidemiological situation and availability of testing and specialized support facilities within State and UTs. She suggested to screen selected Health Conditions for Child Health Screening & Early Intervention Services Defects at Birth Deficiencies Available data bases should be tapped.

**Panel discussions recommendations**

Definition of rare diseases: Different countries have different case definition; speakers suggested for no definition to industry friendly definition. But majority desired to have an India specific definition considering clinical and India policy requirements. Consensus was less than one case in 2500 population and the group left it to NIPER to draft a suitable paragraph and put it on the website for wider acceptance. The group was emphatic: Definition should not address the industry requirements it should address the needs of clinicians.

From oncology perspective no clinical data is available under the category of rare diseases. About 1300 rare cancers are known but no drugs. Clinicians can hardly do anything. TMC has a good laboratory set up and could perhaps of help.
AIIMS may provide significant input to the data registry which should be established.

NORD data base could be used till Indian data base is fully established. 90% of cases are of genetic origin. Focus of the initiative should be that people know that in case of such diseases where they should go. Treatment with growth hormone is costly. Good photos of the case may be used for initial diagnostic tool.

Policy and strategy issues if the initiative is to meet its logical end. If NIPER wants to establish a registry NIB will be able to support its IT requirements. The initiative should have some visibility in public domain to enhance awareness amongst general population.

NIPER with the help of pharmaceutical industry should move forward to take on the issue of Orphan drug act in India so that pharmaceutical industry can get some extra facility like relaxation of duties and licensing requirements and exclusive marketing rights. NIPER Kolkata may identify the molecules and motivate pharmaceutical companies for R&D. Drugs are required to be produced in the country to make available the drugs at an affordable cost. We may take up preparation of essential drugs for rare diseases in the country. Such meetings are to be held in different locations of the country and NIPER-Kolkata should take a lead in this.

A lot of rare cases come to clinical establishments. NIPER should take up R&D work for drug development on a small scale and once the technology is available transfer to the industry.

Ds should be remembered: Definition diagnosis, drugs, data. Defects at birth, Deficiencies, Diseases, Development delays including disability.

Importance of documentation and R&D to bring it to the notice of the Govt for policy inclusion. The Group recommended including rare disease initiative in its upcoming policy document. Issues like tax exemption, CSR, mediclaim insurance provision, Students and clinicians for case detection and diagnosis, inclusion in medical
curriculum, NIPER Kolkata be given the responsibility of coordinating Rare disease registry like ICMR doing it for cancer.

**Criticality of diagnostic issues**

Definition, catalogue/classification, drug availability are important including R&D. NIPER could act as a focal point of surveillance.

**2nd Panel recommendations**

Rare disease are of genetic origin that requires 2\textsuperscript{nd} generation sequencing. Use available facilities for the diagnostic support needed and look for higher diagnostic support where needed,

The need for documentation should be addressed.

Challenges in documentation are charting out relevant epidemiological data region wise 7500 rare disorders. We may take up to do so for West Bengal and north east to start with. Diagnostic support available and needed for each disorder to be worked out and thereafter rare disorders are to be short listed for interventions that are available and also could be possible and thereafter identify priority research and development inputs which NIPER could take up or the industry could be approached.

Approach the physicians for the data. R&D component may have to think of genetic engineering. Regulatory authority may address the needed issues with regard to Orphan drug act. Stem cell bank could be established and it may open up meeting the challenges of treatment.

Need of data base should be addressed, advocacy and needed diagnostic support should be attended to

Available data should be opened up to facilitate the understanding of the problem.

**Round table discussion**

Tentative Course Curriculum including indicative course content for Post-Graduate students of NIPER-Kolkata.
Course Contents:

Rare Diseases History:

Challenging Management
Strategies to address Challenges
Research Gaps
Access to Treatment
Reaching out to the Patients
Assignments

Chapter I

Rare Disease History; Contents

Introduction
Global History of the Rare Diseases
Indian Perspectives
Genesis of Rare Diseases Movement
Geographical Distribution of rare Diseases
Definition, how they are different from common diseases

Classification and causes - genetic, non-genetic and acquired
Diagnosis-Current Status, Clinical diagnosis and Laboratory Diagnosis
Communication, Misconceptions

Chapter – II

Challenging Management

Diagnosis – Clinical, Laboratory, Family, Policy (Review and India scenario)
Community – Myths and misconception, stigma / dis-communication
Support groups – Rehabilitation
Pharmaceutical Challenges
Logistics
Chapter – III

Strategies to address the challenges

Drug discovery
Theranostics
Biomarkers
Companion Diagnostics
Information, Education, Communication
Management – Family and Community based management, Clinical and Drug based management, Technology based management, Genetic counselling.
Policies – Advocacy

Chapter – IV

Research Gaps

Review of current status
Identification of the gaps
Non-availability of data
Current Research Priorities
Epidemiological
Biomarker development
Screening, strategy development
Drug discovery targets
Psychosocial and behavioural

Chapter – V

Access to Treatment
Current Status

Availability
Strategies for facilitating access

Chapter – VI

Reaching out to the patient community
Engaging the community
Awareness and sensitisation
Building Patient groups
Patient Rights and Responsibility
Draft content of course curriculum has been worked out and NIPER academic team to convert into syllabus into hours limited to 50-60 hours etc matching NIPER academic standard.

Chapter – VII

Assignments

Recommendations of data registration session

ORPHANET

- It is the most comprehensive online database of rare diseases.
- The Orpha codes system is designed based on Orphanet data.
- Each of the nearly 7000 rare diseases listed on the Orphanet website has an Orpha code, meaning a larger number than those rare diseases that have either an ICD or SNOMED CT code.
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Recent progress made in this regard:

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- The document includes a recommendation to further promote Orpha codes within the development of ICD11, in order to allow a seamless transition of rare disease classification from Orpha codes to ICD11 when the latter is released.'
While concluding

- Possibility to propose a profound evolution of the organization of chapters II to XVIII
  - With a possible migration of almost all existing codes
  - With a common logics applied to all chapters
  - Putting rare diseases where they should be
- Cross-mapping data sets allows
  - To identify mistakes and improve coding
  - To identify ICD-10 problems, i.e.
- Need for catégories réarrangement
- Need for more specific categories, better reflecting homogeneous groups of rare diseases

Presented some important requirement of the registry from his US experience

The group concluded that NIPER Kolkata team works further on the same and draft a rare disease registry format for consideration in Indian context in the pattern of Cancer Registry and NIPER Kolkata may take up the initiative of establishing a rare disease registry.