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A fair shot for affordable pneumonia vaccine: Why overcoming patent barriers to PCV13 is vital for saving children's lives?*1

Médecins Sans Frontières (MSF)

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pneumococcal conjugate vaccine (PCV), patent, vaccine affordability

1. Introduction

In early February 2018, the international medical humanitarian organization Doctors Without Borders/Médecins Sans Frontières (MSF) filed a third party petition to the Supreme Court of Korea requesting to review the patent granted to the US pharmaceutical corporation Pfizer for its 13-valent pneumococcal conjugate vaccine (PCV13)*2. The filing marks an unprecedented legal action taken by the organization to directly challenge a patent before the highest judicial body of a country. MSF, the biggest non-governmental organization that delivers about 5.3 million doses of vaccines and immunological products every year mostly in low- and middle-income countries, has been advocating for the availability of more affordable alternatives to PCV, while Pfizer's patent in question in Korea could effectively diminish this hope.

2. Public health priority of access to PCV and the challenge of duopoly global market

Globally, pneumococcal infections caused by Streptococcus pneumonia are the leading cause of death for children, representing 16% of childhood mortality*3, and kills nearly one million children under 5 years old every year*4. The vast majority of this burden is disproportionately borne by low- and middle-income countries. Many pneumococcus cases are difficult to diagnose and a number of pneumococcal strains have now become resistant

*1 Japanese translation of this article is published in *Rinsho Hyoka* (*Clin Eval*). 2018; 46(2). Available from: http://cont.o.oo7.jp/46_2/46_2contents.html
*2 https://www.msfaccess.org/resources/press-releases/2886
*3 International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. Pneumonia and Diarrhea Progress Report 2016: Reaching Goals through Action and Innovation. 2016. Available from: http://www.jhsph.edu/research/centers-and-institutes/ivac/resources/IVAC-2016-Pneumonia-Diarrhea-Progress-Report.pdf
*4 http://www.who.int/mediacentre/factsheets/fs331/en/

to the antibiotics typically used to treat these infections. In the context, vaccination with PCV to prevent these life-threatening infections is a public health priority. Therefore, in 2007, the World Health Organization (WHO) recommended PCV for inclusion in all national immunisation programmes, updated it in 2012 to include and focus on the available 10-valent (PCV10) and 13-valent pneumococcal conjugate vaccines (PCV13)*5.

Yet, PCVs are some of the most expensive vaccines, and its price presents a primary barrier for health ministries in developing countries to implement the WHO's recommendation of PCV inclusion in the Universal Immunisation Programme. About one third of the world's countries have not been able to introduce PCV because of its high price*6. One of the key contributing factors to keep PCVs priced out of reach by millions is the duopoly situation. There are only two suppliers of PCVs worldwide: Glaxo-Smith Klein on PCV10 (marketed as Synflorix®), and Pfizer on PCV13 (marketed as Prevnar 13®). Pfizer has made more than US$37 billion so far on its PCV vaccine and it is the world best-selling vaccine*7.

The absence of competition has left immunisation programmes and medical humanitarian organisations, such as MSF, no other choice but to struggle with the unsustainable pricing offered by the companies. According to volumes and prices published by the Supply Division (SD) of the United Nations Children's Fund (UNICEF), PCV prices for Middle-Income Countries (MICs) that are not eligible for donor support are relatively high depending on the country, product, and manufacturers' pricing policies*8.

3. Patent barriers to vaccine competition on PCV

It is a proven fact that competition has played a vital role in reducing vaccine prices in the past. Five-in-one pentavalent vaccine that protects against five life-threatening diseases – Diphtheria, Pertussis, Tetanus, Hepatitis B and Hib – is an example of how market competition has reduced vaccine prices and resulted in greater access to a life-saving vaccine. In 2001, there were only two multi-national pharmaceutical companies producing the pentavalent vaccine purchased by UNICEF; the price of each product was US$3.50 per dose*9. With significant global demand from Gavi, the Vaccine Alliance, which was purchasing pentavalent vaccines for the world's poorest countries, additional manufacturers, especially those from India where no patent barriers existed, have begun to enter the market since 2008 and driven the prices down by 38%*9. By 2016, UNICEF was purchasing from six WHO prequalified pentavalent manufacturers, including a Korean company for a price as low as US$ 1.15 per dose, a reduction of nearly 70%*10.

This has not happened in the PCV market. While bringing competition to PCVs is desperately needed to lower high prices, Pfizer has been

*5 WHO Weekly Epidemiological Record (WER). 2012 April 6; 87(14): 129-44. Available from: http://www.who.int/wer/2012/wer8714.pdf?ua=1

*6 https://www.cdc.gov/mmwr/volumes/65/wr/mm6541a3.htm#F1_down; http://www.who.int/mediacentre/factsheets/fs378/en/

*7 The figure is revenue earnings for Prevnar13® (Pfizer's PCV13 vaccine) from 2009 to 2017, inclusive. Available from: https://investors.pfizer.com/financials/annual-reports/default.aspx

*8 UNICEF Supply Division. Pneumococcal Conjugate Vaccine: Supply and Demand Update. 2016 August.

*9 https://www.msfaccess.org/sites/default/files/MSF_assets/Vaccines/Docs/VAC_report_TheRightShot2ndEd_ENG_2015.pdf page 11.

*10 UNICEF Supply Division. Vaccine Price Database. Available from: https://www.unicef.org/supply/files/DTP-HepB-Hib.pdf

aggressively pursuing frivolous patents to secure its monopoly status and hinder the formation of competition that could offer opportunities to millions of people access to more affordable alternatives of PCVs. Pending before the Supreme Court of Korea, the case involving Pfizer's patent would determine the prospect and timeline of the availability of a long-waited alternative PCV that is being developed and nearly completed by a Korean vaccine manufacturer.

The patent under question before the Korean court concerns the methods of selecting the protein carriers and conjugating serotypes of streptococcus pneumoniae into a single carrier*11. Analysing the claims put forward by Pfizer, the technology described in selecting the protein carrier and the conjugating process are obvious to the conjugate vaccine producers*12. The very technological methods have been disclosed previously and are commonly known and used in conjugate vaccine development. Pfizer's claims for using this old method to conjugate a wide range of serotypes could potentially block not only PCV13 production, but also vaccine production concerning any serotype(s) covered by the claims*13. In summary, the patent that is under scrutiny in Korea now does not present a new technology and if the patent is upheld it could sustain Pfizer's monopoly.

The equivalent patent and application of Pfizer has been challenged in other countries as well. In India, MSF has filed a pre-grant opposition in 2016 and a writ petition in 2017 to challenge this Pfizer patent for its lack of technical merits according to Indian patent law*14. In other places, this patent was revoked in China in 2015*15 and is now under further litigation*16. It was granted and subsequently revoked by the European Patent Office (EPO) following opposition by other major pharmaceutical companies. An appeal by Pfizer is underway in Europe*17. Even in Korea where the case has gone to the highest instance of the proceeding, Pfizer did not get the patent initially, as the patent office rejected Pfizer's application in 2012*18. It was subsequently granted after Pfizer amended the claims and resubmitted them in 2013*18. A local competitor launched an invalidation procedure in 2013, followed by a revocation lawsuit and an appeal procedure to the Supreme Court, which is currently ongoing. Pfizer has also filed several divisional patents in Korea*19, based

*11 Korean Patent Number No. 1298053. Equivalent to WIPO PCT application number WO/2006/110381. Multivalent Pneumococcal Polysaccharide-Protein Conjugate Composition cited 2018 Apr 20]. Available from: https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2006110381&redirectedID=true

*12 See detailed analysis in the amicus brief submitted by MSF to the Korea patent court in 2017. Available from: https://cdn.patentoppositions.org/uploads/patent_opposition/user_uploaded_file/5908670bfb1640400b000000/pdf_cda43310-21c3-0135-5ad3-50e549351d0c.pdf

*13 https://www.msfaccess.org/sites/default/files/VAC_report_A%20Fair%20Shot%20for%20Vaccine%20Affordability_ENG_2017.pdf page 15.

*14 https://msfaccess.org/resources/press-releases/2563; https://www.msfaccess.org/about-us/media-room/press-releases/msf-approaches-delhi-high-court-challenge-unmerited-patent-grant

*15 China and Global Patent Examination Information Inquiry. See CN2006800177768 [cited 2017 Sep 12]. Available from: http://cpquery.sipo.gov.cn/

*16 MSF. Communication with the State Intellectual Property Office of China regarding CN200680017776. 2017.

*17 European Patent Office. Espacenet, EP1868645, Multivalent Pneumococcal Polysaccharide-Protein Conjugate Composition [cited 2017 Aug 8]. Available from: https://register.epo.org/application?number=EP06740419&lng=en&tab=event

*18 See the administrative history of Korean patent No. 1298053 at KIPRIS (Korean Patent Office Public Searching Database) [cited 2018 Apr 20]. Available from: http://engpat.kipris.or.kr/engpat/searchLogina.do?next=MainSearch#page1

*19 For instance World Intellectual Property Organization, Patentscope, KR1020137007564, Novel Polysaccharide-Protein Conjugate Composition [cited 2017 Aug 8]. Available from: https://patentscope.wipo.int/search/en/detail.jsf?docId=KR150893304&redirectedID=true#atapta0

on the primary filing, intending to secure its market monopoly*20.

The dispute in South Korea is particularly significant because a local firm has a follow-on alternative PCV13 product in an advanced stage of development. The current patent dispute could determine whether the local competitor can launch their version of PCV*21.

The approach deployed by Pfizer now on PCV is not uncommon among multinational pharmaceutical companies. Pursuing additional patents on modification of existing technologies has been used as a means to extent monopoly status, as patent protection offers the holders the right to exclude anyone else from using, producing and selling the patented product and process for 20 years starting from the date of filing. This is known as the 'evergreening strategy' in the pharmaceutical industry, and now comes in a different form in the context of PCV. Without bringing technological advancement to the field, Pfizer's patent and its equivalent applications could diminish the chance of bringing much needed competition in the market and drive down the prices of PCV. Pfizer's patent hinders access to more affordable PCV that can save millions of children's lives worldwide.

4. Overcoming patent barriers for more affordable new vaccines

Unmerited patent and application, such as the one that Pfizer is trying to secure now in Korea, could pose continuous barriers to price-lowering competitions to the current duopoly of the PCV market. While potential alternative PCVs are just around the corner, the contestable strategy deployed by companies such as Pfizer needs to be further scrutinized. It is imperative to recall the long-standing international legal principles that have been affirmed especially by the Doha Declaration on TRIPS and Public Health, which stress that the protection of intellectual property should not hinder the rights of protecting public health and promoting access to medicines for all*22.

Overcoming the patent barriers to new vaccines access, as the current experience of PCV shows, requires the clear political commitment of governments to prioritise health needs over extended commercial monopolies. There are also existing legal tools that countries can adapt and use to safeguard public health needs and address the intersection of intellectual property and access to medicines. Also, stricter criteria on assessing the validity of vaccine related patent and application can be used to scrutinize broad claims and those that present obvious modification of old technologies. Countries should also make use of other mechanisms, such as compulsory license to accelerate the entry of follow-on versions of new vaccines*23.

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*20 Divisional patent applications are those filed as a by-product of a main, or parent patent applications. It often involves the practice of splitting broad claims of the original patent applications in to several divisional applications in order to increase the opportunity of getting protection on a wide range of claims. It has been used as a strategy to extent monopoly by patent applicants. Ref. Correa, C. Tackling the Proliferation of Patents: How to Avoid Undue Limitations to Competition and Public Domain. South Centre. Report number: 52, 2014 [cited 2017 Aug 18]. Available from: https://www.southcentre.int/wp-content/uploads/2014/09/RP52_Tackling-the-Proliferation-of-Patents-rev_EN.pdf

*21 https://www.msfaccess.org/sites/default/files/VAC_report_A%20Fair%20Shot%20for%20Vaccine%20Affordability_ENG_2017.pdf page 15.

*22 http://www.who.int/medicines/areas/policy/tripshealth.pdf?ua=1

*23 See the full sets of recommendation on addressing the intersection of patent and vaccine. Available from: https://www.msfaccess.org/sites/default/files/VAC_report_A%20Fair%20Shot%20for%20Vaccine%20Affordability_ENG_2017.pdf page 22-4.