



1. Introduction

1.1 Rare diseases are a large group of diseases that are characterised by a low prevalence in the population.¹ While individually rare, there are more than 7 000 rare diseases collectively affecting 1 in 15 persons worldwide.² Although nearly all genetic diseases are rare diseases, not all rare diseases have a genetic origin. Rare diseases also cover very rare forms of infectious diseases, as well as auto-immune diseases and rare cancers.³

1.2 Rare diseases are serious chronic diseases and are often life-threatening. They pose challenges to the medical sector in view of the diverse types of rare disease conditions that exist, insufficient knowledge or training on the diseases, and the high costs and risks of research and development of drugs (commonly referred to as "orphan drugs") for treating the diseases given the small and dispersed patient base for each disease. As a result, medical care for patients suffering from rare diseases may be hampered by delayed diagnosis, unavailability of treatments, and/or limited access to costly drugs and treatments. These patients and their families are facing immense physical, psychological and economic burdens.

1.3 At its meeting on 19 December 2016, the Panel on Health Services requested the Research Office to study the policy on the provision of support measures for rare disease patients in overseas places to facilitate discussion of the subject matter. This information note studies the United States ("the US"), the European Union ("the EU"), Japan and Taiwan which have devised comprehensive medical care policies over the years to address issues faced by rare disease patients. The paragraphs below give an overview of the rare disease policies in Hong Kong and the overseas places studied, and the

¹ Rare diseases are often referred to as orphan diseases due to the lack of financial incentives for pharmaceutical companies to develop drugs that would treat a small target patient population.

² See De Vruh, R. et al (2013), Shafie, A. et al (2016) and Song, P. et al (2012).

³ See De Vruh, R. et al (2013).

salient features of the latter are compared in the **Table**. It is followed by **Appendices I-IV** which give the details of the rare disease policies in the overseas places studied in terms of the definition of rare diseases, policy framework, relevant legislation, medical and social care support to rare disease patients, and recent developments on the diagnosis and treatments of rare diseases.

2. Rare disease policy in Hong Kong

2.1 In Hong Kong, the Clinical Genetic Service of the Department of Health provides clinical diagnosis, counselling and prevention services for families possibly affected by genetic related diseases. Meanwhile, the Hospital Authority provides medical services for patients suffering from genetic diseases. Furthermore, the Department of Health and the Hospital Authority started the Pilot Study of Newborn Screening for Inborn Errors of Metabolism in October 2015, in an effort to prevent and reduce severe problems arising from inborn errors of metabolism. The number of inborn errors of metabolism covered under the Pilot Study increased from 21 to 24 in April 2016.

2.2 Since 2008-2009, the Government has also subsidized patients who suffer from six specified types of lysosomal storage disorder⁴ and meet the specific clinical criteria to obtain enzyme replacement therapy. Recently, the Government has planned to provide drug subsidies to eligible patients suffering from specified rare diseases (e.g. Paroxysmal Nocturnal Haemoglobinuria) through the Community Care Fund.

2.3 Notwithstanding the above-mentioned medical services provided, the Government has not established any official definition of rare diseases, nor has it set out any specific policy on provision of support for rare disease patients. Indeed, some key stakeholders (particularly patient groups) have criticized the Government for being unable to provide adequate support to rare disease patients, as evidenced by (a) the delay in the time to diagnose rare diseases; (b) limited number of patients receiving subsidies to help cover the high-cost medication; (c) the lack of a comprehensive patient registry to facilitate the

⁴ The six types of lysosomal storage disorders are Gaucher disease, Pompe disease, Mucopolysaccharidosis Type I/Type II/Type VI and Fabry disease. Up to December 2015, the Hospital Authority had provided enzyme replacement therapy to 24 patients with lysosomal storage disorders.

provision of evidence-based treatments to patients; and (d) insufficient provision of social care services to patients and their carers.⁵

3. Rare disease policies in selected places

3.1 The US, the EU, Japan and Taiwan have devised policies over the years to address issues faced by rare disease patients. These places have set out a definition of rare diseases and put in place an orphan drug designation system to encourage the development of orphan drugs for treating rare diseases. They have also implemented other measures to support the medical and/or social care of rare disease patients under their respective policy framework.

Definition of rare diseases

3.2 All the overseas places studied have defined rare diseases in terms of a prevalence rate measured by the total number of rare disease patients (less than 200 000 in the US), the number of rare disease patients in 10 000 persons (fewer than five in the EU and fewer than one in Taiwan), or the proportion of rare disease patients in the total population (less than 0.1% of the population in Japan). In addition, Japan and Taiwan have considered other criteria in their definition of rare diseases such as diseases that are difficult to diagnose and treat.

Orphan drug designation system

3.3 Among the overseas places studied, the US was the first to pass specific legislation (i.e. the Orphan Drug Act) designed to promote development of treatments for rare diseases. The Act contains provisions governing the designation of orphan drugs and granting of incentives and assistance in the regulatory process to encourage pharmaceutical companies to develop orphan drugs. Subsequently, Japan, the EU and Taiwan have also passed legislation to establish a similar orphan drug designation system and provide incentives to address the issue about the limited availability of drugs

⁵ See Minutes of Meeting of the Panel on Health Services of the Legislative Council (2014) and Hong Kong Alliance for Rare Diseases (2016).

and treatments for rare diseases. The incentives granted by the overseas places studied generally include financial subsidies and tax relief on research expenses, fast-track marketing approval process, and marketing exclusivity for a certain number of years after obtaining marketing authorization of an orphan drug.

3.4 As a result of the introduction of the orphan drug designation system, all the overseas places studied have experienced increased orphan drug development activities and greater availability of authorized/approved orphan drugs for treating rare diseases. For example, between 2000 and 2016, the EU has designated 1 805 orphan drugs and granted marketing authorizations to 128 orphan drugs for treating 101 conditions. Likewise in the US, the number of designated orphan drugs totalled 4 023 at end-February 2017. The orphan drug designation system has also successfully enabled the development and marketing of over 575 drugs and biologic products for rare diseases since 1983. In contrast, fewer than 10 such products supported by industry came to market between 1973 and 1983.

Other support measures for rare disease patients

3.5 In addition to the orphan drug designation system, all the overseas places studied have adopted the following common measures to enhance the awareness, early identification, prevention and treatments of rare diseases: (a) providing relevant information on rare diseases through an online information centre; (b) implementing a newborn screening programme; (c) establishing a patient registry or a repository of registries to facilitate information sharing for patient care and research purposes; and (d) committing resources on research and development on rare diseases. It is noteworthy that Japan and Taiwan have specifically addressed the need for social care services among rare disease patients in their policy framework. In particular, they have expanded the definition of persons with disabilities to cover patients suffering from designated rare diseases and provided them with social care services that are stipulated in the relevant legislation.

Table – Rare disease policies in selected places

	The United States	The European Union	Japan	Taiwan
Definition and prevalence of rare diseases				
Definition of rare diseases in terms of prevalence criterion	<ul style="list-style-type: none"> Less than 200 000 patients. 	<ul style="list-style-type: none"> Fewer than five in 10 000 persons. 	<ul style="list-style-type: none"> Less than 0.1% of the country's population. 	<ul style="list-style-type: none"> Fewer than one in 10 000 persons (less than 0.01%).
Other criteria considered for designation of rare diseases	<ul style="list-style-type: none"> Not specified. 	<ul style="list-style-type: none"> Not specified. 	<ul style="list-style-type: none"> Other criteria include: <ul style="list-style-type: none"> (a) causes of diseases not being identified; (b) lacking effective treatments; (c) requiring long-term treatments; and (d) existence of objective diagnostic criteria. 	<ul style="list-style-type: none"> Other criteria include: <ul style="list-style-type: none"> (a) having a genetic origin; and/or (b) being difficult to diagnose and treat.
Number of rare diseases/ designated rare diseases affecting the population	<ul style="list-style-type: none"> About 7 000 rare diseases. 	<ul style="list-style-type: none"> About 5 000 to 8 000 rare diseases. 	<ul style="list-style-type: none"> 306 designated intractable/rare diseases. 	<ul style="list-style-type: none"> About 210 designated rare diseases.
Prevalence of rare diseases	<ul style="list-style-type: none"> Between 25-30 million persons in the US suffering from rare diseases. 	<ul style="list-style-type: none"> About 30 million persons in the EU suffering from rare diseases. 	<ul style="list-style-type: none"> 943 460 patients in Japan suffering from designated intractable/rare diseases as at end-2015. 	<ul style="list-style-type: none"> 7 625 patients in Taiwan suffering from designated rare diseases in 2015.
Policy framework				
Responsible authorities	<ul style="list-style-type: none"> The United States Department of Health and Human Services, the United States Food and Drug Administration, and relevant state authorities. 	<ul style="list-style-type: none"> European Medicines Agency and relevant authorities of individual member states. 	<ul style="list-style-type: none"> Ministry of Health, Labour and Welfare ("MHLW"). 	<ul style="list-style-type: none"> Ministry of Health and Welfare ("MOHW").

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Japan	Taiwan
Policy framework (cont'd)				
Relevant legislation	<ul style="list-style-type: none"> The Orphan Drug Act of 1983 and the Rare Diseases Act of 2002. 	<ul style="list-style-type: none"> The European Union Regulation on Orphan Medicinal Products. 	<ul style="list-style-type: none"> The Pharmaceutical Affairs Act; and the Act on Medical Care and Social Supports for Patients with Intractable/Rare Diseases. 	<ul style="list-style-type: none"> Rare Disease and Orphan Drug Act 《罕見疾病防治及藥物法》.
Policy scope identified	<ul style="list-style-type: none"> Promoting development of orphan drugs. Supporting research and development on rare diseases. 	<ul style="list-style-type: none"> Promoting development of orphan drugs. Supporting member states to ensure their effective and efficient recognition, prevention, diagnosis and treatments of, and research on, rare diseases. 	<ul style="list-style-type: none"> Developing effective treatments, and enhancing medical and social care services for rare disease patients. Establishing a fair and consistent subsidization mechanism. Enhancing public understanding of rare diseases. 	<ul style="list-style-type: none"> Improving the awareness, prevention, diagnosis, and treatment of rare diseases. Enhancing medical and social care services for rare disease patients.
Orphan drug designation system				
Criteria of defining an orphan drug	<ul style="list-style-type: none"> The drug is to treat a disease which (a) affects less than 200 000 persons in the US; or (b) affects more than 200 000 persons in the US but cost of developing the drug is not recoverable from sales in the country. 	<ul style="list-style-type: none"> The drug is intended for treating a life-threatening disease that meets the prevalence criterion and no satisfactory treatment is available. 	<ul style="list-style-type: none"> The drug must meet three criteria: (a) to be used by less than 50 000 patients in Japan; (b) indicated for the treatment of serious diseases and no alternatives are available; and (c) with a scientific rationale to support the need for the drug. 	<ul style="list-style-type: none"> The drug should have major indications for the prevention, diagnosis and treatment of designated rare diseases.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Japan	Taiwan
Orphan drug designation system (cont'd)				
Provision of financial incentives and assistance in regulatory process to facilitate research and development activities	<ul style="list-style-type: none"> Including financial subsidies/tax credit, fast-track marketing authorization and a seven-year period of marketing exclusivity. 	<ul style="list-style-type: none"> Including a 10-year period of marketing exclusivity, research grants and reduced fees for marketing authorization applications. 	<ul style="list-style-type: none"> Including financial subsidies/tax relief, a 10-year period of marketing exclusivity and fast-track marketing authorization. 	<ul style="list-style-type: none"> Including a 10-year period of marketing exclusivity, and allowance for special application for usage reimbursement of designated orphan drugs prior to market approval.
Number of designated orphan drugs	<ul style="list-style-type: none"> 4 023 as at February 2017. 	<ul style="list-style-type: none"> 1 805 between 2000 and 2016. 	<ul style="list-style-type: none"> 327 as at January 2014. 	<ul style="list-style-type: none"> 98 as at January 2017.
Number of designated orphan drugs granted with marketing authorization or approval	<ul style="list-style-type: none"> More than 575 since 1983. 	<ul style="list-style-type: none"> 128 between 2000 and 2016. 	<ul style="list-style-type: none"> 203 as at January 2014. 	<ul style="list-style-type: none"> Information not available.
Reimbursement of drug costs incurred by rare disease patients	<ul style="list-style-type: none"> Drug costs are covered by (a) the public or private insurance schemes that the patients enrolled in; and (b) co-payments by patients. 	<ul style="list-style-type: none"> Reimbursement of drug costs is made in accordance with the healthcare financing systems and reimbursement arrangements put in place by individual member states. 	<ul style="list-style-type: none"> Costs of using orphan drugs granted with marketing approval can be reimbursed under the health insurance system. 	<ul style="list-style-type: none"> Reimbursement of drug costs can be arranged for those drugs which are approved to be on the list of drugs covered by the National Health Insurance Administration. Reimbursement of the costs of using unlisted drugs is allowed if approval is sought prior to drug usage.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Japan	Taiwan
Other support measures for diagnosis and treatment of rare disease patients				
Information provided to enhance key stakeholders' awareness and knowledge of rare diseases	<ul style="list-style-type: none"> • Current and easy-to-understand information provided through the Genetic and Rare Diseases Information Center. 	<ul style="list-style-type: none"> • Comprehensive and updated information provided through the Orphanet portal. 	<ul style="list-style-type: none"> • Information provided through an online resource centre (i.e. the Japan Intractable Diseases Information Center). 	<ul style="list-style-type: none"> • Information provided by MOHW through a specific portal and public education programmes.
Facilitation measure for early identification of rare diseases.	<ul style="list-style-type: none"> • Newborn screening programmes implemented by individual states. 	<ul style="list-style-type: none"> • Newborn screening programmes implemented by individual member states. 	<ul style="list-style-type: none"> • Not specified under the government's policy framework. 	<ul style="list-style-type: none"> • Newborn screening programme covering 11 metabolism disorders.
Facilitation measures for accessing medical care services	<ul style="list-style-type: none"> • Passage of the Patient Protection and Affordable Care Act in 2010 to remove various discriminatory insurance practices against rare disease patients. 	<ul style="list-style-type: none"> • Subject to the policy framework of individual member states. 	<ul style="list-style-type: none"> • Patients only have to bear 20% of the medical costs as co-payment, capped at a monthly limit set by MHLW. 	<ul style="list-style-type: none"> • Patients of designated rare diseases are provided with 80% reimbursement for medical and medication costs under the National Health Insurance programme. Low-income patients can receive 100% reimbursement. • Patients are subsidized to access overseas diagnostic services in case these services are not available locally.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Japan	Taiwan
Other support measures for diagnosis and treatment of rare disease patients (cont'd)				
Facilitation measures for accessing social care services	<ul style="list-style-type: none"> Not specified under the government's policy framework. 	<ul style="list-style-type: none"> Not specified under the policy framework of the European Union. 	<ul style="list-style-type: none"> Provision of social care services through the intractable/rare diseases consultation and support centres. Expanding the definition of persons with disabilities to cover persons suffering from most designated intractable/rare diseases and providing them with relevant social care services. 	<ul style="list-style-type: none"> Expanding the definition of persons with disabilities to cover persons suffering from designated rare diseases and providing them with relevant social care services.
Establishment of a patient registry/reporting system	<ul style="list-style-type: none"> Yes, through the Global Rare Diseases Patient Registry Data Repository to store patient information from different registries set up by patient advocacy groups or researchers. 	<ul style="list-style-type: none"> Yes, member states develop their own patient registries. 	<ul style="list-style-type: none"> Yes. 	<ul style="list-style-type: none"> Yes.
Committing resources on research and development ("R&D") on rare diseases	<ul style="list-style-type: none"> Yes, the Office of Rare Diseases Research under the National Institutes of Health is tasked to promote R&D on rare diseases. 	<ul style="list-style-type: none"> Yes, the European Commission funds collaborative R&D projects conducted by institutions across Europe and other countries. 	<ul style="list-style-type: none"> Yes, MHLW commits resources on R&D projects related to rare diseases. 	<ul style="list-style-type: none"> Yes, MOHW provides incentives to encourage institutions to engage in R&D on rare diseases.

Rare disease policy in the United States

A.I.1 In the US, the federal government enacted as early as in 1983 the Orphan Drug Act to support the medical treatment of rare disease patients. As discussed below, the Act provides for the establishment of an orphan drug designation system and the provision of various incentives to encourage research and development on orphan drugs for the treatment of rare diseases. In 2002, the federal government went further to enact the Rare Diseases Act to boost the research into rare diseases and the development of new treatments.

A.I.2 At the state level, individual states are responsible for setting and implementing their own medical care policies for the diagnosis and treatment of rare disease patients. According to the National Organization for Rare Disorders,⁶ California has put in place a medical care policy with more comprehensive support to rare disease patients than other states.⁷ Against this, the case of California is highlighted below to show how a comprehensive medical care policy could help a rare disease patient.

Orphan drug designation system

A.I.3 The US was the first place in the world to pass specific legislation designed to promote development of treatments for rare diseases, with provisions governing the designation of orphan drugs and granting of incentives to encourage pharmaceutical companies to develop orphan drugs. According to the Orphan Drug Act, the US Food and Drug Administration⁸ will define a drug as an orphan drug if it treats a disease which: (a) affects less than 200 000 persons in the US; or (b) affects more than 200 000 persons in the US but the cost of developing and producing the drug is not expected to be recovered from drug sales in the country.

⁶ The National Organization for Rare Disorders is an independent, non-profit advocacy organization representing rare disease patients and their families in the US.

⁷ See National Organization for Rare Disorders (2016a).

⁸ The US Food and Drug Administration is a federal agency responsible for inspecting, testing, approving, and setting safety standards for foods and food additives, drugs, chemicals, cosmetics, and household and medical devices.

A.I.4 The Orphan Drug Act also provides for various incentives to promote the development of orphan drugs in the US. For example, the manufacturer of a designated orphan drug is entitled to (a) financial subsidies and tax credit on costs of clinical studies; (b) a seven-year period of marketing exclusivity following the grant of marketing approval to protect the drug from competition from similar products; and (c) a fast-track marketing approval procedure. Manufacturers have to obtain marketing approval from the US Food and Drug Administration before they can sell their orphan products in the market. Nonetheless, an orphan drug may be adopted for compassionate use before a marketing approval is granted under specified conditions.⁹

Access to medication of rare diseases

A.I.5 Under the health insurance system in the US, patients' medical and medication costs are covered by the public or private insurance schemes that they have enrolled in and co-payments of patients.¹⁰ Previously, rare disease patients could not access healthcare coverage due to various discriminatory insurance practices. The passage of the Patient Protection and Affordable Care Act in 2010 successfully reformed these practices by forbidding insurers from discriminating against rare disease patients (such as denying coverage for patients having a pre-existing condition) and outlawing annual and lifetime coverage limits.¹¹

⁹ The specified conditions are that: (a) the drug is intended to treat a serious or immediately life-threatening disease; (b) there is no satisfactory alternative treatment available; (c) the drug is already under investigation or trials have been completed; and (d) the pharmaceutical company is actively pursuing marketing approval.

¹⁰ Eligible low-income persons and persons with disabilities are provided with free or low-cost medical benefits under the Medicaid programme jointly funded by the federal and state governments.

¹¹ The Patient Protection and Affordable Care Act has been opposed by some stakeholders as it has brought about issues such as increase in insurance costs from better insurance coverage. Currently, the federal government has been reviewing the health insurance system with a view to repealing the Act.

Other support measures

A.I.6 The federal government enacted the Rare Diseases Act in 2002 to empower the Office of Rare Diseases Research ("ORDR"¹²) under the National Institutes of Health ("NIH"¹³) to promote research and development on diagnostics and treatments for rare diseases. Pursuant to the Act, NIH set up the Genetic and Rare Diseases Information Center in 2002 to provide patients, their families and medical professionals access to current and easy-to-understand information about rare diseases. ORDR also set up a rare diseases clinical research network in 2009 to enhance collaboration and information sharing among research institutions in the US and other countries.

A.I.7 In addition, NIH developed the Global Rare Diseases Patient Registry Data Repository in 2010 to aggregate and store patient information from different registries set up by patient advocacy groups or researchers. The Repository enables stakeholders to access information about multiple rare diseases through a centralized source and facilitates research on rare diseases.

Rare disease policy in California

A.I.8 In California, the California Department of Public Health ("CDPH") has implemented a newborn screening programme to facilitate early identification and intervention of genetic and congenital disorders among babies.¹⁴ At present, the screening programme covers some 80 disorders including metabolic, endocrine and hemoglobin disorders. In 2016, the programme has further been enhanced after the enactment of a law requiring CDPH to expand the programme to include screening for any disease within two years after the disease is included in the list of conditions for screening recommended by the Advisory Committee on Heritable Disorders in Newborns and Children.¹⁵

¹² ORDR was established in 1993 within the NIH Office of the Director. In 2012, ORDR became part of the National Center for Advancing Translational Sciences tasked to develop innovations in an effort to speed the delivery of new drugs, diagnostics and medical devices to patients.

¹³ NIH is an agency under the Department of Health and Human Services responsible for providing leadership and direction to research programmes to improve the health of the public. NIH comprises 27 institutes and centres with each having its own specific research agenda.

¹⁴ All the states in the US have implemented a newborn screening programme as a public health programme. However, the conditions screened under their respective programmes vary.

¹⁵ The Advisory Committee is tasked to advise the Secretary of the Department of Health and Human Services on the development of newborn screening policies and programmes for reducing morbidity and mortality in newborns and children having heritable disorders.

A.I.9 The protection of patients, including those suffering from rare diseases has been enhanced after the recent passage of a law that limits patients' out-of-pocket payments for prescription drugs. Patients' access to appropriate drugs and treatments has also been enhanced by laws stipulating that (a) doctors can appeal against insurers' decision to adopt step therapy¹⁶ for their patients, and (b) pharmacists must communicate to the patients and their doctors if they substitute a biologic drug with a lower cost non-identical alternative.

Recent developments on diagnosis and treatments of rare diseases

A.I.10 NIH estimates that between 25 million to 30 million persons in the US are affected by about 7 000 rare diseases.¹⁷ The enactment of the Orphan Drug Act in 1983 has increased the number of designated orphan drugs to 4 023 at end-February 2017. The Act has also spurred the development of drugs for treating rare diseases, leading to the development and marketing of more than 575 orphan drugs and biologic products. In contrast, fewer than 10 orphan drugs were introduced in the market between 1973 and 1983. As for research on rare diseases, funding of the researches undertaken by NIH amounted to US\$3.8 billion (HK\$29.5 billion) in 2016, up from US\$3.6 billion (HK\$27.9 billion) in 2012.

A.I.11 Nonetheless, patient advocacy groups are concerned that approved orphan drug treatments are only available for less than 10% of rare diseases affecting patients in the US.¹⁸ Besides, they are discontented with the high disparity among states in terms of the coverage of the state newborn screening programmes and the protection provided for patients under the health insurance systems. They have lobbied the state governments to enhance support and protection of rare disease patients.

¹⁶ Insurers may seek to control costs with the use of step therapy requiring insured patients to take one or more different lower-cost medications before getting the one that their doctors originally recommended.

¹⁷ See National Institutes of Health (2016).

¹⁸ See National Organization for Rare Disorders (2016b).

Rare disease policy in the European Union

A.II.1 In the EU, rare diseases were identified, for the first time, as a "priority field" for public health action in 1993. In 1999, rare diseases were further classified as a "priority area" for community action in the context of public health and the first programme of community action was adopted for the period between 1999 and 2003. The programme focused on improving knowledge and facilitating access to information about rare diseases for enhancing health protection of patients. Under the programme, rare diseases were defined as any disease affecting fewer than five in 10 000 persons in the EU.

A.II.2 In 2000, the European Commission¹⁹ established an orphan drug designation system pursuant to the EU Regulation on Orphan Medicinal Products in order to promote the development of orphan drugs for treating rare diseases in the EU. In 2008, the European Commission set out an overall Community strategy for supporting member states in ensuring effective and efficient recognition, prevention, diagnosis and treatment of, and research on rare diseases in the EU. Member states have also been engaging in developing national plans to combat rare diseases since 2009.

Orphan drug designation system

A.II.3 Under the orphan drug designation system, the European Commission will consider to grant orphan drug designation to a medicine if it meets the following three criteria: (a) the medicine must be intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (b) the prevalence of the condition in the EU must be no more than five in 10 000 persons or it is unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; and (c) no satisfactory method of diagnosis, prevention or treatment of the condition concerned has been authorized or, if such a method exists, the medicine will be of significant benefit to those affected by the condition.

¹⁹ The European Commission is the executive arm of the EU and promotes its general interest.

A.II.4 Pharmaceutical companies developing designated orphan drugs are offered with incentives at the EU and individual member state levels to encourage their research and development activities. These incentives include: (a) scientific advice of the European Medicines Agency²⁰ at a reduced fee; (b) reduced fees for marketing authorization applications and other regulatory activities; (c) research grants; and (d) a 10-year period of marketing exclusivity after obtaining marketing authorization.

Access to medication of rare diseases

A.II.5 All designated orphan drugs are required to be assessed through a centralized marketing authorization procedure administered by the European Medicines Agency and granted authorization by the European Commission before they can be marketed in the EU.²¹ Nonetheless, many member states have implemented compassionate use programmes enabling patients to access orphan drugs that are being considered for but not yet been granted marketing authorization under specified conditions.²² The costs of orphan drugs incurred by patients are reimbursed in accordance with the healthcare financing systems and reimbursement arrangements put in place by individual member states.²³

²⁰ The European Medicines Agency is an agency of the EU responsible for the scientific evaluation, supervision and safety monitoring of medicines developed by pharmaceutical companies for use in the EU.

²¹ Under the centralized authorization procedure, pharmaceutical companies can submit a single marketing authorization application to the European Medicines Agency and the authorization is valid across all EU member states once it is granted.

²² For example, Germany allows patients with a seriously debilitating or life-threatening disease to access unauthorized orphan drugs if they cannot be treated satisfactorily with an authorized medicine.

²³ For example, the costs of using authorized orphan drugs are fully reimbursed by statutory health insurance in Germany.

Other support measures

A.II.6 Based on the overall Community strategy on rare diseases adopted in 2008, the European Commission has implemented a series of measures to pool resources across the EU member states to help patients and medical professionals share information and expertise across borders. These measures include: (a) funding operation of the Orphanet portal²⁴ to provide comprehensive and updated information on rare diseases and orphan drugs; (b) providing supporting tools to individual member states to help them develop their national plans on rare diseases; (c) funding the collaborative research projects on the causes of rare diseases, and on preventive, diagnostic and therapeutic interventions; (d) supporting the development of patient registries by individual member states to facilitate clinical research on rare diseases and patient care planning, and developing a European platform on rare diseases registration; and (e) evaluating the current practices of newborn screening for rare diseases in individual member states and exploring potential areas of collaboration among member states in this field.

Recent developments on diagnosis and treatments of rare diseases

A.II.7 At present, it is estimated that there are 5 000 to 8 000 rare diseases affecting about 30 million people in the EU.²⁵ According to the European Commission, the implementation of the overall Community strategy on rare diseases has fostered co-operation and exchange in experiences among the EU member states and other stakeholders. The strategy has also supported the EU member states to develop their national plans for rare diseases. As at February 2017, 22 out of the 28 member states have put in place dedicated plans to combat rare diseases. Besides, the European Commission has funded some 120 collaborative research projects relating to rare diseases between 2007 and 2013 with a total budget of over €620 million (HK\$6,386 million).

²⁴ Orphanet is a free multilingual portal administered by the European Commission on rare diseases and orphan drugs. It contains information on more than 5 000 rare diseases and aims to improve the quality of medical care and provide specialized services for the rare disease community.

²⁵ See European Medicines Agency (2017a).

Appendix II (cont'd)

A.II.8 Between 2000 and 2016, the European Commission has designated 1 805 orphan drugs, and granted marketing authorizations for 128 orphan drugs for treating 101 conditions. Nonetheless, there has been disparity in patients' access to authorized orphan drugs among the EU member states as they have set different pricing and reimbursement mechanisms. Member states have also faced challenge in providing affordable and sustainable access to drugs for rare disease patients as possible treatments are scarce and expensive.

Rare disease policy in Japan

A.III.1 In Japan, rare diseases are categorized as intractable diseases characterized by (a) a lack of an identifiable cause and a clearly established treatment; (b) having a considerable high risk of disability; and (c) posing heavy economic and psychological burdens on the patients and their families. The Japanese government first introduced a dedicated policy to combat intractable/rare diseases in 1972. Under the policy, the Specified Disease Treatment Research Programme was implemented to promote research on intractable/rare diseases and provide financial subsidy to patients. Eligible intractable/rare disease patients who had participated in the research programme were provided with subsidy on their medical costs.²⁶

A.III.2 Japan has seen improvements in the medical treatments for patients suffering from intractable/rare diseases and advancement in related research activities since the introduction of the first policy on intractable/rare diseases in 1972. Nonetheless, in order to further enhance the support provided for intractable/rare disease patients, the Japanese government conducted a review on its intractable/rare disease policy in 2011 and subsequently enacted the Act on Medical Care and Social Supports for Patients with Intractable/Rare Diseases in 2014. The Act lays down the framework for provision of comprehensive support for intractable/rare disease patients in three major areas: (a) development of effective treatments for intractable/rare diseases and improvement of care for those affected; (b) establishment of a fair and consistent subsidization mechanism for patients' medical expenses; and (c) implementation of measures to enhance public understanding of intractable/rare diseases and encourage social participation of patients.

²⁶ For patients participating in the Specified Disease Treatment Research Programme, the co-payment bore by the patients was capped at a limit specified by the Ministry of Health, Labour and Welfare. Patients with low income and those with severe medical conditions were fully subsidized on their co-payment.

Orphan drug/medical device designation system

A.III.3 To encourage the research and development of life-saving but generally unprofitable drugs and medical devices for the treatment of intractable/rare diseases, the Japanese government established an orphan drug/medical device designation system in 1993 pursuant to an amendment of the Pharmaceutical Affairs Act. Under the system, the Ministry of Health, Labour and Welfare ("MHLW") will consider to designate a product as an orphan drug or medical device based on the following three criteria: (a) the product will be used by less than 50 000 patients; (b) it should be indicated for the treatment of serious diseases and there is no appropriate alternative available or is clinically superior to products available in the market; and (c) there should be a scientific rationale for using the product for the target disease and the development plan should be appropriate.

A.III.4 MHLW offers incentives to institutions developing designated orphan drugs/medical devices to support their research and development activities. These incentives include: (a) financial aids such as subsidy and tax relief for research expenses; (b) guidance and consultation from the Pharmaceuticals and Medical Devices Agency²⁷ at a lower fee; (c) a fast-track marketing approval process;²⁸ and (d) a 10-year period of marketing exclusivity. The costs incurred by intractable/rare disease patients on orphan drugs granted with marketing approval can be reimbursed under the health insurance system of Japan at a price set by MHLW.²⁹

²⁷ The Pharmaceuticals and Medical Devices Agency is the government organization in Japan in charge of reviewing drugs and medical devices, overseeing post-market safety, and providing relief for adverse health effects. The Agency charges the pharmaceutical companies for the advice and consultation provided.

²⁸ Institutions intending to manufacture or sell drugs or medical devices in Japan are required to obtain an approval from MHLW for each product. The products will be examined on their efficacy and safety in the approval process.

²⁹ The fees for medical care and medications charged by medical institutions and pharmacies on patients insured under the national health insurance system are set by MHLW based on the recommendations of the Central Social Insurance Medical Council.

Appendix III (cont'd)

A.III.5 In 2015, MHLW implemented a new scheme for subsidizing the medical fees of patients suffering from designated intractable/rare diseases. Designated intractable/rare diseases are defined as those diseases that meet the following criteria: (a) affecting less than 0.1% of the population in Japan; (b) causes not being identified; (c) lacking effective treatments; (d) requiring long-term treatments; and (e) existence of objective diagnostic criteria. The number of intractable/rare diseases covered under the new scheme increased from 56 to 306 by July 2015. Patients are only required to bear 20% of the medical costs as co-payment, capped at a monthly limit set by MHLW. The figure is lower than the 30% co-payment rate applicable to general patients covered under the health insurance system in Japan.

Other support measures

A.III.6 On medical care services, MHLW has improved the service provision by designating hospitals and doctors that are specialized in treating intractable/rare diseases for providing diagnoses and treatments for patients. Designated doctors are required to meet specified level of experience and training. For further improving the quality of medical care for patients, the local public health centres provide outreach and community care services to support these patients. MHLW also commits resources on research on diagnosis, prevention and treatment of intractable/rare diseases, and patients' quality of life.

A.III.7 In addition, MHLW has enhanced the national registry of designated intractable/rare diseases since 2015 to enable collection of data from designated doctors. The enhancement facilitates sharing of patient information among medical institutions and professionals for patient care planning and research purposes.³⁰

³⁰ The national registry was established before 2000 and data had been collected by the local public health centres mainly for administration of the patient subsidy scheme and research on intractable/rare diseases.

Appendix III (cont'd)

A.III.8 As for social care services, MHLW has enhanced the capabilities of the local intractable/rare diseases consultation and support centres³¹ in providing social care services for patients such as counselling and employment support services. These consultation and support centres team up with the local public health centres on providing coordinated social and medical care services for patients. More importantly, patients suffering from most designated intractable/rare diseases are included in the definition of persons with disabilities under the General Support for Persons with Disabilities Act. They are entitled to welfare services stipulated in the Act, which include nursing care services, community life support services, and training services for securing or sustaining employment.

A.III.9 In addition to the above, the Japan Intractable Diseases Information Center has been a major information source for intractable/rare disease patients and other key stakeholders (e.g. patients' families and medical professionals). This online resource centre was established by MHLW in 1997 in corporation with the Japan Intractable Diseases Research Foundation. MHLW has planned to further enhance the content of the Information Centre to promote public understanding of intractable/rare diseases.

Recent developments on diagnosis and treatments of rare diseases

A.III.10 As at end-2015, about 943 460 patients suffering from designated intractable/rare diseases were receiving financial subsidy for their medical costs under the new subsidization scheme set out in the Act on Medical Care and Social Supports for Patients with Intractable/Rare Diseases of 2014. The estimated cost of the subsidization scheme in 2015 was ¥222 billion (HK\$14.2 billion). These compare with 855 061 patients and ¥133.5 billion (HK\$10.6 billion) under the old scheme in 2013. Regarding the development of orphan drugs, MHLW had designated 327 products as orphan drugs as at January 2014, of which 203 products had been granted marketing approval. The majority of orphan drugs approved in Japan are for treating infectious diseases, haematological diseases, neuromuscular diseases, and diseases common in children and infants.

³¹ MHLW has supported the local governments to set up intractable/rare diseases consultation and support centres since 2003 to provide social care services for intractable/rare disease patients.

Rare disease policy in Taiwan

A.IV.1 Prior to 2000, Taiwan's National Health Insurance programme³² did not cover the drug and treatment costs incurred by rare disease patients unless the rare diseases had been defined as major illnesses. In order to enhance the support to rare disease patients, the Taiwanese government promulgated the Rare Disease and Orphan Drug Act ("Rare Disease Act") 《罕見疾病防治及藥物法》 in August 2000. The Act lays down a comprehensive framework to improve the awareness, prevention, diagnosis and treatment of rare diseases in Taiwan. The Taiwanese government aims to provide rare disease patients with easier access to drugs and life-sustaining nutritional supplements by promoting and ensuring the research and development, manufacturing and supply of these products.

Orphan drug designation system

A.IV.2 According to the Rare Disease Act, rare diseases are defined as diseases having a prevalence rate of lower than 1 in 10 000 persons or 0.01%, or diseases meeting other specified criteria such as having a genetic origin or being difficult to diagnose and treat. Applications for designation of rare diseases are reviewed by the Committee for the Review of Rare Diseases and Orphan Drugs ("the Review Committee") under the Ministry of Health and Welfare ("MOHW"). The Review Committee also considers applications for designation of orphan drugs which are defined as drugs having major indications for the prevention, diagnosis and treatment of rare diseases.

³² The National Health Insurance programme is a mandatory social insurance programme to cover the medical and medication costs of the Taiwanese people. The programme is financed by premiums contributed by the insured, employers and the government.

A.IV.3 To encourage the development and supply of orphan drugs for treatment of rare diseases, MOHW offers the following incentives to importers and manufacturers of designated orphan drugs: (a) going through a simplified market approval procedure administered by the Taiwan Food and Drug Administration ("TFDA") under MOHW;³³ (b) reduction in registration fee; (c) granting a 10-year period of marketing exclusivity; and (d) allowing special application for usage and reimbursement prior to market approval. Besides, MOHW has introduced incentive schemes to encourage institutions to engage in research and development and other relevant activities that contribute to the prevention and control of rare diseases in Taiwan.

Access to medication of rare diseases

A.IV.4 Importers or manufacturers of designated orphan drugs have to apply for listing of the drugs by the National Health Insurance Administration ("NHIA")³⁴ before reimbursement of the drug costs borne by rare disease patients can be arranged. However, patients or medical institutions can apply for a permit to import a designated orphan drug without market approval or a non-designated orphan drug on an ad hoc basis.³⁵ For reimbursement of orphan drugs that are not on the NHIA reimbursement list, approval by the Review Committee has to be sought prior to usage of the drugs.

³³ According to the Pharmaceutical Affairs Act, drug importers or manufacturers are required to register their products with and obtain market approval from TFDA before they can sell or manufacture their products in Taiwan. Applicants for registration and market approval may be required to conduct local clinical trials of the drug where necessary.

³⁴ NHIA is an administrative agency under MOHW tasked to administer the National Health Insurance programme.

³⁵ The amount of drug allowed to be imported is limited to the usage amount required by the patient in two years.

Appendix IV (cont'd)

A.IV.5 According to the Rare Disease Act, patients suffering from the designated rare diseases are entitled to reimbursement of up to 80% of the costs of diagnostic services, designated orphan drugs, treatments and supportive equipment, and 100% of costs of designated life-sustaining nutritional supplements³⁶ under the National Health Insurance programme. Patients with low income are provided with full reimbursement of the medical costs. MOHW also subsidizes patients to travel overseas for diagnosis of rare diseases or transfer specimens to overseas laboratories for testing in case the diagnoses or tests cannot be done locally. In addition, MOHW has set up an orphan drug and nutritional supplement supply centre to provide medical institutions with specific orphan drugs and life-sustaining nutritional supplements for emergency use.

A.IV.6 Apart from the support measures on treatment of rare diseases, MOHW has also certified 14 genetic consultation centres and some 30 genetic diagnostic laboratories to provide consultation and diagnostic services for rare disease patients. A central reporting system for rare diseases has been established to facilitate the provision of medical care services for patients, and enhance prevention and control of rare diseases.

Other support measures

A.IV.7 Since 2002, persons suffering from designated rare diseases are included under the definition of persons with disabilities and protected under the People with Disabilities Rights Protection Act 《身心障礙者權益保障法》. Rare disease patients are entitled to specified social services and benefits such as social security benefits, employment assistance services, tax deduction and fare discount for public transport.

³⁶ Applications for designation of life-sustaining nutritional supplements which are defined as foods primarily suited for providing nutrients to rare disease patients are considered by the Review Committee.

Appendix IV (cont'd)

A.IV.8 Meanwhile, MOHW has put in place various measures to promote the awareness and early diagnosis of rare diseases. In 2006, it expanded the newborn screening programme to cover 11 metabolism disorders to facilitate early identification and treatment of babies with genetic disorders.³⁷ Added to this, MOHW has set up a portal for providing information about rare diseases and diagnostic services available, as well as implementing a series of public education programmes since 2000 to raise public awareness of rare diseases and lower the barriers to receiving treatments among patients.

Recent developments on diagnosis and treatments of rare diseases

A.IV.9 According to MOHW, there were about 210 designated rare diseases and 98 designated orphan drugs in Taiwan at end-January 2017. Latest statistics published by NHIA reflected that there were 7 625 patients suffering from designated rare diseases in 2015, and the average drug cost incurred per patient was about NT\$542,000 (HK\$136,000). Nevertheless, the implementation of the Rare Disease Act in 2000 and the various support measures so provided have helped rare disease patients relieve their economic and psychological burdens.

A.IV.10 Nonetheless, as reimbursement of the costs of using designated orphan drugs can be arranged before the registration and market approval process is completed, NHIA has indicated that some drug suppliers are unwilling to complete the process, leading to incomplete information about the therapeutic and adverse effects of the drugs.

³⁷ The newborn screening programme was first introduced in 1985 and only covered five metabolism disorders.

References

Hong Kong

1. Food and Health Bureau. (2016) *Replies to initial written questions raised by Finance Committee Members in examining the Estimates of Expenditure 2016-17*. Available from: http://www.legco.gov.hk/yr15-16/english/fc/fc/w_q/fhb-h-e.pdf [Accessed March 2017].
2. GovHK. (2013) *Press Releases – LCQ 21: Treatment of rare diseases*. Available from: <http://www.info.gov.hk/gia/general/201307/10/P201307100483.htm> [Accessed March 2017].
3. GovHK. (2015) *Press Releases – LCQ 3: Rare diseases*. Available from: <http://www.info.gov.hk/gia/general/201505/06/P201505060526.htm> [Accessed March 2017].
4. Hong Kong Alliance for Rare Diseases. (2016) *Written Submission to the HKSAR Government in response to the Public Consultation for the 2017 Policy Address and 2017–18 Budget*. Available from: <http://www.legco.gov.hk/yr16-17/english/panels/ws/papers/wscb2-535-1-e.pdf> [Accessed March 2017].
5. *Hong Kong Alliance for Rare Diseases*. (2017) Available from: <http://www.hkard.org/> [Accessed March 2017].
6. *Minutes of Meeting of the Panel on Health Services of the Legislative Council*. (2014) 17 March. LC Paper No. CB(2)294/14-15.

Japan

7. Hayashi, S. and Umeda, T. (2008) *35 years of Japanese policy on rare diseases*. Available from: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(08\)61393-8/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)61393-8/fulltext) [Accessed March 2017].
8. *Japan Intractable Diseases Information Center*. (2017) Available from: <http://www.nanbyou.or.jp/english/index.htm> [Accessed March 2017].

9. Kanatani, Y. et al. (2017) *National Registry of Designated Intractable Diseases in Japan: Present Status and Future Prospects*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5243159/> [Accessed March 2017].
10. Ministry of Health, Labour and Welfare. (2009) *Overview of Orphan Drug/Medical Device Designation System*. Available from: http://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/orphan_drug.html [Accessed March 2017].
11. Ministry of Health, Labour and Welfare. (2014) *Orphan Designation System in Japan*. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2014/03/WC500164167.pdf [Accessed March 2017].
12. Song, P. et al. (2013) *Rare diseases and orphan drugs in Japan: developing multiple strategies of regulation and research*. Available from: <http://www.tandfonline.com/doi/full/10.1517/21678707.2013.832201> [Accessed March 2017].
13. 厚生労働省：《難病対策》，2017年，網址：http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryuu/kenkou/nanbyou/ [於 2017年3月登入]。
14. 厚生労働省：《難病の患者に対する医療等に関する法律の概要》，2016年，網址：<http://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000128881.pdf> [於 2017年3月登入]。
15. 難病情報センター，2017年，網址：<http://www.nanbyou.or.jp/> [於 2017年3月登入]。

Taiwan

16. National Health Insurance Administration. (2014) *Policy for reimbursing orphan drugs*. Available from: [http://www.nhi.gov.tw/Resource/webdata/27429_1_03_Policy%20for%20reimbursing%20orphan%20drugs_TWNHIA2014%20\(2\).pdf](http://www.nhi.gov.tw/Resource/webdata/27429_1_03_Policy%20for%20reimbursing%20orphan%20drugs_TWNHIA2014%20(2).pdf) [Accessed March 2017].

17. Orpha News Europe. (undated) *Taiwan Foundation for Rare Disorders*. Available from: <http://www.orpha.net/actor/EuropaNews/2009/doc/Taiwan.pdf> [Accessed March 2017].
18. 行政院衛生署國民健康局：《讓缺陷的生命不再遺憾—罕見疾病政策上路 10 年》，2010 年，網址：<http://health99.hpa.gov.tw/txt/PreciousLifeZone/print.aspx?TopIcNo=620&DS=1-life> [於 2017 年 3 月登入]。
19. 罕見疾病基金會，2017 年，網址：http://www.tfrd.org.tw/tfrd/intro_a [於 2017 年 3 月登入]。
20. 法務部全國法規資料庫：《罕見疾病防治及藥物法》，2015 年，網址：<http://law.moj.gov.tw/LawClass/LawContent.aspx?PCODE=L0030003> [於 2017 年 3 月登入]。
21. 法務部全國法規資料庫：《罕見疾病防治及藥物法施行細則》，2015 年，網址：<http://law.moj.gov.tw/LawClass/LawContent.aspx?PCODE=L0030004> [於 2017 年 3 月登入]。
22. 法務部全國法規資料庫：《罕見疾病醫療補助辦法》，2015 年，網址：<http://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=L0030031> [於 2017 年 3 月登入]。
23. 法務部全國法規資料庫，2017 年，網址：<http://law.moj.gov.tw/Index.aspx> [於 2017 年 3 月登入]。
24. 國立中正大學社會福利研究所：《各國罕見疾病相關法案之比較研究》，2000 年，網址：<http://www.cdc.gov.tw/uploads/files/430b2d95-a4b7-4d83-bbdd-73570d611ece.pdf> [於 2017 年 3 月登入]。

25. 衛生福利部中央健康保險署：《罕見疾病、血友病藥費專款項目之執行報告》，2014年，網址：http://www.mohw.gov.tw/MOHW_Upload/doc/%E7%BD%95%E8%A6%8B%E7%96%BE%E7%97%85%E8%88%87%E8%A1%80%E5%8F%8B%E7%97%85%E8%97%A5%E8%B2%BB%E5%B0%88%E6%AC%BE%E9%A0%85%E7%9B%AE%E4%B9%8B%E5%9F%B7%E8%A1%8C%E5%A0%B1%E5%91%8A_0044710001.pdf [於 2017 年 3 月登入]。
26. 衛生福利部中央健康保險署：《歷年來菸品健康福利捐補助罕見疾病等之醫療費用》，2017年，網址：[http://www.nhi.gov.tw/Resource/webdata/28117_2_%E7%BD%95%E8%A6%8B%E7%96%BE%E7%97%85%E7%AD%89%E9%86%AB%E7%99%82%E8%B2%BB%E7%94%A8\(1060310%E6%9B%B4%E6%96%B0\).pdf](http://www.nhi.gov.tw/Resource/webdata/28117_2_%E7%BD%95%E8%A6%8B%E7%96%BE%E7%97%85%E7%AD%89%E9%86%AB%E7%99%82%E8%B2%BB%E7%94%A8(1060310%E6%9B%B4%E6%96%B0).pdf) [於 2017 年 3 月登入]。

The European Union

27. Belgian Health Care Knowledge Centre. (2009) *Policies for Orphan Diseases and Orphan Drugs*. Available from: http://ec.europa.eu/health/ph_threats/non_com/docs/policies_orphan_en.pdf [Accessed March 2017].
28. Commission of the European Communities. (2008) *Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe's challenges*. Available from: http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf [Accessed March 2017].
29. European Commission. (2014) *Implementation report on the Commission Communication on Rare Diseases: Europe's challenges and Council Recommendation of 8 June 2009 on an action in the field of rare diseases*. Available from: https://ec.europa.eu/health/sites/health/files/rare_diseases/docs/2014_rarediseases_implementationreport_en.pdf [Accessed March 2017].
30. European Commission. (2016) *Inventory of Union and Member State incentives to support research into, and the development and availability of, orphan medicinal products – State of Play 2015*. Available from: http://ec.europa.eu/health/sites/health/files/files/orphanamp/doc/orphan_inv_report_20160126.pdf [Accessed March 2017].

31. European Commission. (2017) *Rare diseases – Policy*. Available from: https://ec.europa.eu/health/rare_diseases/policy_en [Accessed March 2017].
32. European Medicines Agency. (2017a) *Orphan designation*. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&mid=WC0b01ac0580b18a41 [Accessed March 2017].
33. European Medicines Agency. (2017b) *Orphan Medicines Figures 2000 – 2016*. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/04/WC500185766.pdf [Accessed March 2017].
34. European Union Committee of Experts on Rare Diseases. (2014) *2014 Report on the State of the Art of Rare Disease Activities in Europe*. Available from: http://www.eucerd.eu/?page_id=163 [Accessed March 2017].
35. Official Journal of the European Communities. (1999) *Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products*. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:018:0001:0005:en:PDF> [Accessed March 2017].
36. Official Journal of the European Union. (2009) *Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02)*. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF> [Accessed March 2017].

The United States

37. California Department of Public Health. (2017) *California Newborn Screening Program*. Available from: <http://www.cdph.ca.gov/programs/NBS/pages/default.aspx> [Accessed March 2017].
38. California Healthcare Institute. (2014) *Combating Rare Diseases in the 21st Century*. Available from: http://www.chi.org/wp-content/uploads/2014/02/2014-02-Rare-Disease-Brochure_Final-2.20.14.pdf [Accessed March 2017].

39. Everylife Foundation for Rare Diseases. (undated) *Supporting Rare Disease Patients Through State Policy*. Available from: <http://www.womeningovernment.org/sites/default/files/document/events/Julia%20Jenkins%20-%20Rare%20Disease.pdf> [Accessed March 2017].
40. National Institutes of Health. (2016) *FAQs About Rare Diseases*. Available from: <https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases> [Accessed March 2017].
41. *National Institutes of Health*. (2017) Available from: <https://www.nih.gov/> [Accessed March 2017].
42. National Organization for Rare Disorders. (2016a) *State Report Card*. Available from: <http://rareaction.org/wp-content/uploads/2016/12/nord-ran-2016-state-report-card.pdf> [Accessed March 2017].
43. National Organization for Rare Disorders. (2016b) *What is a rare disease?* Available from: http://cdn.rarediseases.org/wordpresscontent/wp-content/uploads/2014/11/NRD-1008-FactSheet_5.pdf [Accessed March 2017].
44. Orphanet. (2017) *Orphan drugs in the United States of America*. Available from: http://www.orpha.net/consor/cgi-bin/Education_AboutOrphanDrugs.php?lng=EN&stapage=ST_EDUCATION_EDUCATION_ABOUTORPHANDRUGS_USA [Accessed March 2017].
45. *Rare Diseases Act of 2002*. (2002) Available from: <https://history.nih.gov/research/downloads/PL107-280.pdf> [Accessed March 2017].
46. United States Food and Drug Administration. (2013) *Rare Diseases and FDA: Perspectives from the Office of Orphan Products Development (OOPD)*. Available from: <http://www.irdirc.org/wp-content/uploads/2013/06/Katherine-Needleman.pdf> [Accessed March 2017].
47. United States Food and Drug Administration. (2017a) *e-CFR 21 PART 316 Orphan Drug & the Orphan Drug Act 1983*. Available from: <https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/ucm124562.htm> [Accessed March 2017].

48. United States Food and Drug Administration. (2017b) *Office of Orphan Products Development*. Available from: <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018190.htm> [Accessed March 2017].

Others

49. De Vruhe, R. et al. (2013) *Priority Medicines for Europe and the World: "A Public Health Approach to Innovation" – Background Paper 6.19 Rare Diseases*. Available from: http://www.who.int/medicines/areas/priority_medicines/BP6_19Rare.pdf [Accessed March 2017].

50. Pacific Bridge Medical. (2014) *Orphan Drugs in Asia 2014 - Guidelines and Regulatory Requirements To Help Orphan Drug Products Enter the Asian Market*. Available from: <http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/Orphan-Drugs-in-Asia-2014.pdf> [Accessed March 2017].

51. Shafie, A. et al. (2016) *State of rare disease management in Southeast Asia*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4969672/> [Accessed March 2017].

52. Song, P. et al. (2012) *Rare diseases, orphan drugs, and their regulation in Asia: Current status and future perspectives*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4204590/> [Accessed March 2017].

Prepared by Ivy CHENG
Research Office
Information Services Division
Legislative Council Secretariat
17 March 2017
Tel: 2871 2143

Information notes are compiled for Members and Committees of the Legislative Council. They are not legal or other professional advice and shall not be relied on as such. Information notes are subject to copyright owned by The Legislative Council Commission (The Commission). The Commission permits accurate reproduction of information notes for non-commercial use in a manner not adversely affecting the Legislative Council, provided that acknowledgement is made stating the Research Office of the Legislative Council Secretariat as the source and one copy of the reproduction is sent to the Legislative Council Library. The paper number of this issue of Information note is IN07/16-17.