A Journey Together: Rare Diseases and Orphan Products in India

I am not alone.....

INDIAN ORGANIZATION FOR RARE DISEASES
March 20, 2015

Indian Organization for Rare Diseases, Plot No. 397, Road 22B, Jubilee Hills, Hyderabad, Telangana – 33,
E-mail ID info@i-ord.org | www.I-ORD.org
A Journey Together: Rare Diseases and Orphan Products in India

Prolog

Until early 1980s, patients with rare diseases in any country on the globe were not included on the agenda of their governments. Patient organizations around the world gave not only a voice to the needs of rare diseases individuals, but also contributed to the consideration of rare diseases as a public health problem. This approach led to the creation of numerous official programs directed at assisting patients and the advent of economic and regulatory incentives for the sponsors of the orphan drug developers. Even after 35-40 years of progress elsewhere in the world, in India even the basic issues such as the definition of rare diseases, the cost of medications to treat these patients etc., have not been addressed. The main challenges in India is balancing the needs and adequately address the demands of patients and the rising costs in the industry due to scientific and technological advancement. In India, there are no effective and safe treatments for many rare diseases and several barriers hinder patient access to specialized treatments and drugs. There is insufficient research and information about these diseases; professionals are in need of training and education which otherwise compromising and delaying diagnosis. Within this complex scenario – a true challenge for health authorities and all segments involved in rare diseases issues exists.

In this document we discuss the national agenda for rare diseases.

In support of a National Policy for Rare Diseases in India, IORD presents a roadmap. Many countries have already established national policies. Therefore we sought the assistance of external experts (former US NIH, FDA executives) to study the size of the
problem, to gather successful examples from their countries, to objectively define the priorities and match the needs of India. It becomes clear, as of now, India does not have an articulated rare diseases policy. It became apparent that without this policy, good intentions are misunderstood. These led to the understanding that the government gives priority to cost, assume that the information has on file has far from reality, government’s neglect is due to lack of sensitivity for the suffering of patients with rare diseases etc. From both the government and society; there is a perception that the solution to these issues will come through the courts. Such misconceptions unfortunately amplify uncertainty and insecurity. We believe a National Policy for Rare Diseases will make everyone to commit to the treatments in a fair and sustainable manner. In addition, we will follow up this effort with a series of activities and events, including seminars and discussions with officials from the central, state and local governments, scientists, industry, patients etc. We wish to contribute to the debate, collaborate with policy makers and help to expand access to treatments to the rare diseases patients. We hope to achieve these goals in very near future.

Ramaiah Muthyala

Ramaiah Muthyala, Ph.D.
President/CEO
Indian Organization for Rare Diseases
A journey Together: Rare Diseases and Orphan Products – India

- Rare Diseases – Global perspective
- Rare Diseases, Orphan products, opportunities – India
- Lessons learned from the experiences of other countries
- Commitment from policy makers
- Expectations and limitations of societal needs
- Power of patient advocacy groups
- Research consortiums
- Orphan product regulations
- Development of National policy for rare diseases
A Journey Together: Rare Diseases and Orphan Products in India

Background

There are more than 7,000 genetic and acquired rare diseases affecting approximately 6% to 8% of the population. This is nearly 18 to 25 million people with a rare disease in the United States with an estimated population of 315 million people. The European Union, comprised of 28 member states, has a total population of nearly 507 million people and has approximately 30-40 million people with a rare disease. There is no universal definition of a rare disease or condition. Based on the interpretation of needs of each country or government, the definition of “rare disease” was determined. A rare disease is defined as a disease with a prevalence of fewer than 200,000 persons in the USA. In the European Union, a rare disease is defined as one with a prevalence of 5/10000 people. In Australia a condition affecting 2,000 patients or less in the Australian population is considered to be a rare disease and in Japan the legal definition of a rare disease is one that affects fewer than 50,000 patients and these disorders are considered intractable diseases. Each country, when establishing their orphan product development or rare diseases research legislation, identified their threshold level and various incentives to address the needs of the rare diseases community in their country.

Research of rare diseases and development of orphan products continues to grow around the world. Obtaining the Orphan Product designation from the Office of Orphan Products Development at FDA, USA provides incentives such as 7 year marketing exclusivity, eligibility for research grants, and possible exemption from an estimated one million dollars in filing fees for an IND or an NDA. In the USA, more than 3,300 active Orphan Product Designations have been made and 60
additional designations with four product approvals have been provided thus far in 2015. There were 286 orphan product designations in 2014. The FDA in the USA has approved products for 46 indications in 2014 and since 1983 more than 485 Approved Orphan Products/Indications by FDA. The Pharmaceutical Research and Manufacturers of America (PhRMA) reported more than 450 compounds in development for rare diseases. Current levels of activities indicate a continued emphasis on rare diseases with an increasing pipeline of potential products.

Most rare diseases affect several organ systems, requiring multiple clinical and research disciplines to be involved in conducting research and providing for most rare diseases. Rare diseases know no geographical, political or historical boundaries. Even-with major efforts by the research community, Federal research and regulatory agencies, private foundations, patient advocacy groups, and members of the pharmaceutical, biotechnology, and medical device industries, the need for interventions exceeds the financial and program capabilities of all of these organizations. In recent years, new models for product development have evolved that utilize the resources available from public-private partnerships.

In most countries, despite extensive efforts, adequate data is not readily available to accurately predict the prevalence of individual rare diseases, that is, people living with a specific rare disease. There is also the need for better data to describe the associated morbidity and mortality of individual diseases and rare diseases in total. As a result, the economic burden of most rare diseases is not known or easily retrievable from existing data sets. In many respects, the lack of accurate data inhibits the public and private sectors in their decision making. In the public sector, government agencies and departments may be unable to predict the associated costs with rare diseases and interferes with their decision making process. In the private sector, industry has mentioned the difficulty in estimating patient population for a rare disease for research purposes and the potential market place
to assist in decision-making to develop a product. In several cases, the pharmaceutical industry has elected to pursue the development of an orphan product for a rare disease regardless of the size of the patient population.

**Emphasizing Rare Diseases in India**

A review of the current situation for Rare Diseases Research and Orphan Products Development is required to provide adequate information for the decision making by the India Parliament considering proposed legislative initiatives and government agencies responsible for the eventual implementation of these initiatives for the entire population of India, now estimated at 1.5 billion people. In many countries with an active research emphasis, research programs in rare diseases and orphan product exist but they are frequently not well coordinated with other programs or are of limited scope for individual rare diseases. This limited emphasis on specific diseases is brought about due to the advocacy role of individuals or a group of individuals with a particular rare disease. Leadership from the Government of India will be required to enable activities to be initiated and implemented for all rare diseases. Special emphasis and leadership will need to be provided by the Executive branch and both bodies of the Parliament, the Lok Sabha and the Rajya Sabha. The burden of rare diseases includes financial, emotional, career, and societal implications for the patients, families, caregivers and clinicians. Even with the tremendous burden of disease associated with the more than 7,000 individual diseases, there are significant research and scientific opportunities available for study in India and throughout the world. The extensive research and development efforts from many other countries can be utilized as a starting point for India. Taking these experiences, it will be possible for the Government of India to consider various programs and determine what is needed and most suitable to meet the needs for all citizens of India.
This is a unique opportunity for India to utilize the numerous available resources and technical skills of its citizens to benefit patients throughout the world. India will become even a greater contributor to the expanding globalization of government and academic research efforts, patient advocacy group collaborations, and the pharmaceutical, biotechnology and medical device industries initiatives. Several actions need to be considered before final decisions are made by elected government officials and civil service staffs of the involved government agencies.

**Reviewing Existing Regulations and Programs.**

Many regulations, programs, and policies may already exist and are being utilized by government organizational structures in day-to-day operations. There is a need to identify in India existing legislation, research, regulatory and health services policies and programs and organizational structures and resources currently utilized to address rare diseases research and product development initiatives which could be expanded or adapted to include provisions for rare diseases and orphan products. Creating an inventory of current activities and identifying unmet needs is a critical major step to be taken and will require a legislative or programmatic mandate to initiate and complete. It is essential to consider in the discussions the numerous views and opinions of all stakeholders.

**Developing Commitments.**

A united approach to rare diseases research and orphan products development is required to be successful. Initiating national government activities with research and regulatory emphasis requires responsible authorities to develop appropriate staff activities, provide sufficient financial resources to address issues, recognize program emphasis, and facilitate global collaborative efforts. Several of the first steps will require (1) an ongoing approach to determine global needs of all stakeholders in India; (2) identify needs of patients, advocacy groups, health care
providers, researchers, industry, payers, and government research, regulatory and health services provider agencies; (3) determine family and societal needs across the lifespan; (4) highlight national government decisions to emphasize needs and develop incentives to meet needs of all patients regardless of (a) prevalence of individual diseases, (b) the severity of diseases in all age groups, (c) expected lifespan of patients with rare diseases, (d) the availability of less than optimal treatments or supportive care, and (e) the cost of treatments that become available for treatment and care.

**Promoting Coordination and Collaboration.**

To be successful, extensive coordinating and collaborative efforts for orphan product development and rare diseases research are required. All activities must promote positive interactions within the rare disease community among the following stakeholders:

- Pharmaceutical, biotechnology, and medical devices industries,
- Academic and private foundation multidisciplinary research communities,
- Medical specialty societies and healthcare providers,
- Patient advocacy groups, families, and individuals with rare diseases, and
- Central government agencies involved with responsibility for...
  - Regulatory Actions
  - Reimbursement policies and procedures
  - Conducting and sponsoring research projects
  - Providing health care services
  - Disease prevention and public health promotion activities

Leadership roles and responsibilities need to be identified and established during the iteration stages of defining necessary activities.
Meeting Societal Needs on a Global Basis:
In the information discovery and planning stages, many needs will be expressed and presented for consideration. These will include the need to mobilize health professionals and society to take action for better treatments and care for the patients with rare diseases by making available safe and effective products for the prevention, diagnosis, and treatment of rare diseases. This can be done by improving health literacy of the entire populations to enable information-based decision making. Ready access to information and interventions for diagnosis, prevention, and treatment of rare diseases will help reduce disparities in health care and treatment. The globalization of many of the stakeholders requires us to identify and expand global partnerships and collaborations of various partners in the public and private sectors. These actions will enable the global rare diseases community to obtain cooperative and collaborative support from all nations and provide partners in rare diseases research and orphan product development.

Identifying the Issues to Be Addressed by Utilizing Previous Experiences.
To initiate discussions among the various stakeholders a major scientific workshop was conducted (a collaborative effort recently in Hyderabad on September 18-19, 2014. Several potential policy matters were discussed in different sessions of the meeting. These issues are presented below as representative of the discussions held on all subjects and do not represent all discussions held at the meeting:

- Develop a mechanism to draft the concept of orphan products and accompanying regulations as a legal framework to encourage research, development, and dissemination of orphan products.
- Identify human, budget and other resources to help gather information for defining rare diseases in India's context.
- Establish policies and guidelines in Rare Diseases Research with fair and adequate earmarked funding.
• Establish new division for rare diseases research under Ministry of Health/Ministry of Commerce/Ministry of Science and Technology

• Establish new division under Drug Controller General for approving designations, approvals and grants; similar to amended Orphan Drug Act of 1983 (USA)

• Link the Orphan Product Framework with the existing patent protection and provide adequate safeguards with additional policies to cover all aspects of Intellectual Property.

• Identify, recognize, and support major and minor ongoing initiatives of rare diseases awareness projects and patient support groups.

• Establish mechanism(s) to identify problems and opportunities for developing diagnostic tools.

• Create a process by which patients’ perspectives can be heard.

• Identify national experts and decision makers to shape public policy and legislative initiatives to be initiated by the Central government.

• Provide support for Newborn Screening or high-risk population screening for rare and genetic diseases.

• Develop an awareness of policies and regulations of other countries and adapt to needs of India.

Expanding the Discussions.

Several issues are presented above for consideration as immediate emphasis can be given to initiate discussions and considerations. Fortunately, considerable information exists from the worldwide published literature and personal experiences to assist in the decision-making.

Other Significant Issues for Consideration,

Several additional issues deserve considerable discussion and can be addressed in numerous forums by the different stakeholders.
Access to Information

We find the needs of the rare diseases community are similar regardless of the home country of individual patients. The major requirement is ready access to useful and reliable information to assist in decision making for patients, families and clinical staff. Considerable information is currently available from public and private resources numerous resources in USA and Europe such as the National Library of Medicine, The Genetic and Rare Diseases Information Center at NIH, Eurordis, Orphanet. National Organization for Rare Diseases, Genetic Alliance and Global Genes.

Obtaining the Diagnosis

One of the first problems encountered by patients is obtaining a quick and correct diagnosis. Access to whole genome, exome, and next generation sequencing techniques will assist in the elimination of the diagnostic odyssey confronted by large segments of the population in the quest for their diagnosis. Ready access to these diagnostic procedures in addition to appropriate newborn screening will lead to improvement in clinical care and treatment of patients with rare diseases and conditions at an earlier period in their lives enabling them to gain the benefits of existing interventions.

Costs of Treatment

Some of these interventions can be very expensive. Extensive discussions will be required to address this need to provide adequate treatments when available. This issue has caused delays in some countries and will need to be addressed appropriately. It is important to note that currently approximately 275 rare diseases have treatments from the 485 products approved in the USA and European Union.
Economic Incentives
Special economic incentives for the industry such as exclusive marketing, tax credits for clinical trial expenses and clinical protocol development assistance have been found to be useful to facilitate the development of interventions. To be effective and address this issue as a major public health issue a coordinated review and development of a centralized approach is required utilizing the resources of the Central, State and Local governments.

Support Services and Care
Ongoing home and hospital care from multiple medical specialists and clinical services such as nursing, pharmacy, physical, occupational, respiratory therapists and other support services are required to assist patient, caregiver and family support services throughout the lifespan.

Patient Advocacy Groups
Providing leadership to patients, healthcare providers and the public are the patient advocacy groups. A significant contribution to the care of the individual is the information provided by these organizations to reflect sharing patient and family experiences and knowledge from living with a rare disease. They are essential in our goal to provide patient centered care. The development of new organizations representing specific diseases and umbrella organizations must be encouraged and facilitated by the Government of India as has been done in other nations throughout the world. The collective voice of the patient is a growing and loud voice articulating a message of the needs of the millions of patients who awake each day with little hope for treatment. The expanded acceptance of patients and patient advocacy groups as research partners has improved the recruitment of patients into clinical trials. Patient advocacy groups themselves have provided a particular emphasis to link with patients and other advocacy groups worldwide to improve opportunities
to share information about their disease, identify ongoing research projects in need of patients, and identify best care practices for their diseases with or without approved interventions for their use.

Research Consortia Network or Centers of Collaboration

Opportunities exist to establish new or to join existing research consortia and networks throughout the world. These organized efforts provide ready access to a critical mass of research investigators, research sites, and patients to facilitate the development of clinical trials, rapid accrual of patients into clinical trials, and lead to the timely completion of a clinical trial operating under a common protocol. India could contribute significantly to these programs by developing new centers and joining established centers of research and treatment excellence. Large cohorts of patients, patient registries, natural history studies, bio-banks, and bioinformatics support are all key elements available from significant contributions by the existing research infrastructure in India.

Regulatory Emphasis on Orphan Products

Expedited product review programs adopted by US FDA continue to move potential products through the research and development continuum to an even speedier approval for safe and effective therapies when adapted in Indian scenario. Utilizing designations such as Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review for potential products provides continued optimism for patients and their families for the quick approval of products for their diseases. Repurposed products now qualify for orphan product incentives at the FDA; should incentivize Indian Pharma to develop new drugs. Compounds included in the Best Pharmaceuticals for Children Act program are eligible for a 6 months extension to existing exclusivity as an incentive to expand the indications for use from the adults to the pediatric population. For antibiotics, a newer incentive program, Generating Antibiotic Incentives Now (GAIN), adds 5 years to existing exclusivity for products
considered a new chemical entity and those included under the US Orphan Drug Act. An additional approach for consideration by FDA involves the use of experts for consultation in pre-approval stage to discuss the severity of rare diseases and unmet medical needs associated with rare diseases. This approach reflects a willingness and ability of individuals with a rare disease to participate in clinical trials following an assessment of benefits and risks of therapies. India can utilize the resources/guidance available at USA Food and Drug Administration and European Union’s Medicines Agency to initiate incentives for product development programs in India.

Conclusion

To address the needs of the Indian rare diseases’ stakeholders, several assessments will need to be made. Alliances of public-private collaborating partnerships are needed to address the significant issues presented by rare diseases research and orphan products development. Numerous public meetings and workshops will provide several reports leading up to proposed legislation. Similar considerations were addressed and ensuing recommendations followed to guide the legislative process in many countries and jurisdictions. Even afterwards, changes continued to be made based on public and private sector involvement in the development of legislative initiatives and implementing programs at the national level. These activities can be found in publicly available reports. Each of these special reports resulted from collaborative partnerships required for advice and consideration of viewpoints from the pharmaceutical, biotechnology, and medical device industries; patients, families and patient advocacy groups; clinical experts, academic research centers, and individual scientists, and government research funding and regulatory agencies. Experienced individuals and countries are willing to assist in all future activities in India. This is a journey to be taken together to maximize the available and limited resources.
INDIAN ORGANIZATION FOR RARE DISEASES

Address:
699 Apache Lane,
St. Paul. MN 55120
USA
Ph. (651) 688 7382