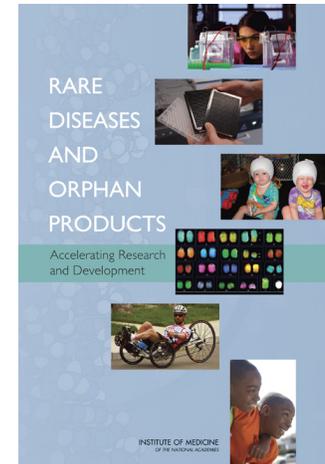


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# Rare Diseases and Orphan Products

## Accelerating Research and Development



**Rare diseases collectively affect millions** of Americans of all ages and additional millions of people globally. Of the estimated 5,000 to 8,000 diseases categorized as rare, some affect only a few individuals, while others affect many thousands of people. Most of the diseases are genetic or have a genetic component. Others arise from such factors as exposure to infections or toxins. Rare diseases often are serious and life-altering; many are life-threatening or fatal.

Because each rare disease affects a relatively small population, developing drugs and medical devices to prevent, diagnose, and treat these conditions is challenging. These difficulties include attracting public and commercial funding for research and development, recruiting sufficient numbers of research participants, designing sound clinical trial strategies for small populations, and assessing the safety and efficacy of products before they are marketed. Scientists, medical products companies, government policy makers, and private advocacy groups have done much in recent decades to respond to these challenges; advances in prevention, diagnosis, and treatment have brought significant benefits for many patients and their families.

Nonetheless, researchers still lack even a basic understanding of the cause or underlying molecular mechanisms of many rare diseases. Also, effective therapeutics are available for only a small fraction of rare diseases—and even when available, some therapies are extraordinarily expensive. To help in accelerating rare diseases research and product development, the National Institutes of Health (NIH), with support from the Food and Drug Administration (FDA), asked the Institute of Medicine (IOM) to examine the opportunities and obstacles in developing drugs and medical devices for treating rare

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diseases—sometimes called “orphan” diseases because their limited prevalence often has discouraged both private and public research.

## **Toward an Integrated National Strategy**

As an overarching goal, the report, *Rare Diseases and Orphan Products: Accelerating Research and Development*, calls for implementing an integrated national strategy to promote rare diseases research and product development. The strategy would include seven key elements:

1. Active involvement and collaboration by a wide range of public and private interests, including government agencies, commercial companies, academic institutions and investigators, and advocacy groups.
2. Timely application of advances in science and technology that can make rare diseases research and product development faster, easier, and less expensive.
3. Appropriate use and further development of trial design and analytic methods tailored to the special challenges of conducting research on small populations.
4. Creative strategies for sharing research resources and infrastructure to make good and efficient use of scarce funding, expertise, data, biological specimens, and participation in research by people with rare conditions.
5. Reasonable rewards and incentives for private-sector innovation and prudent use of public resources for product development when the latter appears to be a faster or less costly way to respond to important unmet needs.
6. Adequate organization and resources, including staff with expertise on rare diseases research and product development, for the public agencies that fund biomedical

research on rare diseases and regulate drugs and medical devices.

7. Mechanisms for weighing priorities for rare diseases research and product development, establishing collaborative as well as organization-specific goals, and assessing progress toward these goals.

Components of each of these elements already exist, some more robust than others. However, it is difficult to achieve coherence, given the array of participants with differing perspectives and priorities, the number and diversity of rare diseases, and the limited and even undocumented resources devoted to them individually and collectively. Thus, the IOM report recommends a number of steps to aid in developing a more integrated approach to rare diseases research and product development.

As one opportunity for improvement, NIH should develop a comprehensive action plan for rare diseases research that covers all institutes and centers and that defines and integrates goals and strategies. This plan should cover program planning, grant review, training, and coordination of all phases of research. Other recommendations span a range of areas, from improving how drugs and medical devices developed for rare diseases are covered under the government’s regulatory umbrella to gaining a better understanding of how public and private insurance programs influence the development and use of such drugs and medical devices.

## **Accelerating Discovery Research**

Basic research, followed by discovery research, is key in identifying the causes and molecular mechanisms of rare diseases and in pinpointing therapeutic targets. In recent years, the research tools available to biomedical investigators have improved dramatically, and some of them hold particular promise for rare diseases research. Also promising is the growth of public-private partnerships and other collaborations that are deploying

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new strategies to bridge the gulf between basic research findings and beneficial products.

Given the small number of patients available to participate in research on rare diseases, as well as limited funding, it is particularly important to make best use of the resources for research and the data and other resources generated by research. The report therefore recommends that NIH work with industry, academia, and voluntary organizations to develop a comprehensive system of shared resources for discovery research on rare diseases and to facilitate communication and cooperation for such research. This effort should include, among other actions, the creation of a repository of publicly available animal models for rare disorders that reflect the disease mechanisms seen in humans and a public repository of biological data on the molecular mechanisms of rare diseases generated by investigators funded by NIH, private foundations, and industry.

### **Supporting Clinical Research**

Once a potential drug has been discovered, the process of developing it into a marketable product begins with preclinical trials and continues through increasingly demanding phases of clinical testing. This process is expensive and risky. The federal government, through the Orphan Drug Act of 1983, provides commercial firms with various incentives for undertaking clinical trials. NIH also supports such efforts through its Rare Diseases Clinical Research Network and other programs. The IOM report recommends that

more be done to identify and implement collaborative strategies to share and leverage resources with a view to decreasing research and development costs without sacrificing product safety or efficacy.

To this end, NIH should increase its capacity and flexibility to support all phases of preclinical and clinical research related to rare diseases, including clinical trials of new and repurposed therapeutic agents. Several opportunities should be explored, including the provision of preclinical development services to nonprofit entities and the creation of standards for data and specimen collection, maintenance, and sharing for patient registries and biorepositories. NIH should also coordinate the new Cures Acceleration Network with the Rare Diseases Clinical Research Network, the Clinical and Translational Science Awards program, the grants programs of FDA's Office of Orphan Product Development, and other existing initiatives.

### **Establishing a Task Force**

To help build on these and other recommendations and existing activities, the IOM report calls for the Secretary of the Department of Health and Human Services to establish a national task force on accelerating rare diseases research and product development. To operate for perhaps four to eight years, the task force would bring together leaders from government, industry, academic and other research institutions, and advocacy groups. Its objectives would be to promote, coordinate,



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monitor, and assess the implementation of NIH, FDA, and other public- and private-sector initiatives on rare diseases and orphan products and to support additional opportunities for public-private collaboration.

### Conclusion

Even as the task force acts to foster cooperation and collaboration, all participants in rare diseases research and product development will need to improve their individual efforts. Individual improvement will strengthen the foundation for collaboration.

Overall, the effort and investment needed to move further toward a collaborative, coordinated, open, and sustained approach to rare diseases will be substantial, but not making the investment will also be costly. The potential benefits justify a renewed commitment to accelerating rare diseases research and orphan product development. 

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