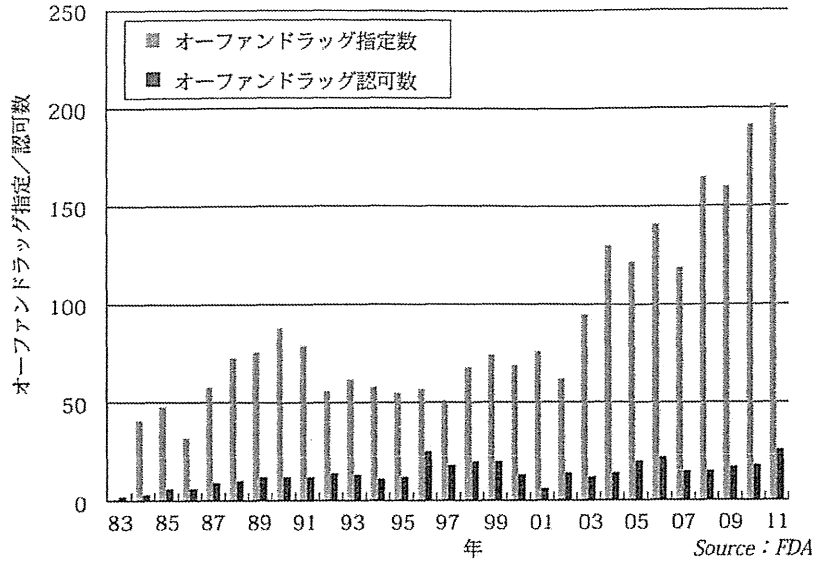


図2　オーファンドラッグ指定および認可されたオーファンドラッグ数（1983-2011）

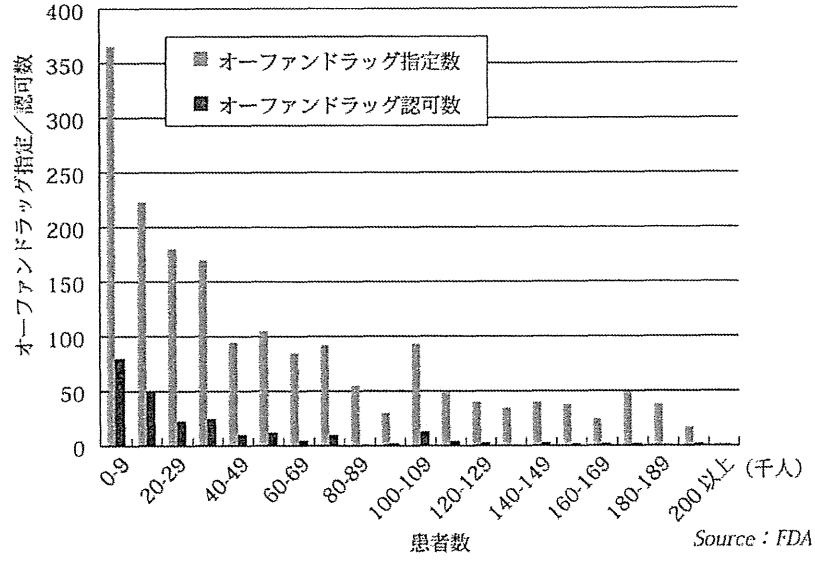


図3　オーファンドラッグを使用する対象疾患のアメリカ国内における患者数

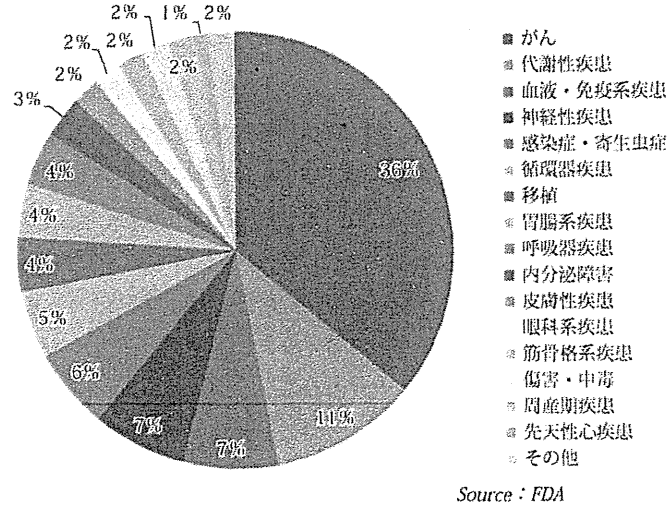


図4　オーファンドラッグ指定を受けた疾患／症状の分野別分類

対象患者数からもわかるように，オーファンドラッグ市場は決して大きくない。しかし，希少疾患は，単一遺伝子異常が原因である場合が多いため，遺伝子を特定するといった研究デザインの工夫により，研究開発の成功確率を高めることが可能である。このような戦略モデルは，大企業より小規模であるベンチャー企業や大学等研究機関に向いているといえる。そのため，米国ではまずベンチャー企業が開発に着手し，販売の目途が立った後に大企業が企業もしくは品目を買収するというモデルが一般的である。このような，基礎研究をおこなっているアカデミック機関と大企業とをつなぐベンチャー企業の存在は，オーファンドラッグ市場にとっては非常に重要である。

6. 患者会の取組 ― NORD ―

National Organization for Rare Disorders（NORD）は，オーファンドラッグ法制定に大きな影響を与えた患者らによって設立された世界最大の希少疾患患者協議会である※25。希少疾病患者，その支援団体のサポートのため，教育，政策提言，研究，奉仕活動を通じて希少疾病の同定，治療，治癒に貢献することを目的として 1983 年に設立された。

1987 年に製薬企業と共同で患者支援プログラムを開始し，2002 年・2003 年には米国ベストチャリティー団体ベスト 100 に選出された。現在 NORD に参加している団体数は 180 を数える。

主な活動は以下の通り多岐にわたっている。

1）教育活動：1,200 件の希少疾患報告書（抄録）を患者およびその家族らのために作成・データベース化している。内容には，症状，原因，治療に加え，問い合わせ先も掲載している。また，電話や Email 等による相談にも対応しており，患者関係者だけでなくソーシャルワーカーや専門医からの問い合わせにも応じている。

2）支援活動：毎年大規模な関連学会に複数回参加し，会員組織の代わりに患者の立場からの支援必要性を訴えている。また，特定疾患患者会に対しては，運営等の支援のためのメンタリングサービスをおこなっている。また，患者会に対する情報提供やネットワーキング活動，事例紹介等も継続的に実施している。

3）研究助成：NORD はアカデミック系研究者に対し研究助成をおこなっている。

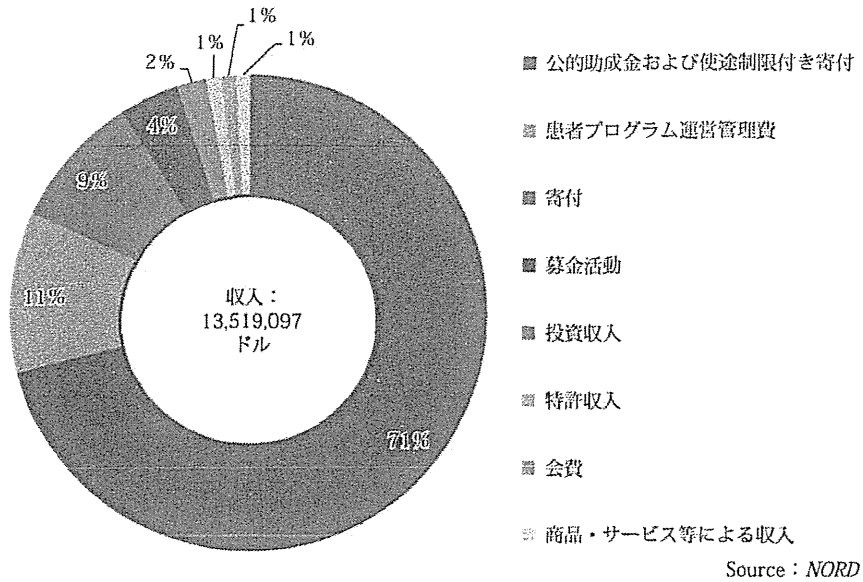
4）医療助成：NORD は 20 年以上にわたって患者医療助成サービスを実施している。1987 年以降，NORD は製薬企業等のパートナーを得て 380 のプログラムを運営し，56 百万ドル分の医薬品無料提供もしくは一部負担サービスをおこなっている※26。

5）国際連携・支援：希少疾患に関する国際連携および相互発信・理解のため，欧州希少疾患患者協議会（EURORDIS）と戦略的パートナーシップ契約を締結しており，欧米状況の共有や毎年 2 月末の Rare Disease Day の開催※27，ワークショップの共同開催等をおこなっている。

図 5，図 6 に 2010 年度の収支状況を示した。

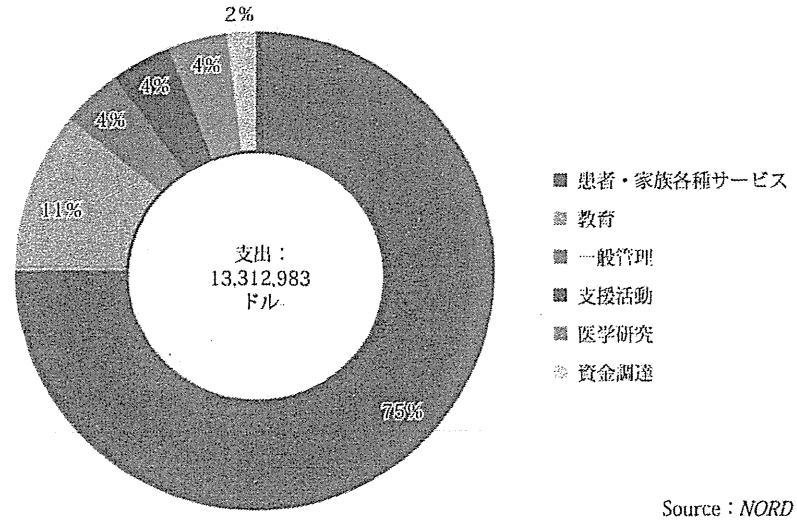
NORD は FDA や NIH といった政府機関とも連携を深めており，FDA には定期的に患者の視点からの政策提言やアドバイスをおこなっている。また，Patient Advocacy Day を共同開催している。NIH とは研究者に対する情報発信やワークショップ開催において協力している。このように，米国では患者会の存在はオーファンドラッグ開発において非常に重要な位置を占めており，その影響力も非常に大きい。

※ 25 http://www.rarediseases.org/
※ 26 http://www.rarediseases.org/industry/patient-programs
※ 27 Rare Disease Day はより良い診断や治療による希少・難治性疾患の質の向上を目指して，スウェーデンから 2008 年から始まった活動であり，日本でも 2010 年から日本各地にて 2 月最終日にイベントを開催している。
http://www.rarediseaseday.jp/



Source：*NORD*

図5　NORD 収支状況（2011 年度）：収入



Source：*NORD*

図6　NORD 収支状況（2011 年度）：支出

7.　まとめ

本稿では，近年の米国におけるオーファンドラッグ開発動向，政府機関や患者会といった関連組織の活動を紹介するとともに，日本の現状との比較をおこなった。米国では，基礎研究支援が創薬・医療などの応用分野のそれと密接に結びついていると同時に，行政も医薬品開発を積極的に支援し，審査の迅速化をおこなってきている。また，同制度を利活用するベンチャー企業が多いことや，それら市場側の対象を意識した支援がおこなわれていること，つまり，制度を漠然と設計するのではなく，利活用する側の利便性をも考慮して，サービスとしての支援プログラムを設計し実行しているところが日本との大きな違いといえる。

希少疾患は，一国ごとの患者数で考えると「希少」といえるが，だからこそ情報の共有化や共同研究推進と言った国際連携は必須である。企業だけでなく，患者会や政府機関もその重要性を十分に理解し，米国をはじめとした前例に学び，参画するべきである。特に政府レベルでは，我が国の医薬品開発が安全かつ遅れをとることのないよう，オーファンドラッグ担当部署の設立を進めるとともに，国際連携の舞台でリーダーシップをとる存在になることを期待する。

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VIEWPOINT ARTICLE

The need for worldwide policy and action plans for rare diseases

John Forman (exec.director@nzord.org.nz)[1], Domenica Taruscio[2], Virginia A Llera[3], Luis A Barrera[4], Timothy R Coté[5], Catarina Edfjäll[6], Désirée Gavhed[7], Marlene E. Haffner[8], Yukiko Nishimura[9], Manuel Posada[10], Erik Tambuyzer[11], Stephen C Groft[12], Jan-Inge Henter (jan-inge.henter@ki.se)[7], on behalf of the International Conference for Rare Diseases and Orphan Drugs (ICORD)

1.New Zealand Organisation for Rare Disorders, Wellington, New Zealand
2.National Centre for Rare Diseases, Istituto Superiore di Sanità, Rome, Italy
3.Fundación GEISER, Mendoza, Argentina
4.Institute of Inborn Errors of Metabolism, Javeriana University, Bogota, Colombia
5.National Organization for Rare Disorders, Washington, DC, USA
6.Shire Human Genetic Therapies, Shire AG, Eysins, Switzerland
7.Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Karolinska University Hospital Solna, Stockholm, Sweden
8.Haffner Associates, Rockville, MD, USA
9.Promotion Research on Intellectual Property, The University of Tokyo, Tokyo, Japan
10.Research Institute for Rare Diseases, Instituto de Salud Carlos III, Madrid, Spain
11.ABConsult, Leuven, Belgium
12.Office of Rare Diseases Research, National Institutes of Health, Bethesda, MD, USA

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Correspondence
John Forman, New Zealand Organisation for Rare Disorders, PO Box 38-538, Wellington Mail Centre, Wellington 5045, New Zealand.
Tel: +64 4 471 2226 |
Email: exec.director@nzord.org.nz
or
Jan-Inge Henter, Childhood Cancer Research Unit Q6:05, Karolinska University Hospital, SE-171 76 Stockholm, Sweden.
Tel: +46 8 5177 2536 |
Fax: +46 8 5177 3184 |
Email: jan-inge.henter@ki.se

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ABSTRACT

There are more than 6000 rare diseases (defined as affecting <5/10 000 individuals in Europe, <200 000 people in the United States). The rarity can create problems including: difficulties in obtaining timely, accurate diagnoses; lack of experienced healthcare providers; useful, reliable and timely information may be hard to find; research activities are less common; developing new medicines may not be economically feasible; treatments are sometimes very expensive; and in developing countries, the problems are compounded by other resource limitations. Emphasis is required to support appropriate research and development leading to better prevention, diagnosis and treatments of rare diseases. Notably, clinical trials using already existing drugs may result in new, affordable, treatment strategies. Moreover, rare diseases may teach us about common disorders.

Conclusions: Countries are encouraged to implement specific research and development activities within their individual capabilities, so that patients worldwide have equal access to necessary interventions to maximize the potential of every individual.

INTRODUCTION

There are more than 6000 rare diseases, currently defined as affecting <1 per 2000 individuals in Europe or <200 000 people in the United States (1). Many rare diseases are diagnosed at the age of childhood, making diagnostic awareness and knowledge on treatment and care particularly important for paediatricians. The rarity of these diseases can create special problems for affected populations including the following:

1 Difficulties in obtaining timely and accurate diagnoses.
2 Lack of experienced healthcare providers.
3 Useful, reliable and timely information may be hard to find.
4 Research activities are less common.
5 Developing new medicines may not be economically feasible.
6 Treatments are sometimes very expensive.
7 In developing countries, the problems are compounded by other resource limitations.

Rapidly expanding scientific and technological advances are greatly improving our ability to intervene in various health conditions, including rare diseases. In the US and EU, legislation including the Orphan Drug Act (1983) and the Orphan Regulation No 141/2000 has brought many rare disease treatments into clinical practice (1,2). Rare disease issues feature increasingly in US and EU policy papers, as the EU Council Recommendation on rare diseases (2009), new action plans (http://www.europlanproject.eu), the EU Committee of Experts on Rare Diseases reports on the state of art of rare disease policy and research, and the International Rare Disease Research Consortium. However, numerous challenges lay ahead (3). Many countries do not

yet have policies for rare diseases and orphan products research and development.

The International Conference on Rare Diseases and Orphan Drugs (ICORD, http://www.icord.se) is a non-profit society, drawing together members from academia, patient advocacy, medicine regulatory, healthcare industry, healthcare services, and public policy agencies and organizations around the globe. Our mission is to improve health and welfare of patients with rare diseases and their families worldwide and reflect on rare disease policies for the future. We try to increase awareness and action internationally by using best practices and examples from all over the world and by bringing together top level experts from different stakeholders worldwide. We present this position statement as a basis for information to and discussion with national governments and international health bodies about rare disease policies.

HEALTH PRIORITIES, AND LEGAL, ETHICAL AND SOCIAL ISSUES

The United Nations Universal Declaration of Human Rights (Article 25.1), the International Covenant on Economic, Social and Cultural Rights (Article 12.1) and the United Nations Convention on the Rights of the Child include important statements about rights to health care. Moral philosophy offers additional guidance. The ethical principle of Justice requires that the needs of rare disease populations are specifically addressed, as for any minority or underserved community. A global approach to rare diseases is needed to utilize the experiences and knowledge gained from rare diseases research and orphan products development.

Key principles for adoption in health policy include:

1 Rare diseases are a significant public health issue. Together they may affect up to 8% of the population, corresponding to a significant minority population.
2 Health care and treatment for rare diseases is a human rights issue. Non-discrimination, justice and equity of access to health care all require that specific policies are put in place to address the needs of people affected by rare diseases.
3 Every country is encouraged to have a rare diseases research development program, with emphasis adjusted to its existing capabilities.
4 A comprehensive approach to rare diseases is needed, including education, prevention, diagnosis, care and treatment, social support and inclusion as well as support of both basic and clinical research.
5 Quality information, informed consent and autonomous decision-making are critical for upholding the rights and protection of patients and their families. Combining genetic knowledge with screening to identify risks should be actively pursued to provide choices about prevention, balanced with careful attention to informed consent and autonomous decision-making.
6 Patient groups play an important role in the development of knowledge about rare diseases and are suggested to be included at all levels in the development of their policies and services.

AN ACTION PLAN FOR IMPLEMENTING RARE DISEASES POLICIES

These twelve points are provided as guidance for the implementation of rare disease policies:

1 **Action plans**. Governments should recognize that rare diseases create disparities and vulnerabilities in health status for affected populations.
2 **Specific programs and policies**. Governments should recognize the human rights issues inherent in rare disease care and treatment across the lifespan. Specific programs and policies may be needed to protect those rights.
3 **Allocation of resources**. Governments should adopt policies for equitable allocation of resources towards all aspects of rare diseases, including information resources, basic research, clinical care, treatment development and clinical research. Moreover, support for clinical trials using already registered existing drugs and other treatments but for new indications should also be considered because this may be effective and cost-effective, as shown in many childhood cancer where remarkably improved outcomes have been achieved by repeated clinical trials using established drugs in new combinations (4).
4 **Specific counterbalancing policies**. Governments and health systems should offer incentives to encourage development of rare disease treatments and recognize problems with the research and development costs of such treatments. Regulatory requirements for clinical trials are important protections for patient safety, and it should be considered to approach these requirements differently for rare and very serious diseases.
5 **Cost effectiveness assessment should consider wider factors**. Health economics criteria, if used and if applicable, should not only consider the cost of treatment but also take into account personal, social and economic benefits of treating diseases.
6 **Specific benefits of research into rare diseases**. Research policies should note the specific benefits of research into rare diseases for gaining information, such as the cause of more common and multi-factorial diseases (5,6). This may justify weighting of research funds towards rare diseases.
7 **Recognition of gaining knowledge to aid prevention**. Gaining knowledge of disease processes may be as relevant for prevention as for treatment of a disease. Opportunities to prevent serious rare diseases should also be a research priority.
8 **Encouragement of industry to contribute to rare disease knowledge**. Industry should be encouraged to increase its 'public good' contributions to rare disease knowledge, such as through donation of products or techniques.

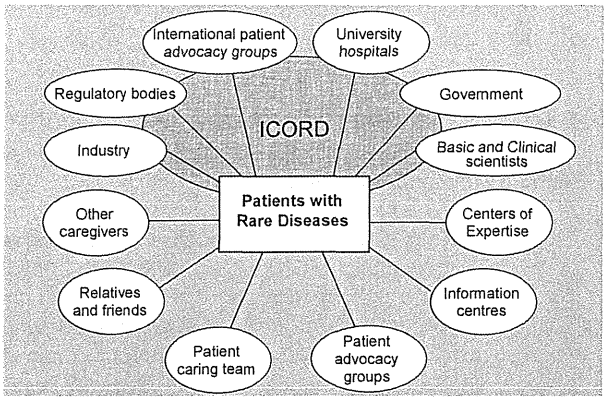

Figure 1 International Conference for Rare Disease and Orphan Drugs (ICORD) aims to facilitate contacts and networking among the many stakeholders involved in the health and welfare for patients with rare diseases. ICORD is a multidisciplinary non-profit society, drawing together members from healthcare services, patient advocacy groups, academia, medicine regulatory bodies, healthcare industry, and public policy agencies and organizations around the globe. In addition to the regular caring team, there are often other caregivers, supporting relatives and friends, and ideally a centre of expertise that can advice. To improve diagnostics, disease monitoring and treatment, both basic and clinical expertise is necessary, typically affiliated with university hospitals. Further information on diseases and treatments can be provided by information centres such as Orphanet (www.orpha.net). National governments and international health bodies have a central role on rare disease policies, and regulatory bodies review and support new drugs and medical devices developed by industry or academia. Patient advocacy groups can play a central role in many of the activities above.

9 **Patient advocacy groups participation in advisory groups and expert panels**. Patient advocacy groups provide important information and support and should be independently involved in advisory groups and expert panels to consider specific policy, ethical controls, risk management and service planning (7).

10 **Development of information networks and support group capacity**. Good information is an essential component of good health care. It can provide timely, reliable and useful information to enable people to become an expert in managing their own health, in partnership with their healthcare providers.

11 **Criteria for antenatal and newborn screening and ethical controls**. Criteria for antenatal and newborn screening and ethical controls for other predictive testing need regular reconsideration in the light of changes in knowledge of disease causes, patient and support group awareness, and prevention possibilities.

12 **Recognition of specific problems of rare diseases in developing nations**. Governments should recognize the specific problems of rare diseases in developing nations and investigate ways in which screening, diagnosis, treatment and clinical training can be provided in aid programs or other arrangements.

CONCLUSIONS

The diagnosis, prevention and treatment needs of patients with most rare diseases and conditions remain largely unmet despite the significant efforts of many stakeholders (Fig. 1). For several selected rare diseases, remarkable basic research, clinical research and orphan products development activities have occurred leading to suitable treatments (1–6). However, more emphasis is required to support appropriate research and development activities leading to the development of prevention, diagnosis and treatments of rare diseases. Notably, clinical trials using already existing drugs and other treatments may be successful in finding new, affordable treatment strategies.

All countries are encouraged to implement specific research and development activities within their individual capabilities. Only when this has occurred will all patients around the world have equal access to necessary interventions to maximize the potential of every individual.

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事務局：一般社団法人日本難病・疾病団体協議会（JPA）
〒162-0822東京都新宿区下宮比町 2 -28飯田橋ハイタウン610号
TEL03-6280-7734　FAX03-6280-7735　E-mail : jpa-kenkyu@nanbyo.jp