MEDCHI, THE MARYLAND STATE MEDICAL SOCIETY
HOUSE OF DELEGATES

Resolution 27-17

INTRODUCED BY: MedChi Medical Student Section

SUBJECT: Reforming the Orphan Drug Act

Whereas, Congress passed the Orphan Drug Act (ODA) of 1983 in response to declining pharmaceutical investment of "orphaned" drugs through clinical trials following the Kefauver-Harris amendments of 1962 because of increased development costs;[1] [2] [3] and

Whereas, The "orphan" designation often refers to drugs that target rare conditions affecting fewer than 200,000 Americans[4], and are thus often deemed "unprofitable" due to the unlikelihood of a company to recuperate development and marketing costs[5]; and

Whereas, To promote the research of therapies against rare diseases and conditions for which sales revenue alone are unlikely to recover the costs of development, the ODA offers a variety of incentives, including 1) 7 years of market exclusivity, 2) a tax credit up to 50% of clinical trial costs, 3) direct federal grants to the pharmaceutical company up $500,000 per year for 4 years, and 4) a waiver of marketing user application fees;[6] [7] and

Whereas, Although the ODA has been praised as highly successful for introducing over 400 orphan drugs since becoming law,[1-3] physicians, researchers, and policymakers have raised concerns about potential abuses of the Act;[8] [9] [10] [11] [12] and

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[1] Orphan Drug Act, Pub. L. No. 97-414 (1983).
[2] Boat TF, Adamson PC, Asbury C, et al. Rare Diseases and Orphan Products, Accelerating Research and Development Institute of Medicine (US) Committee on Accelerating Rare Disease Research and Orphan Product Development. Washington DC: National Academies Press; 2010.
[3] Haffner ME, Whitley J, Moses M. Two decades of orphan product development. Nature Reviews Drug Discovery 2002;1:821–5.
[4] Wellman-Labadie O and Zhou Y. The US Orphan Drug Act: rare disease research stimulator or commercial opportunity? *Health Policy*; 2010; *95*: 216-228.
[5] Office of Orphan Products Development. US food and drug administration. Available at: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018190.htm. Accessed August 10, 2017.
[6] Orphan Drug Act, Pub. L. No. 97-414 (1984 as amended).
[7] Haffner ME. Adopting orphan drugs - two dozen years of treating rare diseases. *New England Journal of Medicine*. 2006; *354*: 445-447.
[8] Burns TM, Smith GA, Allen JA, Amato AA, Arnold WD, Baron R, et al. Editorial by concerned physicians: unintended effect of the Orphan Drug Act on the potential cost of 3,4-diaminopyridine. *Muscle & Nerve*. 2016; *53*: 165-168.
[9] Daniel MG, Pawlik TM, Fader NA, Esnaola NF, Makary MA. The Orphan Drug Act: restoring the mission to rare diseases. *American Journal of Clinical Oncology*. 2016; *39*(2): 210-213.
[10] Gary A. Pulsinelli, The Orphan Drug Act: What's Right with It, 15 Santa Clara High Tech. L.J. 299 (1999).
[11] Hilts PJ. Bush won't sign for-profit drug bill. *The New York Times*. Published November 9, 1990. Available at: http://www.nytimes.com/1990/11/09/us/bush-won-t-sign-drug-profit-bill.html. Accessed August 11, 2017.

Whereas, One such concern is that despite the Act's original intent of incentivizing the development of "non-profitable" therapies treating fewer than 200,000 Americans,[1] several drugs have obtained "blockbuster status," indicating $1 billion in sales annually, through a multitude of loopholes;[4,9] and

Whereas, An example of such a loophole is the approval for "orphan designation" - and therefore, ODA benefits - on existing compounds and mass-market drugs, as is the case for 3,4-DAP,[8] ascorbic acid,[13] calcium carbonate,[14] Humira, and Crestor;[15] and

Whereas, A pharmaceutical company may strategically submit a drug for approval of a single indication - "one that is narrow enough to qualify for orphan drug benefits"[16] - and once approved, the drug is utilized for a variety of off-label uses,[9] as demonstrated by the drugs rituximab, modafinil, and a variety of oncology drugs;[16] [17]and

Whereas, A pharmaceutical company may strategically apply for additional approval for new indications, as has been demonstrated by rituximab, imatinib, and epoetin-alfa; [9,18] [19]; and

Whereas, The ODA's 7-year marketing exclusivity benefit may extend beyond the trademark office patent, and can "run concurrently or sequentially on the basis of number of indications for the drug, effectively providing pharmaceutical companies with government-sponsored monopolies";[9,] [20] and

Whereas, Although each indication of an orphan drug at the time of FDA approval may treat fewer than 200,000 Americans, the total number of indications for a drug can result in treating a larger population, and

Whereas, The exploitation of these and other potential loopholes within the Act have resulted in both exorbitant price hikes and increasing sales, contributing up to one-fifth of global prescription sales by 2020 despite the original purpose of treating small populations;[9] [21] [22] therefore let it be

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[12] Timeline: the Orphan Drug Act. *Kaiser Health News*. Published January 17, 2017. Available at: http://khn.org/news/timeline-the-orphan-drug-act/. Accessed August 9, 2017.

[13] US Food and Drug Administration: For Industry. U.S. Department of Health & Human Services, Available at: https://google2.fda.gov/search?q=cache:qzKcvrZK-DsJ:www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/officeofscienceandhealthcoordination/ucm215811.xls+ascorbic+acid+charcot&client=FDAgov&proxystylesheet=FDAgov&output=xml_no_dtd&site=FDAgov&ie=UTF-8&access=p&oe=UTF-8. Accessed August 10, 2017.

[14] Tribble, J. and Sydney, L. Three Key Senators ask GAO to investigate abuses of the Orphan Drug Act *Kaiser Health News*. March 7, 2017

[15] Tribble SJ and Lupkin S. Drugs for rare diseases have become uncommonly rich monopolies. *National Public Radio*. Published January 17, 2017. Available at: http://www.npr.org/sections/health-shots/2017/01/17/509506836/drugs-for-rare-diseases-have-become-uncommonly-rich-monopolies. Accessed August 9, 2017.

[16] Kesselheim AS, Myers JA, Solomon DH, et al. The prevalence and cost of unapproved uses of top-selling orphan drugs. *PLoS ONE*. 2012;7:2.

[17] Casali PG. The off-label use of drugs in oncology: a position paper by the European Society for Medical Oncology. *Annals of Oncology* 2007;18:1923–5.

[18] Hornberger J, Chien R, Friedmann M, et al. Cost-effectiveness of rituximab as maintenance therapy in patients with follicular non-Hodgkins lymphoma after responding to first-line rituximab plus chemotherapy. Informa Healthcare. 2012;53:2371–2377.

[19] Seoane-Vazquez E, Rodriguez-Monguio R, Szeinbach SL, Visaria J.Incentives for orphan drug research and development in the United States. *Orphanet Journal of Rare Diseases* 2008;3:33.

[20] Cheung RY, Cohen JC, Illingworth P. Orphan drug policies: implications for the United States. Canada and developing countries. *Health Law Journal* 2004;12:183–200.

[21] Faloon W. Unsustainable, cancer drug prices. Life Extension Magazine. 2014 April. Available at: http://www.lef.org/magazine/2014/4/Unsustainable-Cancer-Drug-Prices/Page-01. Accessed August 10, 2017.

[22] Hadjivasiliou A, Gardner J. Orphan Drug Report 2014. EvaluatePharma. 2014.

Resolved, That MedChi's AMA Delegation submit a resolution to the AMA that requires the AMA to support efforts to reform the Orphan Drug Act to protect the Act's original intent and prevent identified abuses of the Act.

At its meeting on September 23, 2017, the House of Delegates referred Resolution 27-17 to the Board of Trustees for decision.