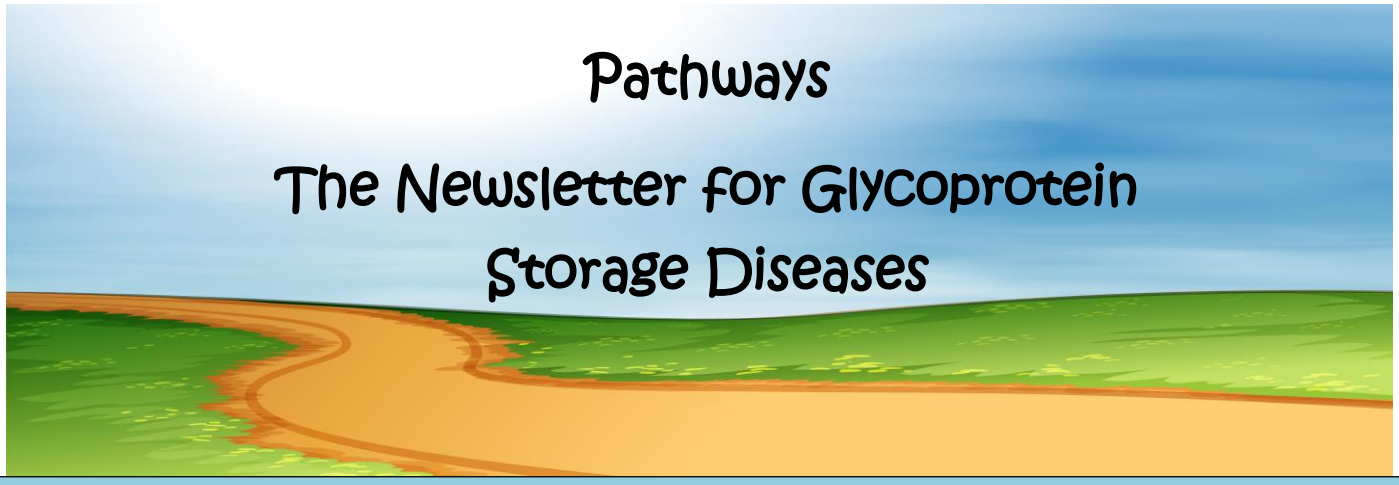

ISMRD, a 501 © not-for-profit organization, FEIN 53-2164838 | website www.ismrd.org

Our Mission and Vision

ISMRD is the leading advocate for families world-wide affected by Glycoprotein Storage Diseases.

Through partnerships built with medicine, science and industry we seek to detect and cure these diseases, and to provide a global network of support and information.

We seek a future in which children with Glycoprotein storage disease can be detected early, treated effectively and go on and live long healthy and productive lives.

ISMRD supports the following disorders

Alpha Mannosidosis, Aspartylglucosaminuria, Beta Mannosidosis, Fucosidosis, Galactosialidosis, Mucolipidosis II alpha/beta(I-Cell Disease), Mucolipidosis III alpha/beta (Pseudo-Hurler Polydystrophy),Mucolipidosis III Gamma, Schindler Diseases and Sialidosis

In this Issue

Follow us on
https://www.facebook.com/groups/82945687520/

https://twitter.com/ISMRD

Donations ISMRD is a 501(c) charitable organisation based in the United States serving a global constituency. We provide our services, which include our newsletter, website, outreach activities and support of research, without requesting monthly dues or any other financial restrictions. We gratefully accept donations that will enable us to continue toward our goal of a future free of the tragic consequences of Glycoprotein Storage Diseases.

Donations can be made via our website using

PayPal Secure Payments

Contact Us

The International Advocates for Glycoprotein Storage Diseases
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Saratoga
CA 95070
USA
email: info@ismrd.org

From the President's Desk

By Mark Stark
President, ISMRD

Welcome to the ISMRD spring newsletter! Here in the US it has been a winter of severe weather, especially in the Eastern and Southern states, but it is finally spring. (Of course, it is fall for our families in Australia and New Zealand!). After the year-end holidays, the ISRMD board has begun serious work to plan for the next combined scientific and family conference scheduled for 2015. There will be more details about the conference coming soon; we will be asking all of you to help make this the best conference ever.

Our goal at ISRMD is to help all those affected by rare diseases by providing information about treatment and care options to parents of affected children, and by providing a community of families that support each other. This newsletter is one of the ways we provide this support to those who may not be in regular contact with ISRMD, as well as provide news about activities and upcoming events that are important to everyone concerned with curing these debilitating disorders. This edition of the newsletter has a focus on information about resources that are available for caregivers and families, and the challenges still facing India; these articles include links to more detailed publications. There are also two articles about therapy for rare diseases in the United States, pointing out the role of patient advocacy groups in getting new treatments implemented for rare diseases. As always, there is a list of upcoming conferences and a thank you message to our donors.

I would like to thank everyone who has already contributed this year to ISRMD; both financially and with your time. We are launching our fund raising campaign for the 2015 combined scientific and family conference on glycoprotein diseases. The last conference in July 2012 was very well-attended, and received high marks from both professional and family attendees. We are setting the bar even higher for the conference next year; if you would like to help, please contact any of our board members and they will be happy to finds ways you can contribute.

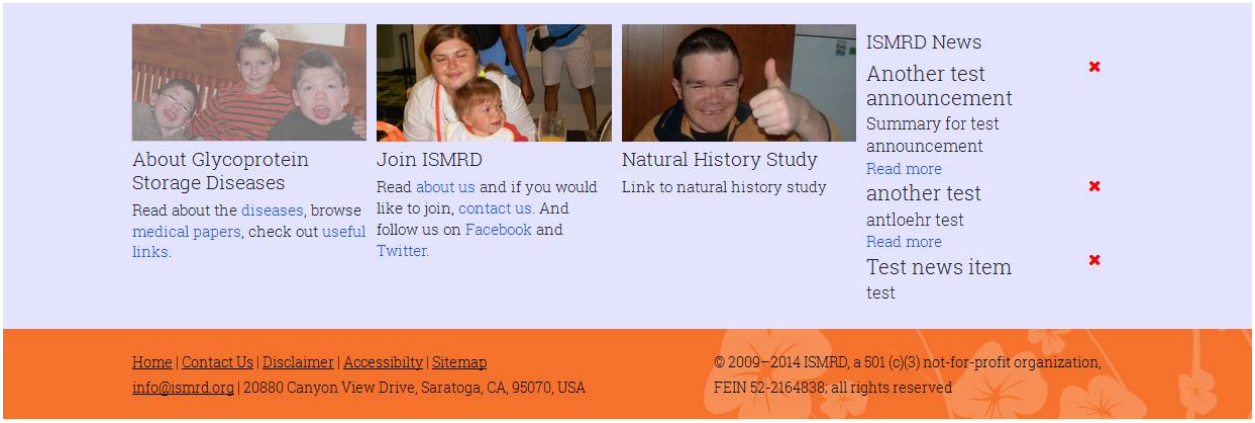
Thank you!

Mark Stark
President
ISMRD

A sneak Preview of our new Website

We have been working on a new and improved website for ISMRD and hope to have this go live by the end of this month. The photo that you see on the home page will be like a video and will keep changing. Ben our webmaster has put a lot of time into the design and Jenny has been doing the re-writing and organization of the information. There is still a lot to be done but we are getting there.

We are still looking for families who would be willing to have their story in our family story section in particular those whose children have ML II and ML II/III and Fucosidosis . If you would like to submit your journey with your particular disorder we would love to include it please contact Jenny Noble jenny.noble@xtra.co.nz



Report on Rare Disease Day

It is now 7 years since the celebration of Rare Disease Day began. Rare Disease Day has been an iconic celebration of our appreciation for rare disease patients and stakeholders for their efforts. This year, a record number of countries from all over the world participated in the celebrations. There were 84 participating countries with 410 events worldwide. Patient organizations from 9 new countries participated for the first time this year: Cuba, Ecuador, Egypt, Guinea, Jordan, Kazakhstan, Kenya, Oman, and Paraguay. To see a list of participating countries, go to http://www.rarediseaseday.org/events/world

This years' slogan - ***Join Together For Better Care*** - urges us to explore how we can assist to gain better care for the patients, be it in obtaining access to medications, or access to expert services or access to social services.

New global, online forum for rare disease caregivers

In honor of this year's International Rare Disease Day theme of "*Join Together for Better Care*", the Caregiver Action Network (CAN) has launched a new global, online forum for rare disease caregivers**.** The purpose of CAN's new website is to provide support and resources to a critical element in the lives of all rare disease patients -- the role of the caregiver.

"Caring for Rare Disease Caregivers**"** will continue to evolve and improve over the coming year based on user feedback and input. In the initial version of the site, several key resources are translated into Spanish, French and German. The website contains important resources for caregivers with information and tools to help caregivers care for themselves, reenergize, and deal with complex emotions and challenging family situations. Perhaps more importantly, it is a tool that will enable caregivers to connect with one another across the globe via an online forum.

Anybody can join ISMRD

What's happening around the world?

Dutch National Plan for Rare Diseases.

On October 10, 2013, a delegation of The Netherlands Organization for Health Research and Development (ZonMw) presented the National Plan for Rare Diseases (in Dutch: Nationaal Plan Zeldzame Ziekten, NPZZ) to Minister Schippers of Health, Welfare and Sport (VWS). The Dutch National Plan identifies bottlenecks and recommendations, and it encourages field parties to feel responsible. The key bottlenecks for the plan include lack of knowledge about rare diseases, insufficient medical research on causes and course of rare diseases as well as inability of patient organisations to work well together. NPZZ recommends emphasising knowledge about rare disease through training and establishment of expert centers, making the information widely accessible to diverse audiences; making financial resources available for research and development of treatment as well as maintaining consistent policy for claims and reimbursement of orphan drugs. Finally NPZZ aims to appoint a director or coordinator to promote all recommendations, and avoid fragmentation and unnecessary duplication within the rare disease field.

For more information please visit the Dutch Orphanet website.

New organization of services on Rare Disorders in Norway

There are now 10 different centres for rare disorders in Norway. They cover a broad range of diagnoses and diagnostic groups. The Norwegian Ministry for Health and care services decided to organise these centres under one national service for rare disorders. In 2013, Oslo University Hospital organised a project to establish a brand new national service, functional from January 2014. Now there is one National Advisory Unit on Rare Disorders (NAURD) in Norway, which oversees the ten other centres. The purpose of this co- organization is enhanced quality of services through strengthened user participation, better coordination and cooperation, better visibility, services for more rare diagnoses and greater efficiency. The new service, NAURD, will operate the Norwegian Help-Line on Rare Disorders (+47 800 41 710). For more information and links to the different Centres for Rare Disorders **visit the website** http://www.oslo-universitetssykehus.no/omoss/avdelinger/nasjonal-kompetansetjeneste-for-sjeldne-diagnoser/Sider/enhet.aspx

Lack of policies in rare disease in India highlighted

A press release from the newly formed Organisation for Rare Diseases India (ORDI) has expressed discontent and frustration over the absence of adequate policy in India towards assisting rare disease patients. Currently, research and development towards understanding rare diseases and finding appropriate therapeutic interventions for them is lacking in India, according to ORDI.

Risky Business: The FDA and Drug Development For the Fatally Ill

If you've ever waited for treatment in the ER—for yourself or perhaps for a child suffering a broken bone or an asthma attack—then you're familiar with how agonizing it can be, knowing that the answer might be just on the other side of the swinging doors. For parents of seriously ill children, this kind of waiting can last for years. And when treatment options are still stuckin the development, testing, or approval processes, the wait can cost patients their lives.

The FDA has set up these processes for good reason; they protect the public from experiencing severe, unexpected side effects due to unsafe drugs, which could actually make people even sicker than they already were. But for seriously ill patients, sometimes the risk is worth taking if there's any chance of increasing their survival rates. In these cases, the burdensome approval process to get drugs on the market—which can take up to 18 years—is detrimental both to pharmaceutical companies and to patients. The recent controversy over the FDA's refusal to approve eteplirsen, a drug intended to treat Duchenne muscular dystrophy, is a prime example of this. Eteplirsen has shown some promising results in clinical trials, but the data still isn't satisfactory enough for FDA approval, since it has a hard time assessing benefit and risk across a spectrum of perspectives and experiences. Patients and their families beg for access to the drug, to no avail.

Unlike other industries, pharmaceutical companies are also legally restricted from directly marketing to consumers or including them in the prototyping phase of the design process. This can prevent consumers from providing vital feedback that could shape drug effectiveness, as well as from learning about experimental options when they are available. With most conditions, the risks of experimentation would be too high. But if you had a fatal disease and were told you only had one year to live, wouldn't you prefer to be allowed to make your own choice?

Sharon Terry, an Ashoka Fellow, and Genetic Alliance have developed a platform that facilitates the responsible engagement of the FDA with patients such as these, and they're getting patients directly involved in voicing their concerns about the current system. The FDA's initiative is called Patient-Focused Drug Development (PFDD), and it is designed to assess risks and benefits for specific patient communities. Genetic Alliance is crowdsourcing input for the FDA to hear from patients. Terry hopes to increase the available pool of information—information about patients' genetics and other personal

data—to help accelerate discovery. She'd like to see a systemic solution across all diseases, rather than solutions that work on a case by case basis. To do that, she and her partners are putting in place a structure to empower disease groups and patients to vocalize their needs to the FDA and determine how and with whom their data is shared. Currently Genetic Alliance works with eight disease groups on PFDD and has enabled patients from each community to serve as guides with the goal of getting input from patient communities. It hopes to expand its work to more diseases in the next few years, and eventually to every disease.

Terry's initiative has recently been awarded a $1 million contract from the Patient Centered Outcomes Research Institute to be a part of the National Patient Centered Clinical Research Network. This news could mean big things ahead for patients with genetic diseases.

If their work is successful, the FDA will begin to distinguish between the process for approving standard use drugs and the process for approving drugs that are designed to treat or cure severe disease. With increased collaboration between pharmaceutical companies and patients with a high risk tolerance, the FDA can gain data to stand on, which could help speed up drug patent approval. Patients would also be able to participate in drug design, thus improving the development process.

Quality of life of caregivers of rare disease patients in the Czech Republic

A paper published in *Procedia - Social and Behavioral Sciences* describes selected results of an extensive study monitoring the quality of life of caregivers of a child with a rare disease. The authors evaluated questionnaires from parents of children with the following diseases: cystic fibrosis (CF), spinal muscular atrophy (SMA), mucopolysaccharidosis (MPS), group of metabolic disorders (MP) and achondroplasis (ACH), confirming that most monitored areas deteriorated during the care. The study results showed that the socio-economic status of the these caregivers deteriorated considerably and their outlook of the future was fairly grim. This difference was statistically significant between the respondents from the groups: caregivers who care for a family member with a rare disease and persons who care for a child without disability or disease - the control group - were confirmed. The authors recommend that considering the immense financial and social strain on these families, it is necessary to focus on better support of caregivers as well. Read the open access article

Patient Advocacy
Understanding the role of Regulatory Affairs in orphan drug availability

It takes a great deal of knowledge and skill to be a truly successful patient advocate. With so much to master, one area that can sometimes get overlooked is the role of Regulatory Affairs (RA) within industry. It is important to understand what RA does and how the process works, because new therapies do not get approved without a long journey through the regulatory process. For patient advocates both in and out of industry, it's also important to understand how RA professionals can be critical allies in making therapies available to patients. Having worked on the Regulatory Affairs end of biotech for many years, I thought I would share some insights I've gleaned over the years.

Broadly speaking, Regulatory Affairs is the department that exists within pharmaceutical and biotechnology companies that interacts and works with the regulatory authority within each government. Of course these regulatory authorities or agencies have control and oversight of the products companies are developing or manufacturing. Examples would be the Food and Drug Administration (FDA) in the U.S. and European Medicines Agency (EMA) in Europe.

So what does RA do? It may be easier to start with what it doesn't do. It doesn't actually run pre-clinical experiments or generate data from manufacturing studies. But it does need to have an in-depth understanding of both. RA advises scientists to ensure they are following regulations. It deciphers and summarizes complex scientific data for submissions to authorities like the FDA. RA is responsible for transmitting vast amounts of data to FDA and similar agencies in other countries to review and approve, which can be an enormous undertaking.

All of this goes on for years, throughout the drug development process, and leads up to the big moment – the submission of a marketing application (in the U.S., a New Drug Application or NDA). In the old days, when applications were actually printed on paper, they were so massive that they actually needed to be driven from biotech or pharmaceutical company headquarters to the FDA in Bethesda, MD in an 18-wheel truck. Nowadays they are sent on CDs or electronically.

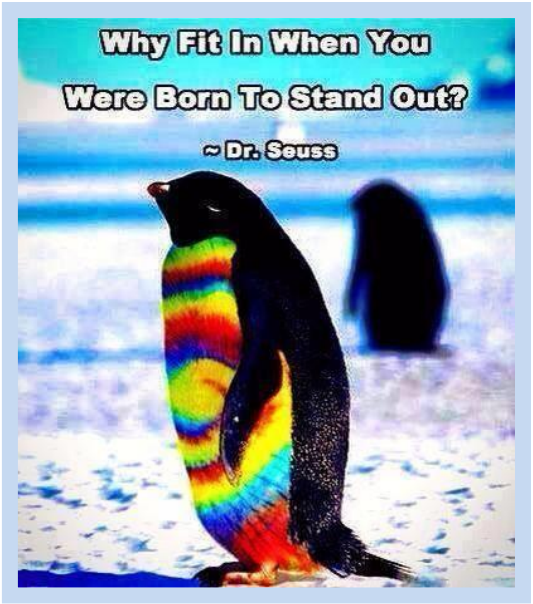
But the work of regulatory affairs doesn't end there. In the U.S., for example, the FDA will have hundreds -- if not thousands -- of questions on all aspects of a NDA to ensure that the product is both safe and effective. This process can take years if there is an issue with the application or the FDA believes the data is not sufficient. Hopefully it ends with an approval, but some products will not withstand the rigor of this review and are not approved. The work of RA doesn't stop even if a drug is approved. There are regular reports that need to be sent to regulatory authorities on any continuing clinical work; safety updates; and even seemingly insignificant changes to the manufacturing process need to be communicated for the life of the product.

Now, I have primarily been using the FDA as an example. Take this and multiply it by the world! Every developed country and most developing countries have their own regulatory agency, and their requirements and processes are unique. A new drug submission for the EU, will have different requirements than that of the US, or China, or Colombia, or Egypt or Australia. There have been efforts to "harmonize" requirements by the International Conference on Harmonization (ICH) but even for countries that have signed on, differences persist. For the EU and countries like Brazil or Japan, filing the new drug submission can happen in parallel with the US, but many other countries require an FDA or EU approval before they will even consider accepting an application. The result is often a "drug lag" which can be frustrating to patients who know there is a safe and effective therapy available, but not yet in their country.

However, patient advocates can have an impact in the regulatory world. When I was working on a team that was trying to get an enzyme replacement therapy approved in Japan, we were stymied by the Japanese regulatory authority's slow progress. Local patient advocates worked with a popular Japanese pop band to urge the government to move faster. The product was approved in nine months, which was a record at the time.

Patients can get involved in working with the U.S. FDA by joining the FDA Patient Representative Program. Advocates can educate themselves by going to an organization like the Regulatory Affairs Professional Society (RAPS) that has courses in EU, US, and Japanese regulations. I have even talked to amazing parent advocates who have basically learned Regulatory Affairs the hard way – learning on their own by authoring and submitting periodic reports to the FDA for the trials they are collaborating with researchers on.

By learning how the regulatory world works, you can be a more effective and powerful advocate. And as your influence grows, agencies around the world will listen to you.



Conferences around the world

7th European Conference on Rare Diseases & Orphan Products

Date: 8-10 May 2014

Venue: Berlin, Germany

The European Conference on Rare Diseases & Orphan Products (ECRD) promises to be an enlightening forum for rare disease stakeholders across various disciplines across in European countries. It aims to cover research, development of new treatments, healthcare, social care, information, public health and support. **For further details**

The World Orphan Drug Congress Asia 2014

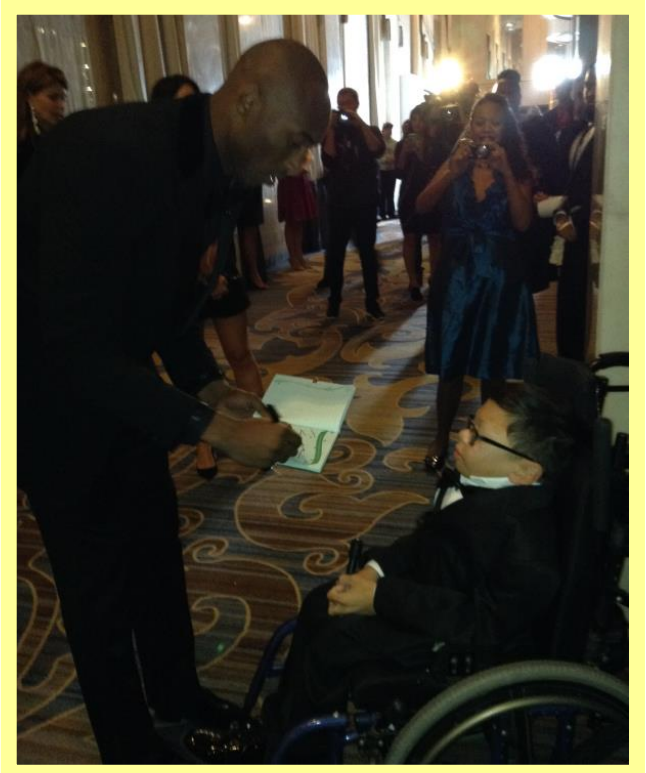
Date: 10-11 June 2014

Venue: Singapore

The World Orphan Drug Congress Asia 2014 focuses on fostering partnerships and relationships between industry, governments, payers, investors and patients as well as to expedite orphan drug development and articulating its value, from discovery to clinical development, to license, to manufacturing, to launch and to sustainability of supply, so that manufacturers are guaranteed full and speedy reimbursement.
For Further Information

Penguins you can eat

ISMRD member Spencer Gates meets Kobe Bryant and Andy Garcia at Make A Wish dinner



ISMRD warmly welcomes the following people to our family

- **Stacy and Tim Buchanan** - USA who have two children with ML III Ariel and Timmy
- **Nicole Potts** – USA who has a son Tyler with ML III
- **Nagila Naiara** - Brazil who has a sister with ML III
- **Holly Thompson** – USA who has a daughter Madison with ML III
- **Jens Blom and Ingrid Lovsland** – Norway who have a son Agnes with Alpha-Mannosidosis
- **Kimberly Puenete** USA who has a daughter with Galactosialidosis
- **Patricia and Vladimir Gribel** – Brazil who have a daughter with Sialidosis type I

The following people have joined us on our Facebook page.

- **Ivana Kohoutová**
- **Shirley Zang**
- **Katie Rheaume**
- **Kurt deParade**
- **Mickey O'Rourk**
- **Louise Buckle**
- **Beth Bruck Clark**

ISMRD gratefully acknowledges the following people for their very generous donations.

Without this kind of support we would not be able to carry out our mission and vision for ISMRD.

Jean Leonard
Carolyn Paisley-Dew
Laura Palmgren
Vice O'Connell
Viv Roll
Steve and Dianne Smith
Ann Woodhouse
Robert and Melody Voltz.

ISMRD FUNDRAISING

Gofundme - Fundraiser

This is our ongoing fundraiser through gofundme. We hope to be able to raise $70,000 which will help support the Natural History Study thus ensuring that new families are able to participate in the study.

To make this fundraiser work we are asking our families and those searching our website to share the link via your social media links such as Facebook and Twitter.

Please use the link to go to our gofundme page where donations can be made and you can meet some of our very special people. http://www.gofundme.com/5rpjhw

ISMRD'S Sunshine Care Committee

ISMRD has a group of parent volunteers called the **"Sunshine Committee"**. Our purpose is to coordinate support for families in need. The type of support varies on the circumstance -- from birthday and weddings, an illness or death in the family, or a family experiencing surgery or a medical crisis. In any case, we provide a little "sunshine" for the family by providing flowers, encouraging messages via email, cards or a phone call --- whatever we think the family would find most helpful. In order to help others, our group relies on the support of all families because, in essence, we are all part of the ISMRD "Sunshine Committee".

If you are in need of assistance or know someone in our Penguin community who is in need, **please contact Susan Kester**. She will coordinate with the appropriate parties to determine how we can best help.