Asia-Pacific
Economic Cooperation

APEC | Action Plan on Rare Diseases

I. PREAMBLE

The 7th APEC High-Level Meeting on Health & the Economy (HLM7) in Ho Chi Minh City, Viet Nam in August 2017 "welcomed the launch of a new APEC initiative to address barriers to the diagnosis and treatment of rare diseases in the region" and "noted that such efforts will improve the economic and social inclusion of those affected by rare diseases, including caregivers, and ensure a more inclusive Healthy Asia Pacific 2020." The HLM7 also "welcomed the development of an action plan to facilitate greater alignment of domestic policies and best practices and to provide a framework for regional collaboration." The APEC Life Sciences Innovation Forum (LSIF) established the tripartite APEC LSIF Rare Disease Network (RDN) with participation from government, academia, and industry. The Rare Disease Network's first task was to identify and compile information on the various barriers that economies face in addressing rare diseases. Over time, the RDN plans to continue to scale in size, diversity, and depth of engagement as the entity shifts from its role of informing the development of an APEC strategy on rare diseases to supporting economies in implementing the strategy. In 2018, the RDN organized a series of Stakeholder Consultations in Australia; People's Republic of China; Republic of Korea; Chinese Taipei; Thailand; and Viet Nam to learn more about the local, frontline experiences with rare disease. Hearing a diversity of perspectives and patient experiences were the priority objectives; the RDN leadership connected with government officials, academics, industry representatives, and other members of the rare disease community including patients in these six (6) economies.

The information assembled through the stakeholder consultations informed the development of a 2-day policy dialogue: the inaugural APEC Policy Dialogue on Rare Diseases in Beijing, China in June 2018. The event facilitated candid discussion between senior leadership from government agencies overseeing health and social services, academic experts from universities and teaching hospitals, industry executives, and leaders from civil society, including patient groups. At the widely-attended dialogue, APEC economies shared best practices and policies for addressing rare diseases and began to collaborate on the development of this APEC Action Plan on Rare Diseases.

> *"When it is obvious that the goals cannot be reached, don't adjust the goals—adjust the action steps."*
>
> **- Confucius**

II. FRAMEWORK

APEC Action Plan on Rare Diseases

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2.1 Vision 2025

APEC member economies will aim to improve the economic and social inclusion of all those affected by rare diseases by addressing barriers to healthcare and social welfare services.

2.2 Objectives

The objectives of the APEC Action Plan on Rare Diseases ("Action Plan") are to:

1. Facilitate greater alignment of domestic policies and regulations;
2. Support urgent implementation of proven best practices; and,
3. Promote multisectoral collaborations and patient partnership.

2.3 Pillars

The Action Plan has 30 targets across 10 pillars:

1. Define rare diseases and orphan products with policies and processes;
2. Raise public and political awareness of rare disease issues;
3. Promote innovative research and development;
4. Build human resource capacity in medical, nursing, nutrition, and other allied health and non-health sectors;
5. Facilitate early, accurate, and systematic diagnosis;
6. Coordinate patient-centered care across medical and other health disciplines, life course, and location;
7. Deliver new and accessible treatments to patients;
8. Support financial and social needs of patients and their families;
9. Manage pooling and usage of patient data securely and effectively; and,
10. Prioritize comprehensive domestic rare disease policy integrating Pillars 1-9.

2.4 Structure

Each pillar has three (3) related recommendations with the following structure:

- A Context section to establish the key issues APEC member economies face in addressing the pillar, along with findings from the 1st APEC Policy Dialogue on Rare Diseases and Stakeholder Consultations;
- A substantive Target which envisions an outcome for economies to work towards;
- A quantifiable and achievable Indicator to measure progress against the target; and,
- A set of Actions to consider implementing domestically to help achieve the target.

2.5 Implementation

APEC member economies are encouraged to pursue implementation of the recommended actions immediately and proceed in a pragmatic, stepwise manner that takes into account local context and public healthcare policy of individual member economy.

2.6 Background

Rare diseases have characteristics that make them one of the significant health challenges of our time. Between 5,000 and 8,000 rare diseases have been identified (Rath & Janmaat, 2018). These diseases are uncommon individually, hence their name; but as a group they affect 6 to 8% of the global population (Barakat et al., 2014). This "paradox of rarity" presents unique problems for not only the individuals living with rare diseases but for caregivers, researchers, policymakers, and industries as well (Schulenburg & Frank, 2015).

More than 80% of rare diseases are caused by genetic or congenital aberrations, and 75% present with a wide range of neurological symptoms and physical and intellectual disabilities (McClellan & King, 2010). Rare diseases mostly affect children or young adults, and several siblings can be affected in the same family. As such, these diseases come with substantial hardship for both parents and patients. Many rare diseases are fatal with no known treatment or cure—almost one-third of those born with a rare disease die before the age of five (Institute of Medicine, 2010).

2.6 Background
(Continued)

In general, healthcare professionals are not trained to recognize diseases that occur infrequently, leading to misdiagnosis and inappropriate medical intervention. This lack of knowledge and treatment options is an issue shared by most rare diseases whether they are genetic disorders or not. Patients finding no respite among medical professionals and no answers to their questions can face stigma, social isolation, and disadvantages in education and employment. Rare diseases severely affect the lives of caregivers, too, with dire economic consequences for patients, families, and society in general.

However, with opportune medical intervention, some rare diseases can be controlled (Valdez et al., 2016). Some of these diseases when detected early can benefit from dietary and nutrition management, food supplements, or medicines. Families can benefit from genetic counselling services and other community support and in return, families and patients can better contribute to a more inclusive society. Additionally, a range of activities and comprehensive public health approaches can be undertaken to control rare diseases and their impact.

To achieve this, economies and their healthcare systems can address barriers that prevent individuals with rare diseases from accessing high-quality, patient-centered healthcare services. This means designing health interventions that facilitate the right diagnosis early and delivers the right care at the right time in the most effective, efficient, and equitable way possible (Valdez, 2016; Ferrelli, 2017). The definitions of 'high-quality' healthcare services and the 'right' health interventions will be defined commensurate with the level of economic, health, social, and other resources available not just for rare diseases but for all chronic conditions and for patients and the public in general.

To this end, APEC economies are encouraged to define rare diseases and orphan products with policy and process; raise public and political awareness of rare disease issues; promote innovative research and development; build human resource capacity across health professions, other allied health and non-medical sectors; facilitate early, accurate, and systematic diagnosis; coordinate patient-centered care across specialties and disciplines, life course, and location; deliver new and accessible treatments to patients; support financial and social needs of patients and families; manage pooling and usage of patient data securely and effectively; and prioritize comprehensive domestic rare disease policy.

III. RECOMMENDATIONS

APEC Action Plan on Rare Diseases

3.1 Define rare diseases and orphan products with policies and processes

Context:

Government administrations rely on clear and consistent definitions for health policy development and planning. Most health authorities use incidence or prevalence rates as the metric to determine whether a condition is considered a rare disease. As such, the definition varies around the world from 1 in 500,000 individuals in some jurisdictions to 1 in 2,000 individuals in others (Dawkins et al., 2018). Since the incidence and prevalence rates of a given condition may vary according to different jurisdictions, a rare disease in one population is not necessarily one in another population. The question for many emerging economies is how to formalize a seemingly static parameter like prevalence when populations are still growing rapidly (Dong & Wang, 2016). This is exactly why Europe has opted for a relative threshold (5 in 10,000 individuals) while the United States is using an absolute threshold (less than 200,000 individuals). Another issue is that the exact prevalence of a rare disease is often unknown—the prevalence calculations available in the literature are approximations that can overestimate or underestimate the occurrence of disease in any given population. As estimates based on the number of known cases in a population exclude undiagnosed cases, prevalence will increase as screening services are established and patients secure an accurate diagnosis.

To circumvent the downsides of a broad prevalence-based definition, some economies maintain a list of officially recognized rare diseases based on expert opinions and on local epidemiologic data when available. When relying on a list of rare diseases to design policies, it is important to keep the list current and in line with newly acquired knowledge, real-world evidence, and new treatment options. One concern is the time it takes to add a rare disease to the list when no specific definition exists: many economies either do not have a definition or have one that is unofficial or informal, and still criteria are often inconsistent and lacking clarity and transparency on inclusion criteria and methodology for which conditions are eligible. Among APEC member economies that do have an official or formal definition, these definitions are embedded in domestic legislation while others are codified by health ministries or drug administrations. As such, for many economies the formal definition is not necessarily consistent across the health system. For example, some economies have a definition for regulatory purpose, but not for reimbursement. Some are determined with broad input from researchers, clinicians, industry, policymakers, and patient groups, while others are modeled after guidance from the United States (U.S.) Food and Drug Administration (FDA) or European Commission.

Whether the definition of rare disease is an official one or the one most commonly accepted by other jurisdictions, the resulting list should be transparent and easily accessible. Beyond prevalence, the severity of the disease and availability of treatment should also be considered. There are challenges maintaining such a record however as a list cannot be comprehensive and will exclude many from medical attention or intervention. No economy has it all, but for developing a rare disease definition, economies should start early, prepare for a long-term process, and incorporate personalization based on their specific context at all steps. At the same time, economies should ensure that their definitions of rare disease are consistent with international definitions. Having standard definitions aligned globally will allow standard setting in a transparent manner and facilitate further harmonization in the orphan product designation and approval process.

RECOMMENDATION 1.1

2025 Target: APEC member economies each have an official definition for rare disease which serves as the basis for regulatory frameworks, policy frameworks, and other policy of relevant local agencies and providers.

Indicator: Percent of APEC member economies with an official definition for rare disease.

Actions:

- Implement a formal definition in consultation with health professional organizations, academia, industry, and civil society, including patient groups, that (1) has a clear objective criteria and a quantifiable prevalence for what constitutes a rare disease; (2) is not too restrictive by focusing only on the smallest populations; (3) is in line with international standards such as those set by the U.S. FDA or the European Commission; (4) is flexible to be reviewed and updated on a regular basis for list-based definitions that still lack convergence with international standards; and (5) includes consideration for severity, epidemiology, and unmet medical need.

- Until such a definition is established, support the development of an unofficial and/or informal definition with early and close consultation with a diversity of stakeholders.

- Work towards the harmonization of rare disease definitions across APEC economies.

RECOMMENDATION 1.2

2025 Target: APEC member economies each have established a transparent process for regularly reviewing the definition of rare disease with input from academia, industry, civil society, non-government organizations and patient groups.

Indicator: Percent of APEC member economies with a review process for updating the definition.

Actions:

- Establish a regular and transparent process in close consultation with a diversity of stakeholders including health professional organizations, academia (researchers, clinicians, etc.), industry, civil society, non-government organizations, and patient groups to review (1) the definition of rare disease, (2) the resulting list of recognized rare diseases if applicable, and/or (3) the designation process in light of new knowledge, treatments, and real-world evidence.

- Provide adequate time for all stakeholders to consider adjustments and submit feedback, and organize the process under a dedicated cross-agency working group or public forum.

RECOMMENDATION 1.3

2025 Target: APEC member economies each have established policies and fit-for-purpose protocols for orphan product assessment, including international alignment and expedited registration pathways.

Indicator: Percent of economies with dedicated assessment of orphan drug status and mechanisms for accelerated assessment.

Actions:

- Maintain a fair and transparent decision-making process to assess orphan products.
- Set up an accelerated regulatory process that (1) is clear in eligibility requirements and provisions; (2) allows for international data rather than requiring local data; (3)allows for exemption of local manufacturing requirements, drug product testing, domestic good manufacturing practice inspection requirements; (4) is applicable to all orphan products; (5) is applied in practice by trained regulators; (6) shortens review duration and/or allows exemptions from typical technical dossier requirements within a specific time frame; (7) makes submission guidelines for manufacturers easily available and accessible; and (8) does not discriminate based on disease area or predictive criteria.
- Consider mutual reliance of regulatory decisions from other APEC economies to improve harmonization across the region, and expedited registration pathways at the relevant domestic regulatory authorities.
- Establish a regional network or partner with an existing one to facilitate the sharing of best practices related to the policy, regulatory, and reimbursement decisions of rare disease.

3.2 Raise public and political awareness of rare disease issues

Context:

Given the low prevalence of rare disease and thus the small number of patients, awareness of their characteristics and challenges among both the general public and communities of policy makers and elected officials is low. This diminished understanding can lead to stigma and discrimination, further compounding the barriers to awareness among the public and political communities. With a high fatality rate and short life expectancy, there are a limited number of individuals living with a rare disease who can help better inform these communities and correct misunderstandings. In addition, unlike in the case of many infectious or communicable diseases, there is a rarely a dramatic cure or change in condition, so the stories of these individuals living with a rare disease are not easily dramatized or broadcast by traditional media, and thus are not sufficiently captured by the attention of the public. Limited political attention leads to equally limited policy attention, which cascades into parallel limitations in the awareness among public health professionals, industry, academia, and even healthcare professionals. For this reason, and because of the complexity of their causes, even patients themselves and their families are often lacking in sufficient education about their condition—they do not engage the healthcare system when they should, sometimes seeking other non-scientific solutions to their illnesses. The reality highlights why patient organizations such as Rare Disease International have been and continue to be central to raising awareness among patients, public, and political audiences.

RECOMMENDATION 2.1

2025 Target: APEC member economies each have established some policy and/or program to support the establishment and development of groups to represent rare disease patients and their ability to engage central and local governments.

Indicator: Percent of economies that have established some policy and/or program to support patient organizations.

Actions:

- Ensure patient groups, in collaboration with each other, international coalitions, and industry, have sufficient access to the resources they need (1) to support individuals living with a rare disease and their families, and (2) to educate the public and political communities about rare disease issues.
- Explore with the relevant authorities a special entity status and registration process for patient group organizations to reduce administrative burden where possible.
- Seek to provide accommodations for awareness-raising activities in public spaces, and to facilitate access to public, private, and hybrid grant funding and in-kind support to improve the depth and diversity of engagements with all stakeholders.
- Take steps to ensure agencies, employees, and elected officials are open and willing to engage and participate in regular activities organized by patient groups to educate them on the issues of rare diseases and their political and policy implications.
- Seek leadership and coordination from patient groups to contribute meaningfully to policy design and implementation.

RECOMMENDATION 2.2

2025 Target: APEC member economies each have established a multi-sectoral advisory committee that includes patients and reports directly to the Health Minister to advise the government on rare disease policy.

Indicator: Percent of economies with a high-level advisory committee on rare disease established.

Actions:

- Convene a special advisory committee which (1) meets regularly; (2) has clear terms of reference and obligations to consult with the rare disease community on government policy impacting those living with a rare disease; and (3) includes but is not limited to orphan product researchers and manufacturers, clinicians and other representatives of the healthcare system, patients and representatives of patient organizations, scientists and other representatives of academic or research institutions, and other policymakers and regulators from outside the Ministry of Health.

- Outline processes for (1) changing composition of the special advisory committee on a regular basis, (2) reporting to the Minister of Health directly on a regular basis, (3) managing potential conflicts of interest, and (4) ensuring any recommendations put forth by the committee are open and transparent to the wider rare disease community.

RECOMMENDATION 2.3

2025 Target: APEC member economies each have allocated time and other resources in public information, education, and communication, including social mobilization and advocacy, to highlight the lives of individuals living with rare diseases and their families.

Indicator: Percent of APEC economies with public broadcasting related to rare diseases.

Actions:

- Encourage allocation of time and financial resources within public broadcasting and state media agencies to develop and deliver programming about rare diseases and the lives of patients, their families, and caregivers.
- Encourage allocation of private resources to fund television programs, films, documentaries, public service announcements, theatrical performances, books, newspaper articles, and internet media to focus attention on the challenges of rare diseases.

3.3 Promote innovative research and development

Context:

Though much progress has been made in rare disease research over the last decade, especially with help from the digital and genomic revolutions, the source and benefit of this knowledge tend to be unevenly distributed within and between APEC economies. Furthermore, in comparison to other regions of the world, Asia Pacific appears to publish less on rare disease. A Google Scholar search in January 2018 for ["rare disease*" and "Europe*"] returned more than 50,000 results, while ["rare disease*" and "Asia*"] returned less than 15,000. Research also mainly focuses on underlying disease mechanisms and metabolism; more research is needed on the social and economic burden of these diseases and patient characteristics of specific population groups (Angelis et al., 2015).

One hurdle to doing innovative research is the lack of investment in sometimes-costly infrastructures. Research related to rare diseases is relatively expensive due to the use of sophisticated equipment and the costs of organizing small trials (Angelis et al., 2015). Funding for some rare diseases research is limited and covered somewhat by a patchwork of private initiatives, public research grants and support from patient organizations. At a regional level, the European Union (EU) has demonstrated a strong commitment to rare disease research through the EU Framework Programme for Research and Innovation. Under the Seventh Framework Programmes for research (2007–2013), over $727 million USD in support was granted to over 120 collaborative research projects on rare diseases. The funding facilitated the formation of multidisciplinary teams from universities, research organizations, industry, and patient organizations from across Europe and beyond (European Union, 2014). More recently, Horizon 2020, which runs from 2014 to 2020, continues the EU's strong commitment to funding rare disease research (European Commission, 2014). At an economy-specific level, France, which currently funds over 300 clinical research projects with collaborations across domestic and international institutions, is seen as a leader in the research space (France Diplomatie, 2013). In Germany, the Federal Ministry of Education and Research (BMBF) is currently funding 12 research consortia since 2012, with more than $27 million USD for three years and has supported additional funding through initiatives such as the National Genome Research Network (http://www.ngfn.de/en/).

In addition, the high fatality rates and the low prevalence of some rare diseases means longitudinal studies are especially scarce and difficult to organize (Valdez, 2016). Classical clinical trial designs and methods are not always feasible in rare disease populations. To address the unique quantitative challenges of rare diseases alternatives are needed for clinical trials adapted to small population and infrastructures to collect rigorous and replicable real-world evidence (Knowles et al., 2017). The International Rare Diseases Research Consortium (IRDiRC) Small Population Clinical Trials (SPCT) Task Force has done some work on this issue and has published a report, which includes recommendations and guidelines for the design of small population clinical trials in the field of rare diseases. Collaborative platforms such as the International Rare Diseases Research Consortium, RD-Connect (http://www.rd-connect.eu), and Rare Connect (http://www.rareconnect.org) are essential for connecting not only researchers but also individuals living with rare diseases.

Similarly, patient registries can also help collect data on demographics, diseases, and treatments. France is a model for domestic coordination of registries with their Banque Nationale de Données Maladies Rares, a domestic organization collecting and organizing data from centers of expertise (Choquet & Landais, 2014). French patients enter the registry via the center at which they receive care. In contrast, the UK, Bulgaria, and Argentina, have domestic patient registries in various stages of planning, but not implemented as of yet. To help support the standardization and sharing of information across rare disease registries, the European Commission, within the EU Program of Community Action in the field of Public Health, has initiated the establishment of a European Platform for Rare Disease Registries to address the challenge of standardizing and sharing information across rare disease registries (EpiRare, 2011). However, numerous challenges remain to privately and securely capturing, standardizing, and sharing health information between patient registries and with researchers. The benefits extend beyond just the rare disease community. A better understanding of rare disease mechanisms has the potential to inform future research on common diseases such as hypertension, diabetes, and cancer.

RECOMMENDATION 3.1

2025 Target: APEC member economies each have established innovative mechanisms to provide seed funding for early-stage and benchtop research on rare diseases and development of orphan products.

Indicator: Percent of economies with R&D seed funding mechanisms.

Actions:

- Fund and manage with collaboration and co-investment from industry and civil society a public grant program for rare disease research and orphan product development.
- Align funding with economy strengths, support academic institutes to increase production of basic research, and encourage additional public-private-patient partnerships to fund deeper applied and clinical research.
- Lead efforts to advance international and regional collaboration for research and development.

RECOMMENDATION 3.2

2025 Target: APEC member economies each have established financial and in-kind incentives to encourage and support commercialization of domestic rare disease research and development of orphan products.

Indicator: Percent of economies with incentives and support programs for commercialization of R&D.

Actions:

- Provide a menu of tax credits and/or fee waivers for clinical trial activities related to rare diseases and orphan product development.
- Establish a centralized entity that oversees commercialization to coordinate activities across universities and public research institutes while supporting regulatory agencies to provide scientific assistance for marketing authorization requests.
- Convene regulatory and patent authorities to determine and establish a specific and enforceable market exclusivity period for orphan products.

RECOMMENDATION 3.3

2025 Target: APEC member economies each have streamlined their respective processes for research and clinical trial design, method, and ethics approvals in consultation with industry and patient organizations.

Indicator: Percent of APEC economies with streamlined approval process for research.

Actions:

- Harmonize ethical review procedures for clinical trials, working towards acceptance of a single ethical review for multicenter rare disease research and adoption of common policies, procedures, and forms across APEC economies.

- Introduce policy on clinical trials that (1) provides an incentive to reach at most a 60 calendar day timeline for both ethics and governance review for which sponsors would pay a defined additional amount to support increased efficiency; (2) supports at most a 120 calendar day maximum timeline for governance review; (3) supports at most a 120 calendar day maximum timeline for ethics review, the compliance with which would be a condition of certification of ethical review processes; (4) allows concurrent review of the ethics and governance components of a clinical trials; and (5) allow a 'stop clock' during efficient ethics and research governance review when additional input is required before consideration can continue.

3.4 Develop human resource capacity in medical and non-medical sectors

Context:

Across economies and in a variety of disciplines, there is a scarcity of knowledge and experts with an interest in rare diseases (Holmes, 2012). Significant progress has been made, especially within universities and teaching hospitals, but several barriers remain to attracting new professionals to become researchers and clinicians with a specific interest in rare diseases. There is also a need for formalizing and scaling new professions such as genetic counseling (Wicklund et al., 2018). For researchers, the limited public funding and grants available means the field is highly competitive and lacks strong financial incentive (Hoskovec et al., 2018). Specialists clinical practices especially in rural and underserved hospitals remain small, nascent, or nonexistent, meaning employment opportunities are sparse and salaries are limited (Emmet et al., 2018). One adaptation emerging from and simultaneously addressing one human resource challenge is the multidisciplinary professional—individuals that may for instance practice clinical medicine part-time while also leading research investigations part-time into the rare diseases they treat (Milewicz et al., 2015). As this is already a common structure in developed academic settings, universities with teaching hospitals can be effective platforms in APEC emerging economies for supporting multidisciplinary professionals working on rare diseases.

Similarly, many families of individuals living with rare diseases also require professional support as they maintain their jobs while taking on responsibilities of a caregiver. Especially in low-resource settings, patient groups also sometimes function in much broader capacities than usual, often shepherding patients and their families through their journeys to secure diagnosis, access treatment, coordinate care, and pay for it. In addition to recruiting new clinicians and researchers and supporting professionals that perform both these functions, the rare disease community could also be more inclusive and supportive of non-medical professionals like lawyers. The issues of rare diseases are interdisciplinary; as such, they require a team of professionals from a variety of disciplines, both medical and non-medical, to address them effectively and efficiently. Lawyers and policy professionals have a crucial role to play in improving the process of orphan product approval, registration, and post-market vigilance. That said, beyond growing the number of human resources for rare disease, APEC economies must also navigate ways to improve the capacity of existing human resources. It is up to public and private medical, legal, and public policy education institutions to ensure rare disease is included in the curriculum early and with sufficient depth, so more healthcare, law, and policy practitioners are better prepared to design solutions to these challenges. Where this is absent, patient groups again have filled the vacuum, but need partners to support effective professional education activities.

RECOMMENDATION 4.1

2025 Target: APEC member economies each have conducted an audit of clinical skills needed to address rare disease, identified gaps in the professional workforce, and developed pre-service and in-service training curricula to build capacity.

Indicator: Percent of economies with a completed audit, human resource inventory, gap analysis, and training curricula.

Actions:

- Facilitate engagement between appropriate clinical bodies and medical schools to develop training modules for utilization in medical schools, and engage with medical schools to ensure these modules are delivered as part of medical training.
- Implement plans to address skills gaps in the form of new training opportunities and support for medical students from across the APEC region.
- Encourage regional networks for human resource capacity-building in medical and non-medical sectors, especially around specific rare diseases or clusters.
- Build on existing programs and centers to offer cross-border clinical training and internships
- Encourage and provide opportunities for public-private partnerships in medical and non-medical training and investment in regional comprehensive clinics and regional centers of expertise (hub-and-spoke model).
- Support twinning programs for training and ongoing consultation and support.
- Facilitate partnerships with clinical geneticists and other sub-specialties to conduct risk assessments for families of newborns with rare diseases and discuss diagnostic testing options with family or guardians and the implications of results as needed.
- Formulate and publish practice guidelines for genetic counselors in the APEC region that encounter and handle patients and families with rare diseases.
- Support mechanisms to provide education on genetics to families of individuals living with rare diseases by community-based providers such as nurses, midwives, social workers, other healthcare professionals, and hospital-based clinical staff.

RECOMMENDATION 4.2

2025 Target: APEC member economies each have designed and implemented multi-professional and multi-disciplinary capacity development programs to raise awareness of rare disease issues among healthcare providers and social workers, and medical, nursing, and other allied health students.

Indicator: Percent of economies with professional development programs for providers and students.

Actions:

- Translate audit and gaps analysis of clinical skills into general training curricula and specific strategies to enhance the rare disease components of public and private medical, nursing, other allied health, and social work education, using licensing and/or accreditation systems as vehicles for enforcement.
- Direct educational resources at healthcare providers including but not limited to primary healthcare physicians, generalists, pediatricians, nurses, midwives, nutritionists, dieticians, and geneticists, as well in the form of professional development opportunities delivered via digital training and tools.

RECOMMENDATION 4.3

2025 Target: APEC member economies each have established programs to develop, support, and utilize underrepresented professionals including genetic counselors, clinical geneticists, rehabilitation therapists, and allied healthcare workers.

Indicator: Percent of economies with programs for genetic counselors, clinical geneticist, and allied healthcare workers.

Actions:

- Design and implement policies in partnership with industry, academia, civil society, non-government organizations, and patient organizations that create an enabling environment for the development and proliferation of (1) prenatal genetic counseling for pregnancies with family history of rare diseases; (2) post-diagnosis support for parents from genetic counselors, rehabilitation, and psycho-social professionals; and (3) appropriate referral to ongoing support for the management of conditions identified.

- Support researchers and academics that may provide ad hoc or otherwise informal advice to patients and families on rare diseases in collaboration with professional associations and societies.

3.5 Facilitate early, accurate, and systematic diagnosis

Context:

In seeking a diagnosis, individuals living with a rare disease face unique journeys often so complex they are likened to "medical pilgrimages" (Dharssi et al., 2017). A 2012 study of 12,000 individuals found that 25% had to navigate this "patient odyssey" for between 5 to 30 years before obtaining a diagnosis, 25% had to travel to a different region in the process, and almost half of these patients received at least one misdiagnosis prior to the accurate one (EURORDIS Survey, 2012). When misdiagnosed, patients are at risk of receiving the wrong treatment with potentially complicating or fatal results; and when undiagnosed they carry the emotional and psychological burden of living without a name for their sickness (Schulenburg & Frank, 2015). Some of these patients are at risk of self-excluding themselves from the health system out of frustration. For over 40% of rare disease patients, misdiagnoses cause treatment delays (EURORDIS Survey, 2012). Even when diagnosed accurately or quickly, underlying disease mechanisms can remain unknown (Valdez, 2016). Many individuals living with a rare disease never receive a diagnosis in part because diagnostic tests exist for only 3,000 rare diseases (Melnikova, 2012; Orphanet).

Widespread underdiagnosis of rare disease has not only clinical implications for patients but also political ones: government officials often do not realize the magnitude of the issue. In many places, the clinical community is unfamiliar with signs and symptoms of rare diseases; and with such heterogeneity among clinical presentations of even the same condition, case definitions for surveillance are usually lacking and confusion is common between similar conditions (Valdez, 2016). Over the last decade, advancements in molecular genetics have certainly helped to characterize the causes of many rare diseases and provide unprecedented opportunities for diagnosing individuals and determining phenotypes (Austin et al., 2018). However, genome sequencing and lab capacity in general is limited and still unaffordable, meaning rural areas of APEC economies will lack access to diagnostic tests, which has a significant impact on the speed and accuracy of diagnoses (Schulenburg and Frank, 2015).

If designed, implemented, and sustained, newborn screening is a proven best practice with the potential to contribute to universal early diagnosis and management of a significant portion of treatable rare diseases. Where these programs are already in place in APEC economies, they can improve by updating procedures to account for new diagnostic technologies and techniques. For example, most programs are not mandatory or use an opt-in system of participation, which may be insufficient to detect a small number of patients within a general population. In general, neonatal screening has the potential to contribute to an early diagnosis and management of a fraction of rare diseases when there is an effective intervention which can avoid or mitigate severe consequences and/or death if provided early enough. Multiple conditions can be identified from a single bloodspot collected at birth. Where neonatal screening does not exist yet, investing in underlying genetic testing and diagnostic infrastructure like laboratories and trained staff in hospitals and clinics is the first essential step.

RECOMMENDATION 5.1

2025 Target: APEC member economies each have established a regional network to build and share genetic testing and diagnostic infrastructure and capacity that leverages each economy's strengths.

Indicator: Percent of economies engaged in the network and building core diagnostic infrastructure.

Actions:

- Adjust trade policies in collaboration with industry, diagnostic professionals, and patient organizations to improve the ease of transporting anonymized patient data and/or tissue samples across domestic borders, and pilot the innovative security capabilities of digital technologies.
- Increase both financial and non-financial incentives for industry and academia to further advance diagnostic techniques and technology to bring down cost and increase accuracy, speed, and coverage.
- Leverage these coordinated efforts and regional partnerships in balance with local data privacy policies to generate and capture sufficient quantity and quality of Asian genetic reference sequences and make them widely accessible and available to researchers and clinicians.

RECOMMENDATION 5.2

2025 Target: APEC member economies each have established newborn screening programs that are fully reimbursable for testable and treatable rare diseases and reviewed every three (3) years.

Indicator: Percent of economies with mandatory and reimbursable newborn screening programs; average number of diseases included in baseline screening programs per economy.

Actions:

- Implement an economy-wide newborn screening program that (1) is fully reimbursed under the social and/or public healthcare system; (2) is mandatory or opt-out; (3) is available to all newborns across hospitals, other birthing facilities, and home births; (4) is required or strongly recommended for accreditation or licensing of public and private hospitals, birthing facilities, and clinics; (5) covers rare diseases that are amenable to testing and early intervention and treatment; and (6) requires timely patient and clinician notification so that appropriate action can be started immediately, especially for those newborns and infants with rare diseases amendable to interventions.

- Review the programs and their conditions at least every two (2) years to ensure they remain up-to-date with current quality standards, scientific evidence, and advancement of testing capabilities. Once all testable and treatable rare diseases are part of the screening programs, more conditions may be added.

- Encourage a regional network of newborn screening programs (1) to crowdsource interpretation of test results, (2) to promote collaboration and innovation in programs, and (3) to cultivate the training and development of genetic counselors.

RECOMMENDATION 5.3

2025 Target: APEC member economies each have established domestic referral networks that guide newly-diagnosed individuals to the most appropriate place in the healthcare system to begin treatment and care.

Indicator: Percent of economies that have established a domestic referral network.

Actions:

- Leverage digital technology in coordination with industry, healthcare systems, and patient organizations to design and implement a robust referral network which bridges public and private healthcare facilities and allows for patients to effectively and efficiently move across geographic borders.
- Consider how such a referral network uses trained staff to help lead patients and their families to and through the appropriate pathway given their unique situation, location, and context.
- Make special considerations for how to diagnose symptomatic adults and individuals with late-stage disease onset who were not identified through newborn screening programs.

3.6 Coordinate patient-centered care across medical specialty, life course, and location

Context:

In addition to the journey to secure a diagnosis, individuals living with rare diseases and their caregivers must also navigate an equally arduous process to secure treatment and rehabilitation from multiple providers within the healthcare system when available. Problems arise frequently from this fragmentation of care, which can have a significant impact on clinical outcomes. As such, it is critical that economies implement solutions to improve coordination of patient-centered care across medical specialty, life course, and location. Defined referral networks for rare diseases and designated centers of excellence can be effective in helping coordinate these components, but they remain unofficial and underfunded in many economies. Where these mechanisms are weak, patient groups play an active role in coordinating patient-centered care (Dharssi et al., 2017). In many economies, improved coordination is needed between primary care providers and specialized medical services (Holmes, 2012; European Union, 2012). Trained specialists like cardiologists, nephrologists, and pulmonologists and clinical technicians that oversee enzyme replacement and proton beam therapy must work together with general practitioners to direct care that is holistic especially as patients living with rare diseases can have complicated comorbidities. It can be challenging to coordinate treatment schedules and payments between the various care providers. These issues weigh heavily on patients, who feel consistency of key contacts and good collaboration with the family doctor are some of the most important elements of their care (Schulenburg & Frank, 2015).

Due to the chronic nature of rare diseases, coordination is also critical across the life span, especially during the transition from pediatric to adult care (Holmes, 2012). Geography adds an additional dimension to the challenge of coordinating patient-centered care (Toumi et al.). Individuals living with rare diseases and their families may be forced to travel temporarily, or even move permanently across provincial or international borders to access various components of their care. However, patients face many barriers to coordinating care across borders. Starting with identifying the disease within the healthcare systems, the codes of the WHO International Classification of Diseases (ICD) are limited to covering 500 rare diseases, often understood differently, and applied inconsistently between jurisdictions (Yu et al., 2016). Moreover, transitioning medical records across different systems and borders has its own web of issues around data privacy and security. While costs and technical needs are still high, many domestic rare disease patient registries have designed innovative solutions to these problems with digital technologies (Gliklich et al., 2014).

RECOMMENDATION 6.1

2025 Target: APEC member economies each have established Centers of Excellence in meaningful locations given their respective domestic context for comprehensive diagnosis and initial treatment of rare diseases.

Indicator: Percent of economies with Centers of Excellence for diagnosis and treatment of rare diseases.

Actions:

- Establish Centers of Excellence in partnership with industry, academia, and healthcare professionals in meaningful locations, such as in population centers, and eventually expand them into a domestic network of Centers for rare disease diagnosis and initial care organized as a hub-and-spoke model.

- Ensure Centers (1) integrate with the broader healthcare system with clear, digitally-enabled pathways for patients to be referred for diagnosis and treatment initiation; (2) provide the full multidisciplinary scope of services from specialist clinicians, allied healthcare professionals, genetic counselors, and patient coordinators for rare disease patient care; and (3) be accessible and affordable for patients to attend.

RECOMMENDATION 6.2

2025 Target: APEC member economies each have established a clear and efficient process to ensure patients and their families can transition from Centers of Excellence to localized facilities to continue their care.

Indicator: Percent of economies with transition processes for patients to move from Centers to local facilities.

Actions:

- Partner with industry, clinicians, and patient groups to employ digital tools to overcome geographic barriers to the flow of information between patients and physicians such as remote detailing, online knowledge portals, and mobile applications to complement face-to-face interactions with physicians.
- Establish a process following treatment initiation at a Center of Excellence to efficiently refer the patient back to a healthcare setting closer to their home, or another location that is more convenient for the patient, and to co-manage the patient with local healthcare professionals for effective, patient-centered community care under direction of the Center of Excellence.

RECOMMENDATION 6.3

2025 Target: APEC member economies each have established a regional network of Centers of Excellence to share best practices and create an enabling environment for innovation in centralized rare disease care.

Indicator: Percent of economies participating in a regional network of Centers of Excellence.

Actions:

- Collaborate with industry, academia, and patient organizations to assemble a regional network of Centers of Excellence for resident healthcare professionals to exchange clinical guidelines and techniques, share best practices, and encourage innovation of rare disease diagnosis and treatment.

- Consider the feasibility of allowing patients (1) to move between Centers across borders for diagnosis and care if more convenient than traveling to a Center within their jurisdiction; or (2) to move virtually, utilizing networks to organize multidisciplinary boards of professionals from different economies and specialties to make diagnosis or treatment recommendations for individual patients anywhere in the region.

3.7 Deliver new and accessible treatments to patients

Context:

Development, delivery, and financing of rare disease treatments are some of the most sensitive issues. For one, treatments are only available for roughly 200 rare diseases, so more than 90% of patients have no medicinal treatment options available to them (Von der Lippe et al., 2017). If treatments are available, they often require highly specialized and coordinated medical care, which can be difficult to provide in economies with developing health infrastructure (Valdez, 2016). Patients also often require an assortment of long-term, non-therapeutic care: from special nutrient foods and other over-the-counter consumables to physical rehabilitation and home-based equipment (Simpson, 2016). That said, rare disease therapies nevertheless do extend the length and quality of life for patients, and recent genetic advancements in gene and cell therapy suggest aspirational cures may be possible for many rare diseases in the near future (Austin et al., 2018).

Yet even if treatment is available alongside well-integrated, high-quality care, the cost of medicine is also a key barrier. For rare diseases, the per-patient cost of treatment tends to be higher in order to recoup the cost of development for and marketing to such a small number of patients (Meekings, Williams, and Arrowsmith, 2012). Ideally, an appropriate mix of regulations and incentives encourages researchers and industry to develop new orphan products, while a patchwork of public, private, and charitable financing and insurance mechanisms help manage the costs (Committee, 2010). Such systems work particularly well for middle-class consumers in smaller, more developed economies (Schulenburg & Frank, 2015). Many patients and caregivers in poor and rural areas however pay relatively more out-of-pocket for care, leaving their financial security at risk (Jütting).

Cultivating a domestic policy environment to help enable biopharmaceutical innovation and access takes time. For one, a standard health technology assessment (HTA) is not suitable for orphan products and rare disease treatments. Stakeholders should work together to find innovative solutions to provide early patient access while addressing evidence needs. Where a value assessment or HTA is to be applied to a rare disease treatment, a tailored approach is required that takes into account: timely access for all rare disease patients; involvement of rare disease experts in the value assessment process; inclusion of all types of evidence; incorporation of multiple criteria in the value assessment; and a flexible approach to accepting greater uncertainty in the evidence at the time of launch. Before such improvements can be made domestically, where economies import a significant amount of therapeutic products, sensible trade policy becomes ever more critical on top of other policies to facilitate orphan drug designation, authorization, early access, and reimbursement programs (Dharssi et al., 2017). Economies must also figure out how to help regulators and reviewers keep up with new technology, techniques, and diseases while managing lean expense budgets (Schuhmacher et al., 2016).

RECOMMENDATION 7.1

2025 Target: APEC member economies each have established regulatory mechanisms with input from orphan product developers to ensure efficient review, approval, and access of new products for patients.

Indicator: Percent of economies with dedicated regulatory mechanisms for orphan products.

Actions:

- Create formal and regular opportunities for direct dialogue between all stakeholders including but not limited to industry, academics, clinicians, and patients.

- Design and implement expedited, flexible, or facilitated regulatory pathways for orphan products that (1) allow and encourage mutual reliance of decisions from other regulators in APEC economies with flexibility to allow consideration of regional factors; (2) ensure sustainability through appropriate application of cost recovery frameworks to allow for decreasing the fee for orphan product review or government funding to supplement cost-recovery mechanisms; (3) establish clear and transparent evaluation processes with defined timelines for review of dossiers and flexible rolling submissions; and (4) remove regulatory barriers such as unnecessary requirements for local quality control testing, clinical trial data, and GMP inspections.

- Establish a mechanism to allow for pre-regulatory early access while broader evaluation or approval is underway where a new therapy may address high unmet patient need—first on a nominative basis and later expanded to cohort schemes as regulatory infrastructure improves—and to fund this short-term access.

- Take steps to ensure alignment and harmonization between regulatory, reimbursement, and health technology assessment bodies within and across APEC economies to promote access.

RECOMMENDATION 7.2

2025 Target: APEC member economies each have established pricing mechanisms with input from the biopharmaceutical industry to make orphan products more available, accessible, and affordable to patients.

Indicator: Percent of economies with collaborative pricing mechanisms dedicated for orphan products.

Actions:

- Establish pricing mechanisms in partnership with industry in tandem with adequate base funding and ongoing review of base funding provided.
- Pricing policy considerations should reflect the benefit orphan products bring to patients and society, existing standards of patient-centered care, the potential of medicines to reduce other healthcare costs, as well as quality and safety.
- Implement a platform for negotiation with industry at listing to determine (1) how pricing policy will be implemented over the lifecycle of the product; (2) a well-defined criteria for pricing policies to be implemented; (3) a review mechanism to determine impact of pricing policy and a process for discretion to waive price reductions based on clinical or market forces; and (4) the ability to expand treatment and reimbursement guidelines, if clinically appropriate, upon reduction of price.

RECOMMENDATION 7.3

2025 Target: APEC member economies each have established a reimbursement structure with input from industry to make funding decisions for orphan products more transparent and effective for payers and patients.

Indicator: Percent of economies with dedicated reimbursement structures for orphan products.

Actions:

- Host consistent opportunities to engage with patients, caregivers, healthcare professionals, and industry to obtain their views and input throughout the reimbursement process.
- Design and implement a process to establish clear and fair reimbursement guidelines based on expert advice, with assistance from health technology assessments (HTAs), and with consideration for clinical outcomes.
- HTA decision-makers should be experienced in the appraisal of orphan products and any HTA process should be oriented to capture unmet need and clinical value as a measure of cost-effectiveness. In order to do this, decision-makers need access to all available relevant data from sources including randomized and non-randomized controlled trials, real-world evidence, and patient-reported outcomes.
- Undertake regular review of HTA process to ensure the system remains fit for purpose in the assessment of new therapies, especially new cell and gene therapies, and recognizes that returns are not only uncertain but also could come far into the future.
- Establish a formal process to provide for named patient access (NPA), including publishing list of drugs currently being provided through NPA.
- Sufficient funds should be allocated for the reimbursement of orphan products and care (1) using earmarked funding from new sources, (2) through pooled funds that could include many private and public payers with potential rebates, and (3) that explicitly include rare disease as its focus for coverage by including a prevalence-based definition that governs eligibility for funding.

3.8 Support financial and social needs of patients and their families

Context:

The first tier of support for the financial needs of rare disease patients is the patchwork of public, private, and charitable financing and insurance mechanisms designed to minimize the amount they pay out-of-pocket. The costs owed can be overwhelming, and some costs go uncovered. Additional yet vital non-therapeutic components of patient-centered care add substantial costs for healthcare systems and out-of-pocket expenses for the patients with rare diseases (Solberg, 2011; Giunti et al., 2013).

The economic burden of rare disease extends far beyond just therapeutic and non-therapeutic costs to indirect costs, which actually account for a significant proportion of total costs (Angelis et al., 2015). If not sufficiently covered by traditional payers, families of patients are often forced to bear a large part of the costs. According to one study, the medical expenses of patients with rare diseases exceeded three-times their individual income and twice their family income—indeed over 90% of patients surveyed were not able to make a living by themselves (Dong & Wang, 2016). Many other rare disease patients, however, are not able to work at all. Sometimes, spouses, partners and parents are not able to work either, having to dedicate their time to caregiving. Due to the actual or sometimes perceived limitations of their rare diseases, these individuals are disqualified, discounted or otherwise excluded from employment opportunities.

In addition to economic hardship, patients also face significant "loss of social support" (Von der Lippe et al., 2017). Given the number of children and young adults living with rare diseases, accessible education is of critical importance. Yet in many economies, this is a rarity itself—to fund specialized public education for children with rare diseases. Still, the consequences are sobering: for example, one study found children with congenital aniridia were not going to school at all because of the lack of trained staff and appropriate books accessible to individuals with blindness (Fioravanti, 2014). In addition to schooling, rare diseases can also force individuals, families, and caregivers into a mostly sedentary lifestyle, thus reducing social activity and interaction.

RECOMMENDATION 8.1

2025 Target: APEC member economies each have established policies and programs to better connect health systems with social welfare or assistance systems for patients and families to attain a minimum standard of living.

Indicator: Percent of economies that have connected healthcare systems with social welfare or assistance systems.

Actions:

- Ensure that an individual diagnosed with a rare disease becomes a beneficiary of new and existing social safety net programs that provide to both the patient and family members involved in their care (1) income supplements in the form of unconditional and/or conditional cash transfers and/or earned income tax credits; (2) sufficient access to credit or micro-credit; (3) long-term and/or temporary tax breaks; (4) food and housing subsidies; (5) and other sales discounts from the private sector.

- Examine efforts to coordinate the operation and funding of social protection programs across multiple parties or ministries and between local and central funding authorities, and consider strategies for enhancing collaboration to maximize resources and synergies.

RECOMMENDATION 8.2

2025 Target: APEC member economies each have established policies and programs to provide some level of publicly funded social insurance in tandem with private social insurance to mitigate risks for patients and families.

Indicator: Percent of economies with social insurance provided by public and private insurers.

Actions:

- Ensure that all those diagnosed with a rare disease and their families have access to social welfare support in the form of social insurance which reduces the risks associated with income loss resulting from unemployment, death, and the impacts of rare disease.
- Publicly funded insurance should include unemployment insurance, housing insurance, life insurance, health insurance, and micro-insurance products directly from governments.
- Create an enabling policy and regulatory environment that encourages and facilitates the development of innovative private insurance schemes.

RECOMMENDATION 8.3

2025 Target: APEC member economies each have implemented adjustments to employment and education systems in collaboration across departments or ministries to improve inclusivity and accommodation for individuals living with a rare disease.

Indicator: Percent of economies with education and employment support programs for patients.

Actions:

- Ensure both built and natural environments are accessible to individuals with rare diseases through minor adjustments in environmental and urban policies and guidelines for programs and projects. This may also require modest investments in infrastructure to ensure public transportation systems are accommodating to individuals living with a rare disease and their families.
- Consider actions to financially support relocation—either temporary or permanent—for patients and families to access employment and education opportunities most appropriate for them given their needs.
- Make investments in and facilitate anti-discrimination campaigns to ensure adequate psychosocial support is given to patients and families who may otherwise be excluded from employment and education environments due to their differences.
- Fund special education and skills training to enhance long-term economic security of patients and families, focusing particularly on women, elderly, and vulnerable groups.

3.9 Manage pooling and usage of patient data securely and effectively

Context:

Better utilization of patient data provides a significant opportunity to better support those living with a rare disease. Its purposeful application provides opportunities for better disease diagnosis and management, personalized therapeutic interventions, and as a catalyst for new and innovative research and development. Rare disease patient data also has the potential to underpin public health and clinical research and to inform health service design and delivery. Furthermore, rare disease data is used to promote and disseminate new knowledge to inform best clinical practice and care, identify and recruit volunteers for clinical trials, and to enable seamless integration with clinical trials.

A patient registry is the term typically used to manage rare disease patient data. A conventional definition of patient registries is that it is an organized system that collects patient data over a period of time in individuals with a specified condition in both a systematic and standardized manner. With more than 94% of rare diseases lacking an approved therapy, there is still much to be done regarding treatment discovery, and continued data sharing and enrollment of individuals into trials using registries is paramount (Austin et al., 2018). However, experience has shown that registries evolve over time. One critical aspect of registries is to ensure that they evolve to meet the evolving needs of stakeholders of governments, industry, researchers, clinicians, and caregivers.

Stakeholders from across APEC are in agreement: access to data is essential to improve the management of rare disease. The challenge this presents is how to manage data in a way that meets the needs of all stakeholders. While the data requirements of clinicians, researchers, patients, government and industry may overlap, their different roles in providing support for the rare disease community mean that bespoke data solutions need to be possible. Therefore it must be recognized that registries can serve different purposes. Registries can be used for clinical trial recruitment, a contact registry to empower rare disease patient advocacy communities, a clinical registry for screening and diagnosis, post market and surveillance and post-authorization and assessment, palliative care to capture patient-reported outcomes.

For example, to help support the standardization and sharing of information across rare disease registries, the European Commission, within the EU Program of Community Action in the field of Public Health, has initiated the establishment of a European Platform for Rare Disease Registries to address the challenge of standardizing and sharing information across rare disease registries (EpiRare, 2011). However, numerous challenges remain to privately and securely capturing, standardizing, and sharing health information between patient registries and with researchers.

The benefits extend beyond just the rare disease community. A better understanding of rare disease mechanisms has the potential to inform future research on common diseases 351 such as hypertension, diabetes, and cancer. The multi-purpose role of registries is critical. These datasets generated and the means to analyse them underpin future health system architecture and will drive new advances in healthcare. However, the variety, veracity and the velocity with which patient data can and should be generated, especially in the era of personalised genomics, presents challenges. Appropriate mechanisms need to be in place in order to rapidly improve patient outcomes. Considerations such as governance and security, consensus on what data should be collected, and who should get access to data, working with differing APEC economy regulatory frameworks covering collection of data, sharing of data across national borders, privacy and how registries are sustainable.

RECOMMENDATION 9.1

2025 Target: APEC member economies each have achieved consensus on governance and capacity-building measures for managing and storing patient data to optimize scientific discovery, innovation, trust, and societal benefit for rare diseases.

Indicator: Percent of economies with governance frameworks for management and storage of patient data.

Actions:

- Convene industry, academia, clinicians, and patient organizations to discuss and design consensus-based codes of conduct to detail a fair and transparent framework for governing the capture, management, storage, and use of patient data, including how and where it should be collected and in what standardized formats based on internationally recognized disease phenotype ontologies (e.g., ORDO, HPO).
- Formalize a working group with participation from clinicians, patient representatives, industry to review these governance structures, provide advice to Health Ministers on issues of patient data, and design and implement feedback loops for patient data to inform drug development, regulatory activity, health technology assessments, funding and reimbursement decisions, and quality control.
- Ensure that the data captured include patient reported outcomes, relevant clinical endpoints, and appropriate quality of life measures.

RECOMMENDATION 9.2

2025 Target: APEC member economies each have made investments in foundational data infrastructure, digital technologies, and capacity-building measures for secure, private, and efficient rare disease patient data capture, storage, and use.

Indicator: Percent of economies with meaningful investments in data infrastructure and digital technologies.

Actions:

- Partner with a multisectoral community of industry representatives to invest in the core infrastructure necessary to ensure secure, private, and efficient rare disease patient data management including traditional hardware components like servers and electronic health record systems to cutting-edge cloud computing.
- Work together across the APEC economies to determine the feasibility and preliminary design of a single regional registry focused on rare diseases for all APEC economies to access and use.
- Establish a working group which includes patients and representatives of patient organizations to explore digital solutions and infrastructure and regulatory hurdles to emerging technology, and to develop, publish, and promote the design and governance of a regional infrastructure platform for collaborative economy usage.
- Invest in and make accessible innovative digital technological solutions to support research and development activities for rare diseases across all disciplines including but not limited to biotechnology, biomechanics, and engineering.

RECOMMENDATION 9.3

2025 Target: By 2025, all APEC member economies will facilitate cross-border data flows while respecting data privacy and applicable domestic laws and regulations.

Indicator: Percent of economies with policies that facilitate cross-border data flows.

Actions:

- Leverage the expertise and activity of the working group in partnership with industry, clinicians, and patient organizations to design and implement policies and processes that create an enabling environment for the sharing of relevant rare disease patient data across disciplines and borders, even regionally, to allow stakeholders to access information about their patients and medical product consumers.
- Ensure these policies and processes allow for sufficient acquisition of full and informed consent from patients and families, interoperability of databases and other digital systems so that integration and collaboration is possible and efficient, and public availability of some meaningful data where appropriate and within the parameters of local privacy and security contexts.
- Considerations should be made to ascertain and adjust accordingly to the impacts of Good Data Privacy Regulations (GDPR) and Cross-Border Privacy Regulations (CBPR) on data related to rare diseases.
- Work with private and public researchers and academia to further facilitate regional and international pooling of trial data to solve some of the challenges related to small patient cohorts in any one jurisdiction.

3.10 Prioritize comprehensive domestic rare disease policy integrating 3.1 – 3.9

Context:

Without a clear definition, it is difficult for health policymakers to allocate resources and design health interventions for rare diseases. This is especially true as the size of the affected population and the size of the potential benefits are influencing awareness, visibility, and the political calculus. That is, where few people are affected and few treatments exist issues are at risk of insufficient political attention and limited public health resource allocation (Norheim, 2016). The voices of individuals living with a rare disease and their caregivers will fill this vacuum. In many economies, patient groups are central to building political capital to prioritize rare disease policy. With so few individuals living with a single rare disease, organizations that have gained momentum are ones capable of building coalitions, expanding their scope, including all rare disease patients in a collective movement (Mikami & Sturdy, 2017). Without a cohesive patient voice, rare disease will be at risk of not been recognized as a public health priority. It takes the entire community of stakeholders to build and sustain political capital, and channel it into comprehensive rare disease policy often in the form of a domestic, whole-of-government plan. However, for many economies enacting comprehensive rare disease policy in a single bill is neither feasible nor effective. Instead, one proven best practice is incorporating small provisions for rare disease into larger and broader legislation with political support. After all, the challenge of rare disease is interdisciplinary and thus must be addressed from all angles—the rare disease community can find support in legislation as far ranging as tax to transportation. In practice though, the difficulties are in the details and all stakeholders need to work together and advocate for prioritizing rare disease policy and improving coordination of policymaking. Rare disease policy is multifaceted and requires a holistic approach from government. While on a per condition basis these diseases are rare, when viewed holistically and cumulatively, the numbers are significant. APEC economies and their respective governments cannot afford to ignore rare disease policy—these patients are sick and utilize healthcare services.

RECOMMENDATION 10.1

2025 Target: APEC member economies each have developed and published non-binding but comprehensive, whole-of-government, and medium- to long-term plans for addressing rare diseases in each of their domestic contexts.

Indicator: Percent of economies with a non-binding, comprehensive domestic rare disease plan.

Actions:

- Generate political will in partnership with industry, academia, clinicians, and patient groups to develop and publish an economy-wide plan on rare diseases and orphan products that (1) incorporates actionable strategies on key policy areas that require development; (2) targets and prioritizes research and development areas depending on economy strengths and needs; (3) evolves over time to match the domestic rare disease context and community; and (4) integrates monitoring and financing components to accelerate action and maintain momentum.

- Identify a government focal point to convene various government entities relevant to addressing rare diseases.

RECOMMENDATION 10.2

2025 Target: APEC member economies each have integrated legislative provisions for rare diseases into other areas of legislation outside healthcare such as social security, disability, employment, and housing.

Indicator: Percent of economies with binding, legislative rare disease provisions in other policy areas.

Action:

- In collaboration across departments or ministries, establish regular reporting on the integration of provisions to assist the rare disease community across government services, including the publication of an annual report detailing (1) steps taken to align policy and regulation, (2) objective and quantifiable measures of improvement to the system, and (3) steps required to continue improving policy and regulatory harmonization across government.

RECOMMENDATION 10.3

2025 Target: APEC member economies each have enacted enforceable, comprehensive legislation, policy, or mechanism at least covering provisions on the research, diagnosis, and treatment of rare diseases.

Indicator: Percent of economies with comprehensive domestic legislation, policy, or mechanism.

Action:

- Utilize rare disease committees to provide advice on the scope and content of legislation to address the challenges of rare disease, including access to diagnostics, appropriate patient-centered care and management, and the regulatory and reimbursement systems relied upon to facilitate access to therapy. Legislation should also coordinate government support to research in rare disease.

IV. IMPLEMENTATION TOOLS & INSTRUMENTS

APEC Action Plan on Rare Diseases

IV. IMPLEMENTATION TOOLS & INSTRUMENTS

APEC LSIF Rare Disease Network

- APEC LSIF Rare Disease Network (RDN) will establish the virtual platform upon which economies can collaborate to implement the recommendations of the APEC Rare Disease Action Plan.
- The RDN will also continue to recruit additional governments, academics, and industry representatives so as to achieve the overarching objective of engaging all 21 APEC economies in the Action Plan.
- The RDN will also establish a resident expert to provide advice to governments in APEC economies.

APEC Policy Dialogue on Rare Diseases

- Organized by the RDN, the annual Policy Dialogue will serve as an opportunity for in-person collaboration and consensus-building for stakeholders involved in implementing the Action Plan.
- Building from the 1st APEC Policy Dialogue on Rare Diseases in June 2018, future events will spotlight specific pillars of the Action Plan to support concerted progress in key areas of challenge or opportunity.
- The RDN will conduct an annual evaluation of the Action Plan and amend it according to scientific advancements and progress made towards implementation, presenting results at the Policy Dialogue.

APEC LSIF Regulatory Harmonization Steering Committee

- Tasked with supporting and encouraging convergence of medical product regulations across APEC, the RHSC will serve as a critical convener of support for success in 3.7 (“Pillar 7”).

APEC Action Plan Regional Collaboration Checklist *(see Appendix 1)*

- A summary checklist of actions that center around or involve regional collaboration.

Remaining Questions and Concerns

- Population and economic development considerations
- Flexibility in the target, indicator, or action
- Monitoring progress by ranking
- Incentives and encouragement
- Ambitious but achievable indicators

V. MONITORING & REPORTING MECHANISMS

APEC Action Plan on Rare Diseases

V. MONITORING & REPORTING MECHANISMS

Implementing the APEC Rare Disease Action Plan will encourage APEC member economies to work together. In order to ensure the successful and effective implementation of the Action Plan, monitoring and reporting will be conducted at an APEC level and at the economy level on a voluntary basis.

APEC Level Monitoring and Reporting

- Quantitative and qualitative feedback from economies to APEC LSIF
- APEC LSIF and APEC LSIF RDN meetings as platforms to highlight progress
- APEC LSIF RDN will aggregate data from economies for a comprehensive status update at 2020 APEC Ministerial Meeting

Economy Level Monitoring and Reporting

- Economy-level monitoring and evaluating systems
- Baseline studies and economy-specific targets and indicators
- Reference of Action Plan to design domestic initiatives

Project or Initiative Level Monitoring and Reporting

- Economies are encouraged to consider the targets and indicators in this Action Plan when designing new projects or initiatives to ensure harmonization, especially metrics that evaluate the number of patients and families assisted and the extent of this assistance.

APPENDIX 1:

REGIONAL COLLABORATION CHECKLIST

APEC Action Plan on Rare Diseases

APEC economies are encouraged to:

- ☑ Consider mutual reliance of regulatory decisions from other APEC economies to improve harmonization across the region; and establish a regional network or partner with an existing one to facilitate the sharing of best practices related to the policy, regulatory, and reimbursement decisions of rare disease. **(Recommendation 1.3)**

- ☑ Lead efforts to advance international and regional collaboration for research and development. **(Recommendation 3.1)**

- ☑ Encourage regional networks for human resource capacity-building in medical and non-medical sectors, especially around specific rare diseases or clusters. Build on existing programs and centers to offer cross-border clinical training and internships. Encourage and provide opportunities for public-private partnerships in medical and non-medical training and investment in regional comprehensive clinics and regional centers of expertise. **(Recommendation 4.1)**

- ☑ Leverage coordinated efforts and regional partnerships in balance with local data privacy policies to generate and capture sufficient quantity and quality of Asian genetic reference sequences and make them widely accessible and available to researchers and clinicians. **(Recommendation 5.1)**

- ☑ Encourage a regional network of newborn screening programs (1) to crowdsource interpretation of test results, (2) to promote collaboration and innovation in programs, and (3) to cultivate the training and development of genetic counselors. **(Recommendation 5.2)**

- ☑ Collaborate with industry, academia, and patient organizations to assemble a regional network of Centers of Excellence for resident healthcare professionals to exchange clinical guidelines and techniques, share best practices, and encourage innovation of rare disease diagnosis and treatment. **(Recommendation 6.3)**

- ☑ Work together across the APEC economies to determine the feasibility and preliminary design of a single regional registry focused on rare diseases for all APEC economies to access and use. **(Recommendation 9.2)**

- ☑ Work with private and public researchers and academia to further facilitate regional and international pooling of trial data to solve some of the challenges related to small patient cohorts in any one jurisdiction. **(Recommendation 9.3)**

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