



Compulsory (CL) and Voluntary Licensing (VL)

Illustrative case Studies

Outline and purpose of the document: These three case studies are designed to illustrate the use of different types of licenses to make technologies available in times of acute crisis.

Target readership: This document is aimed at policy makers and those involved in technology transfer who are relatively new to the subject and would like to see more examples of how CL and VL have been applied in the past and the implications for future use.

Level: This document assumes that the reader has some familiarity with Intellectual Property Rights (IPR) and in particular patent regulations and technology licensing, as well as an awareness of associated international trade regulations e.g. TRIPS (Trade-Related Aspects of Intellectual Property Rights).

Approach: The document is laid out as three contrasting case studies. Two are taken from the COVID-19 pandemic and one from ongoing drugs development for cystic fibrosis.

Sources: The case studies have all been based on publically available information. Sources have been cited

Linked resources: These case studies can be read in conjunction with the IMPAC3T IP FAQ Fact Sheet and literature review on CL and VL licensing.

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1. Rapid voluntary free Licensing (VFL) of technology in times of crisis: the case of the Ventura Ventilator.

In mid-March 2020 the global COVID-19 pandemic was starting to spread. The number of people being admitted to hospital requiring help to breathe was rising sharply. While some patients needed to go on full ventilators, others would be helped if they could access non-invasive ventilation in the form of Continuous Positive Airway Pressure (CPAP) devices. Unfortunately the number of such devices was very low.

A research group from University College London (UCL) in the UK joined forces with University College London Hospital (UCLH) and Mercedes-AMG High Performance Powertrains to respond to this need. Their starting point was an existing 'off-patent' CPAP device that had received regulatory approval in the UK many years ago, but was no longer being produced so there was little documentation to support manufacture. Using reverse engineering, including 3D imaging to produce 2D manufacturing drawings, Mercedes-AMG HPP and the UCL team were able to produce the blue-prints and plans needed to for mass production of the device. Mercedes-AMG HPP had the high quality engineering expertise needed to produce the first devices. These were then rapidly tested by colleagues at University College London Hospital on volunteers to produce the test results needed to seek the necessary regulatory approvals prior to use.

The device was approved for use by the UK Medicines and Healthcare products Regulatory Agency (MHRA) 10 days after the teams first came together and Mercedes-AMG HPP started to manufacture 100 devices a day. After 4 weeks they had delivered 10,000 devices and demand was still rising from many countries.

The designs and manufacturing instructions for the device were released on Tuesday 7 April. As of May 2020, the team had approved over **1,850 requests from 105 countries** spanning Europe, Asia, Africa, Americas and Australasia. Many of these countries and teams were supported to manufacture and adopt through translation, manufacture and distribution. UCL-Venturas are now being used in 29 countries across the globe.

VFL Access Model

The teams made the decision to license all the information needed to manufacture and use the devices free of charge. Download of all the information was subject to approval and made clear the special condition under which the regulatory approval had been granted, namely that the device was a non-CE marked CPAP, given approval for use in the NHS for the interest of public health protection under the Covid-19 pandemic emergency.

Prospective licensees had to meet certain conditions including having local regulatory approval in place, as required in the third party's own country and fully complying with any stipulated conditions, laws and regulations that ensure full patient safety. The terms and conditions also stated that the technical specifications for this CPAP were being shared for humanitarian purposes, to help support the international community addressing pressing demands to care for Covid-19 patients and that there was an expectation that those using these specifications to manufacture these devices would follow the same guiding principles and not seek for commercial gain. In addition, that the instructions for manufacture should be followed precisely to ensure quality and safety, with no deviations or substitutions.

Application to license the device could be made online. Following human approval all documents and the licensing agreement could be downloaded from a website set up for this purpose. In the 2 weeks that followed release 1,080 downloads were approved and made from more than 100 countries.



Support for manufacture and use

The basic information needed to manufacture and use the device was approved for download in conjunction with publicly available information. This included:

- Q&A webinar with the team to support international manufacture
- Q&A webinar on the clinical use of CPAP internationally
- Private Facebook page designed to offer informal space for teams in the process of manufacturing the UCL Ventura CPAP device. Teams could discuss any problems they have, any barriers to manufacture and/or any useful tips that may help others progress.
- FAQ of technical questions
- Instructional video of how to use the CPAP clinically
- Instructions for use of device clinically (written)
- Healthy volunteer test data (clinical)
- UCL Ventura device user manual
- Guidance for international use

Critical success factors

The UCL team highlighted a number of critical success factors in being able to offer the device for licensing so quickly.

- **Regulatory approval:** By starting with an 'off-patent device' that had previously been approved for medical use, the team needed only to demonstrate 'like-for-like' mechanical performance and the results of the volunteer trials.
- **High precision manufacturing capability:** By working with Mercedes-AMG HPP the UCL team knew that they could manufacture the device to the very high specifications demanded for medical devices.
- **Established relationships:** UCL had well established relationships with individuals at UCLH and Mercedes-AMG HPP. This meant that the teams could start collaborating in a highly trustful environment from Day 1

For more information visit: <https://www.ucl.ac.uk/healthcare-engineering/ucl-ventura-breathing-aids-covid-19-patients>



2. Compulsory Licensing (CL) in times of crisis: the contrasting cases of Remdesivir in Hungary and Russia

During the COVID 19 pandemic compulsory licenses for drugs containing the active ingredient remdesivir were sought and granted in Hungary (2020) and Russia (2021). Remdesivir, marketed under the brand name Veklury® was used as a treatment for Covid. It is protected by patents owned by the company Gilead in a number of countries. In late 2020 this product was the only authorized medical product containing remdesivir approved by the European Medicines Agency (EMA) for the treatment of a certain patient population suffering from COVID-19 and pneumonia requiring complementary oxygen therapy (low or high-flow oxygen or other non-invasive ventilation at start of treatment).

Hungary

A compulsory license for Hungary was sought by the Hungarian pharmaceutical manufacturer Richter in November 2020 citing the public interest case of unmet supply need. The application was heard without the patentee Gilead being present. It was granted one week later with only one day of notice being given to the patentee.

The application was contentious both because Hungary was already obtaining the medicine via the EU Joint Procurement Agreement negotiated with Gilead and so there was no unmet need that could form the basis for a compulsory license. Also because of the lack of representation of and notice to the patentee which it was claimed, breach fundamental rights of a patent holder.

Gilead appealed the CL and in October 2023, nearly three years later the Constitutional Court annulled the licence, emphasising the right to be heard as an essential element of client rights in any proceedings. However, in the mean time, Richter had managed to successfully manufacture enough remdesivir to treat 3,000 patients and begin clinical trials. This is a notable outcome of the short-lived CL as undertaking R&D on an in-force patented invention is not permitted as it conveys on the infringing company valuable know-how and arguably a head start towards legal production when a patent expires.

Russia

In 2020 the generic manufacturer Pharmasintez JSC sought a voluntary licence agreement to produce and sell remdesivir at a lower price. The request was refused by Gilead. Pharmasintez then filed a request for compulsory licence with the Russian Government, based on article 1360 of the local Civil Code. This law entitles the Russian Government to grant a compulsory licence by administrative order, *'in the interest of public security, life and health protection of the population'*, and without the consent of the patent holder.

The Government Order granted a non-exclusive right to use five Eurasian Patent that were owed by and stated that 'adequate compensation' should be paid 'within three months' but without making any recommendation on the size of the royalties.

Gilead challenged the CL on the grounds that there were no "national defence" or "security" justifications to grant the licence and that there was no unsatisfied need for the drug in Russia. It also challenged the approach used to determine the cost of the medicine.

In this case, the Supreme court rejected the claim and up-held the CL, citing Article 8 of the European Convention for the Protection of Human Rights and Fundamental Freedoms of 1950 (ECHR) and article 31 of the TRIPS Agreement. The court also held that the amendment to Article 1360 of the Civil Code had not changed its core meaning, but merely specified in which cases compulsory licences can be granted, without affecting the grounds and so that that the order for the CL had been adopted in line with the core principles of Russian law as well as the Eurasian Patent Convention.



Main information sources used to produce this case study:

Scope of Compulsory License and Government use of Patented Medicines in the context of the Covid-19 Pandemic Southcentre.int 2021

<https://ipaccessmeds.southcentre.int/wp-content/uploads/2020/04/Covid-19-CL-Table.pdf>

Compulsory Licensing of Patents During Pandemics Sapna Kumar 2022


https://digitalcommons.lib.uconn.edu/cgi/viewcontent.cgi?article=1510&context=law_review

Compulsory Licences during the Covid-19 Pandemic: A European and International Perspective Bonadio and Contardi 2022.

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4282886

Compulsory licenses, the TRIPS Waiver, and access to COVID-19 medical technologies MSF 2021.

<https://amp.msfaaccess.org/compulsory-licenses-trips-waiver-and-access-covid-19-medical-technologies>



3. Threat of compulsory licensing (CL) to address pricing: the case of Vertex Pharmaceuticals Kaftrio for cystic fibrosis

Cystic fibrosis is a genetic disease estimated to affect 162,428 people worldwide. The condition causes a number of symptoms including recurring chest infections. It can reduce life expectancy to less than 40 as mucus clogs and damages lungs leaving those with the condition prone to infection.

When Vertex Pharmaceuticals developed the drug Kaftrio for the treatment of cystic fibrosis the test performance of the drug was hailed around the world as “groundbreaking”¹. A major trial, published in the New England Journal of Medicine, showed that a combination of drugs could bypass the genetic errors that cause the disease and may increase life expectancy with a proven effectiveness for about 90% of CF patients. Kaftrio is a triple combination therapy made up of the drugs ivacaftor, tezacaftor, and elexacaftor.

Regulatory approval was granted by the European Medicines Agency (EMA) on August 21, 2020, approving it for use throughout the EU. In the UK, Kaftrio became ‘available’ to adult patients in August 2020. The license has since been extended to include younger age groups, (children aged 6–11 in 2020 and children aged over 2 in 2023) and a wider range of genotypes.

However, the therapy was not cheap. In the UK the price set was well over £100,000 a year per patient. With more than 11,000 CF patients in the UK, it would, at list price, have cost the UK NHS (National Health Service) more than £1bn a year. It was deemed too expensive to prescribe in the UK given the limited overall budget of the NHS. The world wide price of the drug makes it expensive and out of reach for many patients, especially those in low- and middle-income countries. A number of national health authorities including the US, Netherlands and Canada called for large price reductions.

Basic production costs for the drugs were estimated to be \$6,000 (£4,790, 5790 EURO) a year per patient. However this price does not take into consideration the money invested into R&D and clinical testing incurred by Vertex Pharmaceuticals over many years to develop the drug and secure regulatory approval so it can be safely used. However, the costs of drug development is rarely if ever transparent making it hard to assess if the price charged represents value for money.

Patents allowed Vertex Pharmaceuticals to protect its monopoly of the drugs. This made it impossible for others to manufacture and compete on price. However, in February 2023 a **compulsory license** was sought in South Africa to force supply of more affordable generic versions of the drug^{2, 3}. Petitions in India, Ukraine, and Brazil also demanded legal action by their Governments to revoke or suspend the patents. A coordinated international campaign by patients and advocacy groups to bring down the price, led by Vertex Save Us and Just Treatment was supported by a large number of organisations and individuals including Third World Network, ABIA, ITPC, and SECTION27.

The UK NHS and Vertex reached an agreement in June 2021. Other countries, including South Africa⁴ have also reached a negotiated agreement with Vertex to make the drugs available at a reduced price without the need for a compulsory license.

In this case a compulsory licence has not been used, but the threat of such an action appears to have helped to influence VERTEX to reduce its prices to a level that is more acceptable to organisations who procure drugs on behalf of governments. However, the treatment remains unaffordable for many individuals who are not covered by private healthcare.

¹ <https://www.bbc.co.uk/news/health-32755065>

² See <https://justtreatment.org/news/cf-patients-launch-global-challenge-to-vertex>

³ See <https://www.theguardian.com/global-development/2024/mar/18/cystic-fibrosis-patient-south-africa-cheri-nel-lawsuit-big-pharma-generic-drugs-trikafta-access-vertex>

⁴ See <https://www.spotlightnsp.co.za/2024/08/06/case-against-vertex-dropped-after-cystic-fibrosis-medicine-price-reduced/>