THE RIGHT TO HEALTH AND ACCESS TO PANDEMIC INFLUENZA VACCINES: PROCUREMENT OPTIONS FOR DEVELOPING STATES

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Abstract

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The impact of influenza pandemics is felt most greatly in developing states, where the close proximity between humans and disease vectors, weak public health surveillance systems, and poor sanitation make these states particularly vulnerable to influenza pandemics. A vaccine is the most effective intervention to minimise the spread and impact of influenza, and yet, developing states are the least likely to have timely access to a vaccine during a pandemic. According to ‘The Committee on Economic, Social and Cultural Rights General Comment No. 14: the Right to the Highest Attainable Standard of Health’ there is a clear positive obligation for states to provide access to vaccines during an influenza pandemic, and this obligation is not waived or depleted merely because developing states have resource constraints. There has been a proliferation of literature recently which has considered access to medicines in developing states and the right-to-health. However, there has been little exploration of this issue in respect of pandemic influenza vaccines. This research explores the manner in which developing states procure influenza vaccines during a pandemic, and determines if the current international legal mechanisms which are available to developing states can be successfully used to enhance procurement, and increase the amount of vaccine developing states can access during a pandemic, to a point where they can discharge their right-to-health obligations. In doing so, I argue that the WHO Pandemic Influenza Preparedness Framework, and the flexibilities of the TRIPS Agreement are not able to enhance the procurement of pandemic influenza vaccines by developing states, to the point where states right-to-health obligations can be said to be discharged. From this, I propose an international ‘Knowledge Clearing House’ as a solution to the problems in procurement which are identified in this research.
Declaration

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CHAPTER I –
INTRODUCTION

In this chapter I argue that access to pandemic influenza vaccines is integral to developing states having an effective response to pandemic influenza. I also argue that a failure to provide access to such vaccines during a pandemic constitutes a breach of states’ obligations regarding its citizen’s right-to-health. I also describe the benchmark of ‘sufficient access’ to pandemic influenza vaccines which needs to be met by a state in order for a state to have discharged the right-to-health obligations regarding its citizen’s access to medicines. Having done so, I justify the approach taken in this research, and outline the structure of the rest of the thesis.

1.1 - What is pandemic influenza?

Influenza is an infectious disease caused by an individual being infected by an influenza virus. Influenza viruses are transmitted through the air, most commonly through coughing and sneezing, although transmission can also occur through contact with animal droppings.\(^1\) Influenza viruses are RNA viruses;\(^2\) their genetic material consists of ribonucleic acid (RNA), as opposed to deoxyribonucleic acid (DNA). This has a significant impact on the evolution of the virus;\(^3\) RNA replication lacks a ‘proof-reading’ mechanism,\(^4\) meaning mutations are more likely to occur during gene replication. Mutations result in changes to the genome, and therefore to viral proteins, over time.\(^5\) As Krattinger and others succinctly noted ‘Flu [sic] virus is

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\(^1\) Gabrielle Brankston and others, 'Transmission of influenza A in human beings' (2007) 7(4) The Lancet Infectious Diseases 257
\(^3\) Robert Webby and Robert Webster, 'Emergence of influenza A viruses' (2001) 356 Philosophical Transactions of the Royal Society of London B: Biological Sciences 1416
\(^4\) N. Lui and others, 'Mutations in influenza virus replication and transcription; detection of amino acid substitutions in hemagglutinin of an avian influenza virus (H1N1)' (2009) 23(10) The FASEB Journal 3377
\(^5\) Y Iwasaki and others, 'Prediction of Directional Changes of Influenza A Virus Genome Sequences with Emphasis on Pandemic H1N1/09 as a Model Case' (2011) 18 DNA Research 125
distinguished from most pathogenic viruses by its extreme variability. Over time the virus can change its surface antigens so completely that an immune response to one infection gives little or no protection against a subsequent infection.\textsuperscript{6} Two main categories of influenza virus evolution can be identified.

Firstly, \textit{antigenic drift} describes the process by which mutations continuously occur during replication of viruses which lead to subtle changes of antibody-binding proteins.\textsuperscript{7} This results in novel viral strains that can evade the immune system as the antibodies developed from previous exposure to influenza no longer recognise the virus. The new strain of virus has a similar structure to a virus already in circulation but with minor, but important, differences. This gives an explanation for annual seasonal influenza outbreaks, and the requirement to develop new vaccine formulations on an annual basis.\textsuperscript{8}

The second mechanism of influenza virus evolution is \textit{antigenic shift},\textsuperscript{9} which is responsible for pandemic outbreaks.\textsuperscript{10} Antigenic shift occurs when one change in the genetic make-up of the virus results in the formation of a novel influenza virus with a significantly different genetic structure to currently circulating influenza viruses,\textsuperscript{11} typically because the virus has crossed the species barrier from an animal host reservoir to humans.\textsuperscript{12} Antigenic shift causing an influenza pandemic is particularly difficult to control and treat as there is no residual human immunity from previous

\begin{itemize}
\item \textsuperscript{6} Anatole Krattiger and others, 'Intellectual Property Management Strategies to Accelerate the Development and Access of Vaccines and Diagnostics: Case Studies of Pandemic Influenza, Malaria, and SARS' (2006) 2(2) Innovation Strategy Today 67
\item \textsuperscript{7} Alan Hampson, 'Influenza Virus Antigens And Antigenic Drift' in C.W. Potter (ed), \textit{Influenza} (Elsevier Science 2002)
\item \textsuperscript{8} CDC, 'Prevention And Control Of Influenza With Vaccines: Recommendations Of The Advisory Committee On Immunization Practices (ACIP)--United States, 2012-13 Influenza Season' (2012) 61 Morbidity And Mortality Weekly Report 613
\item \textsuperscript{10} Maria C Zambon, 'Epidemiology and pathogenesis of influenza' (1999) 44(suppl 2) Journal of Antimicrobial Chemotherapy 3
\item \textsuperscript{11} Haye, (n2) at 6;
\item \textsuperscript{12} Gabriele A. Landolt and Christopher W. Olsen, 'Up to new tricks – A review of cross-species transmission of influenza A viruses' (2007) 8(01) Animal Health Research Reviews 1; Edwin D. Kilbourne, 'Influenza Pandemics of the 20th century' (2006) 12(1) Emerging Infectious Diseases 9
\end{itemize}
infections or vaccinations, therefore the infection is much more virulent and typically requires a two-dose vaccination strategy in order to provide immunity. Pandemic influenza viruses have the potential to spread rapidly across borders in a very short timeframe. During the most recent influenza pandemic, 2009-H1N1, the first case was identified on March 17th 2009; just twelve weeks later 74 countries had officially reported 27,737 cases.

As part of their surveillance and response mechanisms for influenza, the World Health Organisation provides phases of pandemic alert between ‘Phase One’ and ‘Phase Six’, with ‘Phase One’ being the least severe and ‘Phase Six’ being a pandemic, the most severe outbreak. The World Health Organisation describe the characteristics of an influenza pandemic as when

an influenza virus which was not previously circulating among humans and to which most people don’t have immunity emerges and transmits among humans. These viruses may emerge, circulate and cause large outbreaks outside of the normal influenza season. As the majority of the population has no immunity to these viruses, the proportion of persons in a population getting infected may be quite large. Some pandemics may result in large numbers of severe infections while others will result in large numbers of milder infections, but the reasons behind these differences are not completely understood.

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13 Haye, (n2); Shinya Yamada and others, ‘Haemagglutinin mutations responsible for the binding of HSN1 influenza A viruses to human-type receptors’ (2006) 444(7117) Nature 378
1.2 - Pandemic Influenza Vaccines

Effectively combating pandemic influenza requires an international coordinated response which may include surveillance, screening at borders, closure of borders, vaccines, and the use of drugs.\textsuperscript{18} Vaccines are a key component in the response to an influenza pandemic; systematic reviews of clinical studies demonstrate that the timely administration of an influenza vaccine is the most effective public health intervention to halt the spread of infection and prevent mortality from influenza in adults,\textsuperscript{19} the elderly\textsuperscript{20} and children.\textsuperscript{21} Therefore states that have sufficient\textsuperscript{22} access to pandemic influenza vaccines are in a significantly better position to limit the effects of pandemic influenza, and to limit their reliance on drugs to manage complications of the outbreak. This is particularly important for developing states, as many lack health systems with sufficient capacity to manage a pandemic.\textsuperscript{23} Therefore prevention through vaccinations is key.

Developing states lack appropriate access to both the vaccines required in order to minimise the impact of a strain of pandemic influenza, and to the drugs that are required in order to manage the effects of pandemic influenza, such as oseltamivir.

\textsuperscript{19} Tom Jefferson and others, 'Vaccines for Preventing Influenza in Healthy Adults (Art. No: CD001269)' (2010) 7 Cochrane Database of Systematic Reviews
\textsuperscript{20} Tom Jefferson and others, 'Vaccines for Preventing Influenza in the Elderly (Art. No: CD004876)' 7 (2010) Cochrane Database of Systematic Reviews
\textsuperscript{21} Tom Jefferson and others, 'Vaccines for Preventing Influenza in Healthy Children (Art. No: CD004879)' 8 (2012) Cochrane Database of Systematic Reviews
\textsuperscript{22} More on what is ‘sufficient’ access is provided below.
(commonly known by its trade name, Tamiflu). Despite the importance of vaccination, during the 2009-H1N1 pandemic influenza outbreak, there were significant disparities in vaccination coverage between developed states and developing states. Developing states tended to procure less pandemic influenza vaccine, and the vaccine that was procured arrived in developing states later than it did in developed states.

While a range of factors may impact upon a developing states ability to successfully procure pandemic influenza vaccine, such as vaccine financing and healthcare infrastructure, it would be naïve to assume that the law is not a contributing factor. The manner by which states procure vaccines is inextricably linked with legal rules, including contractual relations, intellectual property rights, and the regulatory framework for the licensing of drugs. Therefore, analysing the problem of access to vaccines in developing states from a legal perspective, and seeking legal solutions to the problem, is appropriate.

Claims that law is integral to the problem of access to medicines are not mere speculation: the theory has gained considerable traction in the years following developing states providing patent protection on pharmaceuticals. Claims that law

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24 David Fidler and Lawrence Gostin, 'Biosecurity in the global age: Biological weapons, public health, and the rule of law' (Stanford Law and Politics 2008) 161; However, there are tools available that have been used by developing states in order to improve access to oseltamivir during a pandemic. This is typically achieved through making use of provisions in domestic patent legislation and used where the cost of purchasing directly from the manufacturer was prohibitively high Voluntary licenses were granted to India, Vietnam, and South Korea by Roche for Tamiflu during the H5N1 influenza outbreak. It is argued that the threat of widespread compulsory licenses being issued by the above states pressurised Roche into issuing a license: Esther Van Zimmeren and Gertrude Requena, 'Ex-Officio Licensing in the Medical Sector: The French Model' in Geertrui van Overwalle (ed), Gene patents and public health (Bruylant 2007)


is integral to problems in access and procurement for developing states have further been advanced specifically regarding the impact of law on access to vaccines during an influenza pandemic.27 Discussions regarding the role law plays in access to vaccines were brought to the fore in 2006, when Indonesia refused to comply with international virus sharing norms, citing the unfairness of the procurement process, and the role intellectual property law played in this, as the primary reason for refusal.28

It is clear that, at least to some degree, legal rules impact upon the manner in which developing states access and procure pandemic influenza vaccines. If law is a problem, legal reform has the potential to provide a solution to developing states’ inabilitys to procure sufficient vaccine. I would contest, therefore, that analysing the legal aspects of the procurement of pandemic influenza vaccines could provide valuable insight, which could better enable developing states to procure pandemic influenza vaccines in the future.

1.3 - The Need for a Solution
The fact that pandemic influenza vaccine (henceforward PIV) manufacturing capacity was significantly below that required, and that developing states lacked access to PIV as a result,29 was first acknowledged in a Resolution of the World Health Assembly in 2005. In this Resolution the Assembly called upon the World Health Organisation (henceforward WHO) to develop a strategy to address the shortfall in PIV

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production. Subsequent acknowledgements of the problem, and calls to improve the situation, were made by the Assembly in 2008, and 2012.

As a result of this call to action in 2006 the WHO created the Global Action Plan for Influenza Vaccines (GAP), with the primary objective of ‘reducing the present global shortage of influenza vaccines for both epidemics and pandemics’. At the time global manufacturing capacity for PIV was approximately 350 million doses per annum. GAP sought to increase capacity in two ways: first, by encouraging domestic policy-makers to develop an immunization policy to increase demand for seasonal vaccines, thereby creating market incentives for manufacturers to enhance production capacity; and second, by promoting the creation of new production facilities in ‘developing and/or industrialised states’. As a result of GAP, PIV capacity increased by 600 million doses between 2006 and 2009. However, capacity grew predominantly in developed states, and the extent to which developing states benefitted from the increased capacity during a pandemic was minimal.

The most recent figure estimating pandemic influenza vaccine manufacturing capacity was given in 2013, with capacity being approximately 1.4 billion doses per annum, and the most recent GAP report proposed strategies for increasing capacity to approximately 1.7 billion doses by 2015. A more accurate figure of global capacity is

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34 Ibid. 13.
35 Ibid. 4.1.1
36 Ibid. 4.2.1(2)
37 Nicolas Collin and Xavier de Radiguès, 'Vaccine production capacity for seasonal and pandemic (H1N1) 2009 influenza' (2009) 27(38) Vaccine 5184
38 Jeffrey Partridge and Marie Paule Kieny, 'Global production capacity of seasonal influenza vaccine in 2011' (2013) 31(5) Vaccine 728
39 Ibid
likely to be provided at GAP III in November 2016. At the most recent meeting of the
GAP Advisory panel in March 2015, it was noted that

[s]ignificant increases in global pandemic vaccine production capacity were
reported from the United States of America (USA) and potentially from Japan
through partnering of the USA licensed recombinant influenza vaccine
manufacturer with a Japanese company and the licensing of the first cell-based
influenza vaccine production facility in the USA. Production capacity increases
in GAP-supported countries have been modest and it is expected that several
of the GAP-supported countries/companies will not reach the targets for a
variety of reasons.40

While this lack of progress in developing states is clearly concerning, it is worth noting
that WHO acknowledged in its review of GAP that even if the 1.7 billion doses had
been realised ‘global capacity will still be insufficient to allow all developing states to
procure sufficient levels of pandemic influenza vaccine in a timely manner’41, and
should an influenza pandemic emerge in the near future, vaccine supplies would fall
short of the anticipated global demand by over one billion doses.42 This has led to
corns that it is quite likely, in the face of more virulent pandemic that governments
with domestic vaccine manufacturing capability will not donate or export any of their
nationally produced vaccines to WHO or developing states until domestic demand is
satisfied.43 The inability of developing states to obtain sufficient access to pandemic
influenza vaccines in order to immunise their population may have implications for
the ability of these states to meet their right-to-health obligations during an influenza
pandemic.

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40 WHO, ‘The global action plan for influenza vaccines report of the tenth meeting of the advisory group
of the WHO global action plan for influenza vaccines’ (WHO, 2015)
41 http://apps.who.int/iris/bitstream/10665/182733/1/WHO_HIS_PHI_TTI_15.1_eng.pdf?ua=1&ua=1
42 WHO, ‘Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine
deployment initiative’ (WHO, 2011)
43 Klaus Stohr, ‘Public Health Enhanced: Will Vaccines Be Available for the Next Influenza Pandemic?’
1.4 - The Right to Health

The right-to-health has been referenced in international agreements since the 1940s. The right-to-health was first articulated in the Preamble to The Constitution of the World Health Organisation, which states that ‘[t]he enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition.’ The right-to-health was also referenced at Article 25 of the United Nations Universal Declaration of Human Rights, which states that ‘[e]veryone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services.’

The right-to-health has since been referenced in a number of international and regional agreements. The clearest articulation of the right-to-health has come in The International Covenant on Economic, Social and Cultural Rights (ICESCR), adopted by the United Nations (UN) General Assembly in 1966. Article 12 of the Covenant states that:

1. The State Parties to the present Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.
2. The steps to be taken by the States Parties to the present Covenant to achieve the full realization of this right shall include those necessary for:

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(c) The prevention, treatment and control of epidemic, endemic, occupational and other diseases;

(d) The creation of conditions which would assure to all medical service and medical attention in the event of sickness.\(^47\)

The Covenant built upon the ideas put forward in the WHO Constitution and the Universal Declaration of Human Rights, and, in placing obligations upon states, outlined what sort of action a state could take in order to ensure that the highest attainable standard of health could be enjoyed by its citizens. Within the context of pandemic influenza vaccine access, clearly 2(c) is most directly relevant: action necessary for ‘[t]he prevention, treatment and control of epidemic, endemic, occupational and other diseases’; as noted above, pandemic influenza vaccines are the most effective method to prevent and control a pandemic outbreak within a population.

Despite its long history, the right-to-health has, until fairly recently, remained largely a statement of intent without any real legal weight, as opposed to being a justiciable right a citizen can enforce against the state. Despite the fact that, since the original references to the right in the Constitution of the WHO and the Universal Declaration of Human Rights, the right-to-health has been referenced in numerous international agreements and documents, it lacks the level of enforcement enjoyed by other human rights.\(^48\) However, since the 1980s, and largely driven by the drastic health impact that

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\(^48\) In contrast, the right to intellectual property, which is included in both the UNDHR at Article 27(2) and the ICESCR at Article 15(C) is a right which has long been enforceable (see: Brad Sherman and Lionel Bently, *The making of modern intellectual property law* (Cambridge University Press 2008). Interestingly, the right to intellectual property is sometimes seen as being in conflict with the right-to-health, and the differing levels of protection each right is afforded is key to this conflict see: Jamie Crook, ‘Balancing intellectual property protection with the human right-to-health’ (2016) 23(3) Berkeley Journal of International Law 524 and Graeme W. Austin and Laurence R. Helfer, *Human rights and intellectual property: Mapping the global interface* (Cambridge University Press 2011)
the HIV/AIDS epidemic has had on developing states, the right-to-health has begun to move into legislative chambers\textsuperscript{49} and court houses,\textsuperscript{50} particularly in developing states.

1.4.1 - The Right to Health, and Access to Medicines

The rights-based discourse is largely focused on the extent to which citizens of states can use the right-to-health in order to compel the state to act in a certain way to improve individuals’ health, such as providing for access to specific medicines. This rights-based approach has been particularly successful in improving access to medicines in developing states, particularly HIV/AIDS medicines.\textsuperscript{51} This rights-based approach to healthcare tends to result in two sorts of obligations upon states: positive obligations that require states to act in a certain manner in order to improve an individual’s health (for example, to ensure that an individual has appropriate access to essential medicines, without undue restrictions); and negative obligations, in effect, not to place unnecessary restrictions on an individual that can interfere with their ability to attain the highest standard of health (for example, to not place unnecessary restrictions on accessing medical treatment, based on race, gender, or sexuality). The rights-based approach to access to medicines, encapsulated within the right-to-health, creates a positive obligation upon the state to take appropriate action in order to ensure the right can be realised. Within the context of access to medicines, the state’s attempt to fulfil this positive obligation has typically manifested itself through legislative or policy changes intended to improve access, such as limiting the


\textsuperscript{50} Rajshree Chandra, ‘Right to Health and TRIPS: The Glivec Patent Case’ in Thomas Pogge, Matthew Rimmer, and Kim Rubenstein (eds), Incentives for Global Public Health: Patent Law and Access to Essential Medicines (1st edn, Cambridge University Press 2010) at 383 discusses the judgments of Superior courts in India, Venezuela, Bangladesh, South Africa and Ecuador - all of whom, to varying degrees, have recognised the right-to-health as enforceable at the domestic level against the state.

patentability of pharmaceutical products,\textsuperscript{52} the issuing of compulsory licenses,\textsuperscript{53} or using nationalised manufacturers to cheaply manufacture medicines.\textsuperscript{54}

Access to medicine, as a component of the right-to-health, was elaborated upon in The Committee on Economic, Social and Cultural Rights General Comment No. 14: the Right to the Highest Attainable Standard of Health.\textsuperscript{55} General Comment 14 holds that states have a tripartite obligation to respect, protect, and fulfil the right-to-health.\textsuperscript{56} Within the context of access to pandemic influenza vaccines, two of the ‘core obligations’ of states are relevant:

States must ensure provision of health care, including immunization programmes against the major infectious diseases\textsuperscript{57}

The creation of conditions which would assure to all medical service and medical attention in the event of sickness...includes the provision of equal and timely access to basic preventive, curative, rehabilitative health services and...the provision of essential drugs\textsuperscript{58}

It is clear that providing full access to vaccines during an influenza pandemic would enable a state to discharge its obligation fully in this regard. However, it remains unclear to what extent states can fail to provide full access to pandemic influenza

\textsuperscript{52} For example see S.3(d) The Patents (Amendment) Act 2005 in India, which excludes certain pharmaceutical substances from being patentable. Carlos Correa, ‘Is Section 3(d) Compatible with the TRIPS Agreement?’ (2013) 32 Economic and Political Weekly
\textsuperscript{53} Indeed, A recent Commission on Intellectual Property Rights, Innovation and Public Health study found, ‘virtually all developing and least developed countries [who had implemented the Agreement] provided for the granting of compulsory licenses’: WHO Commission on Intellectual Property Rights, (n26)
\textsuperscript{54} The Butantan Institute in Brazil is an example of a state-owned pharmaceutical manufacturers that has been particularly successful in addressing health needs in a developing state: Marcelo De Franco and Jorge Kalil, ‘The Butantan institute: History and future perspectives’ (2014) 8(7) PLoS Neglected Tropical Diseases e2862
\textsuperscript{56} para. 33, ibid.
\textsuperscript{57} para. 36, ibid.
\textsuperscript{58} para. 17, ibid.
vaccines (for whatever reason) and still be considered to have discharged their obligation.

Generally, states party to the Covenant undertake to  

[t]ake steps, individually and through international assistance and co-operation, especially economic and technical, to the maximum of its available resources, with a view to achieving progressively the full realization of the rights recognized in the present Covenant by all appropriate means, including particularly the adoption of legislative measures.59

However, this is weakly worded and filled with uncertainty, particularly in relation to what ‘the maximum of its available resources’, ‘achieving progressively’ and ‘all appropriate means’ relate to.60 Given that a sufficient benchmark for a state having discharged its obligations in relation to access to vaccines is not provided in the Covenant, it is necessary to turn to General Comment 14 for further guidance. In the context of access to medicines, the provision of ‘essential’ medicines is a core, non-derogable obligation, which states must fulfil as a minimum criterion to meet their obligations under the Covenant.61 The ICESCR does not provide an exhaustive list of which drugs constitute ‘essential medicines’, instead relying upon the WHO Model List of Essential Drugs.62 While not listed on the current Essential Drugs list,63 influenza vaccine was listed as an ‘essential medicine’ on the 200964 and 2010 lists65, when 2009-H1N1 was prevalent.

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59 Article 2(1), ICESCR.
61 para. 43(d), General Comment 14.
62 Ibid.
1.4.2 - The Right to Health, and Access to Pandemic Influenza Vaccines

Despite the clear obligation to provide pandemic influenza vaccines as an essential medicine, during the most recent influenza pandemic (2009-H1N1), access to the required vaccine was very poor in developing states, with most states either not accessing the vaccine at all, or accessing it significantly later than their developing neighbours.\(^6^6\) If a rights-based approach to 2009-H1N1 is adopted, one could argue that developing states failed to meet their obligations regarding the right-to-health by failing to provide an ‘immunization programme against a major infectious disease’\(^6^7\), and failing to ‘provide essential drugs’\(^6^8\) for their population. However, such an approach may be too simplistic; developing states have long complained that they are unable to access influenza vaccines during a pandemic, despite their best efforts.\(^6^9\) This serves to highlight one of the significant drawbacks with the rights-based narrative regarding access to medicines in developing states: it presupposes that the state is capable of adequately addressing the problem with the resources that it has available to it. What of the state that lacks the means to secure access to medicines on behalf of its population? It would of course be unfair to claim that such states have failed to meet their positive obligations in regards to the right of health, when they lack the means to discharge the obligation. This is neatly highlighted by contrasting Article 2(1) of the ICESCR, which states that

\[
\text{[e]ach State Party to the present Covenant undertakes to take steps, individually and through international assistance and co-operation, especially economic and technical, to the maximum of its available resources, with a view to achieving progressively the full realization of the rights recognized in the present Covenant by all appropriate means, including particularly the adoption of legislative measures}}^7^0\text{[emphasis added]}
\]

\(^{6^6}\) See 3.4.1 for further information  
\(^{6^7}\) para. 36, General Comment 14  
\(^{6^8}\) para. 17, General Comment 14  
\(^{7^0}\) Article 2(1), ICESCR
With paragraph 47 of General Comment no. 14, which states that

[i]f resource constraints render it impossible for a State to comply fully with its Covenant obligations, it has the burden of justifying that every effort has nevertheless been made to use all available resources at its disposal in order to satisfy, as a matter of priority, the obligations outlined above. It should be stressed, however, that a State party cannot, under any circumstances whatsoever, justify its non-compliance with the core obligations set out in paragraph 43 above, which are non-derogable.  

Both the provision of essential drugs, and the provision of immunization against major infectious diseases are core obligations within General Comment 14. Therefore, it is clear that not providing vaccines during an influenza pandemic constitutes a failure on the part of a state to meet its ICESCR obligations regarding the right-to-health, and resource constraints are not an adequate justification for failing to provide pandemic influenza vaccines. In short, states, including developing ones, must provide pandemic influenza vaccines to their population, or they will not have fulfilled their obligations under the ICESCR.

1.4.3 - the Right to Health and the Pharmaceutical Industry

Clearly one of the predominant actors in this discussion about access to pandemic influenza vaccines is the pharmaceutical industry - pandemic influenza vaccines are manufactured by a small number of established manufacturers, the majority of whom are large, multinational pharmaceutical corporations. Traditionally private corporations are not included in discussions about international human rights, as it is states, not private business that are the subjects of international law, and therefore, any rights based obligation is binding upon the state, not upon private corporations.

71 para. 47, General Comment 14.
72 para. 43(d), ibid.
73 para. 44(c), ibid.
74 Perhaps the most notably exception to this is the Butantan Institute in Brazil - which is a state pharmaceutical manufacturer. More information about Butantan, and how it established its influenza vaccine manufacturing capacity is provided at 8.1.1
75 I discuss this in more detail at 8.2.1 in the context of reform of the PIP Framework
However, more recently some academics have argued that “the application of human rights to non-state actors like the pharmaceutical industry is not a settled question within international law.”76

More specific arguments have been presented by the UN Special Rapporteur on the Right to Health - both Paul Hunt and Anand Grover in this role have argued that there are direct Right to Health responsibilities that pharmaceutical companies need to uphold in respect of access to medicines.77 Hunt also drafted the “Human Rights Guidelines for Pharmaceutical Companies in Relation to Access to Medicines,” a set of 47 guidelines on the Right to Health responsibilities of pharmaceutical companies, which was presented to the UN General Assembly.78 Most notably for the discussion in this thesis, Guideline 33 provides that a pharmaceutical company “…should give particular attention to ensuring its medicines are accessible to disadvantaged individuals, communities and populations, including those living in poverty and the very poorest in all markets.”79 Moreover, the United Nations Special Representative of the Secretary-General on the issue of human rights and transnational corporations has provided a report to the UN Human Rights Council80. This report argued that that private corporations “should avoid infringing on the human rights of others and should address the adverse human rights impacts with which they are involved”81, and

79 Para 33, ibid.
81 Para 11, ibid.
“avoid causing or contributing to adverse human rights impacts through their own activities, and address such impacts when they occur”82 This report was endorsed by the UN Human Rights Council in 2011.83

Despite this, the pharmaceutical industry itself is strongly resistant to any Right to Health obligations being binding upon them. This issue has been directly addressed by both Novartis and GlaxoSmithKline, both of whom are major manufacturers in the field of pandemic influenza vaccines. Both companies have stressed that any obligation upon them to alleviate the health problems in developing states, or improve access to medicines in those states should be, and are, of a voluntary nature.84

Despite the limited extent to which it can be claimed that the Right to Health is directly binding upon the pharmaceutical industry, that is not to say that the Right is of no relevance to the industry itself. General Comment. 14 states that ‘States parties should take appropriate steps to ensure that the private business sector and civil society are aware of, and consider the importance of, the right to health in pursuing their activities.’ 85 Meaning that it is pursuant upon states to regulate the pharmaceutical industry within their territory in such a way so as to ensure the industry respects and upholds the Right to Health. Potential opportunities for this are discussed at 7.2, 7.4, 7.4.2 and 8.2.1.

1.5 - Beyond the Rights-Based Discourse

Within this thesis I intend to step beyond the rights-based narrative, and examine the available resources a developing state could use to procure vaccine during an

82 Para 13(a), ibid.
83 ibid.
85 para. 55, General Comment 14.
influenza pandemic, in order to ensure that the right-to-health obligations can be met. To this end, a number of questions arise. The first is this: what resources do developing states have available to them in order to ensure access to pandemic influenza vaccines? Second: are these resources sufficient to enable a state to achieve the full realisation of the right-to-health during an influenza pandemic? Finally: what, if any, technical or economic assistance will developing states require in order to ensure they can provide access to pandemic influenza vaccines?

In order to answer these questions, it is necessary to make a determination regarding the threshold of vaccine access that needs to be met by a state in order for it to be considered to have discharged its right-to-health obligations regarding access to pandemic influenza vaccines. On this point General Comment no.14 states that ‘[f]unctioning public health and health-care facilities, goods and services, as well as programmes, have to be available in sufficient quantity within the State party’\(^\text{86}\) but no further guidance is provided as to what ‘sufficient quantity’ means in this context.

For the purposes of this research the notion of ‘sufficient access’ is used, and ‘sufficient access’ is based on two interlocking factors: vaccination levels and vaccination timings. If a state achieves ‘sufficient access’ to vaccines during an influenza pandemic, for the purposes of this research, they are considered to have satisfied the requirements to have discharged their obligations regarding the right-to-health - full vaccination is not required to have discharged right-to-health obligations in this context.

1.5.1 – Vaccination Levels
The World Health Organisation recommends that, at a minimum, ‘at risk’ groups should be vaccinated during an influenza pandemic.\(^\text{87}\) The WHO categorises at-risk groups for influenza vaccines as ‘pregnant women, health-care workers, the elderly, 

\(^{86}\) para. 12(a), General Comment 14
\(^{87}\) the campaign to eradicate polio by vaccination began in 1988, and is still ongoing: Bruce Aylward and Rudolf Tangermann, ‘The global polio eradication initiative: Lessons learned and prospects for success’ (2011) 29 Vaccine
those with risk conditions and children aged 6-59 months.’

Within the EU, it is estimated that 49.1% of the population fall into one or more of the WHO’s at-risk groups for the purposes of influenza vaccination. Data are not available from developing states as to what proportion of their population falls into these categories. Moreover, who is ‘at risk’ from the virus is subject to fluctuation with each mutation of the virus. For instance, the 1918 ‘Spanish Flu’ outbreak disproportionately killed men and women aged 15-44, who are not typically considered to be in one of the ‘at risk’ groups for influenza immunisation. Therefore, as it cannot accurately be determined what percentage of the population of developing states falls into this category, and because this figure may fluctuate between developing states, and pandemic strains, it would not be appropriate to base ‘sufficient’ vaccination levels on this concept.

When discussing access to oral solid dose drugs it is fairly straightforward to determine when a state has discharged its right-to-health obligations in respect of access to that drug - the right can be said to be discharged when all patients that require access to that drug have access. For example, the antiretroviral drug zidovudine which is used to treat HIV infections appears on the WHO Essential Medicines list, therefore access to zidovudine constitutes a core obligation under General Comment no.14, in much the same way access to pandemic influenza vaccines does. The right-to-health obligations in respect of zidovudine can be said to have been discharged when there is ready access to zidovudine for all patients who require it in order to treat their HIV infection. However, that is not the case when discussing vaccines - the beneficial effects of a vaccine are not just felt by the

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89 James Ryan and others, ‘Establishing the health and economic impact of influenza vaccination within the European Union 25 countries’ (2006) 24(47-48) Vaccine 6812


individual receiving the vaccine, but by those in the wider community too, due to community immunity. Community immunity is the immunity against an infectious disease that occurs when the vaccination of a significant portion of the community provides protection for individuals who have not developed immunity by reducing transmissibility, has come to be one of the most important concepts in vaccination policy and public health.

Due to the mutations that occur with each strain of influenza virus, the vaccination coverage required in order to establish community immunity has fluctuated with each pandemic since 1900. Aside from 2009-H1N1, which was noted for having a particularly low mortality and infection rate when compared with more typical pandemics, a minimum vaccination coverage of at least 33% has been required in all pandemics in order to establish community immunity and slow down the rate of infection.

When discussing access to pandemic influenza vaccines as a right-to-health obligation, we are not just discussing access to pandemic influenza vaccines on an individual basis, but also the right to benefit from the herd immunity which is established within a community when sufficient vaccine is administered. To that end, within this research, enough vaccine to immunise at least 33% of a state’s population will be taken to be ‘sufficient access’. This threshold is taken as it is sufficient to provide the

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92 Also Referred to as ‘Herd Immunity’ or the ‘Herd Effect’.
93 Paul Fine, Ken Eames, and David L Heymann, ‘Herd Immunity: A rough guide’ (2011) 52(7) Clinical Infectious Diseases 911
95 Pedro Plans-Rubiò, 'The vaccination coverage required to establish herd immunity against influenza viruses' (2012) 55(1) Preventive Medicine 72
97 Edwin D. Kilbourne, (n12); Jeffery K. Taubenberger and David M. Morens, '1918 influenza: The mother of all Pandemics' (2006) 12(1) Emerging Infectious Diseases 15
98 Pedro Plans-Rubiò (n82) at Table 2.
beneficial effects of community immunity. Therefore, if sufficient vaccine has been procured in order for community immunity to be achieved within a population, it is possible to argue that states’ right-to-health obligations have been discharged in respect of pandemic influenza to the entire community which is benefiting from the immunisation campaign, not just the individuals that have received the vaccine directly.

1.5.2 – Vaccinating Timings

Pandemic influenza strains predominantly emerge in, and spread rapidly through, developing states.99 The states that are at a heightened risk from pandemic influenza are the most likely to be reliant upon donations from the WHO to gain access to PIV.100 These donations from the WHO arrive in much smaller batches than in developed states, and much later than in self-procuring developed states.101 This significantly hampers these states’ abilities to combat pandemic influenza outbreaks, meet community immunity thresholds, and limit or prevent the spread of the disease beyond its borders. Therefore, it is not just the amount of PIV that a state can access that is of relevance to this research, but also when access is gained.

WHO Guidelines first recommend use of PIV at Phase 4 of the pandemic102; more direct language is use at Phase 5-6, where states are urged to ‘[i]mplement medical prophylaxis campaigns for antivirals and/or vaccines according to priority status and availability in accordance with national plans’.103 Such language suggests that this is the optimum time of the pandemic to implement a vaccination programme. In contrast, the post-pandemic phase guidance advises that states should ‘[c]onduct a

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100 See: WHO ‘Global survey on national vaccine deployment and vaccination plans for pandemic A(H1N1)’ (2010) <http://www.who.int/influenza_vaccines_plan/resources/2010_H1N1_NVDP_WHO_Survey.pdf?ua=1> for an overview. Further details are provided in Chapter III ‘Vaccine Procurement’.
101 See Chapter III ‘Vaccine Procurement’.
103 Ibid, 43
thorough evaluation of all the pharmaceutical interventions used, including: vaccine coverage, effectiveness, and safety’ and ‘continue with vaccination programmes in accordance with national plans, priorities, and vaccine availability’, implying that the majority of the vaccinations in states should already be completed by this stage. During the post-pandemic phase the virus’ transmission levels and intensity is considered more akin to a seasonal influenza outbreak, than that of a pandemic, and the vaccine has reduced impact on a population due to the number of people already exposed to the outbreak.

Despite this, during 2009-H1N1 there was a delay of at least four months between PIV being administered in developed states, and the first doses arriving in developing states. Of the 78 million doses of PIV WHO distributed during 2009-H1N1, over 30 million of these doses were delivered to developing states in the ‘post-pandemic phase’, when the virus’ transmission levels and intensity is considered more akin to a seasonal influenza outbreak. Such a delay in PIV availability in developing states is undesirable, and hinders developing states’ ability to protect their population and reduce cross-border spread, as ‘speed is of the essence to deliver a pandemic vaccine...and [being able to administer a PIV] as quickly as possible, reduces disease transmission, and uses the efficacy of the vaccine to fight the disease.

As the timing of vaccination administration is so important for an effective domestic and international response to the pandemic, for the purpose of this research ‘in

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104 Ibid, 47
106 Neuzil, (n27)
107 Jeffrey Partridge and Marie Paule Kieny, 'Global production of seasonal and pandemic (H1N1) influenza vaccines in 2009–2010 and comparison with previous estimates and global action plan targets' (2010) 28(30) Vaccine 4709
sufficient time’ is taken to mean developing states accessing PIV within the same timeframe as developed states.

1.6 – Focus of the research

This research is focused on two mechanisms that could improve the procurement of PIV by developing states, and in doing so, would enable said states to meet their right-to-health obligations regarding access to pandemic influenza vaccines. The two mechanisms to be examined are the Pandemic Influenza Preparedness Framework,110 which has been a major development in relevant international law post-2009-H1N1; and the TRIPS Agreement.111 The flexibilities of both have been presented as potential solutions to the problem of access to medicines in the developing world.

1.6.1 – The Pandemic Influenza Preparedness Framework

The Pandemic Influenza Preparedness Framework was enacted by the World Health Organisation (WHO) in 2011. The WHO aspires to realise ‘the attainment by all peoples of the highest possible standards of health’112, through ‘stimulat[ing] and advanc[ing] work to eradicate epidemic, endemic and other diseases.’113 The WHO has traditionally played a major role in the management of pandemic influenza outbreaks since its inception,114 even going as far as to procure vaccines, and distribute them to developing states that lack access during a pandemic, though this has been done on a largely ad-hoc basis.115

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112 PIP Framework, Article 1
113 Article 2, ibid.
115 WHO, (n41); for a discussion of the ad-hoc nature in which vaccine were donated to the Vaccine Deployment Initiative during 2009-H1N1, and the impact this had on developing states being able to meet their vaccination target levels see: Chapter III Vaccine Procurement.
Regarding the PIP Framework and pandemic influenza vaccine procurement, the Framework aims to improve the procurement of pandemic influenza vaccines by developing states by creating a more structured approach to collection and distribution of donated PIV than the traditional ad-hoc manner in which the WHO has collected and donated vaccines. This is intended to ensure that the PIV donated from manufacturers is not just given on an ad-hoc basis after orders from fee-paying states have been fulfilled, or once self-procuring states have determined they have excess PIV to meet their needs, as was the case with Vaccine Deployment Initiative (henceforward VDI) donations during 2009-H1N1. Instead, donations of pandemic influenza vaccine may be included within the company obligations within Standard Material Transfer Agreements completed via the PIP Framework, which mandate that a proportion of the real-time PIV production are reserved for, and transferred to, the PIP stockpile. This is intended to enable the WHO to manage a stockpile of ‘around 150 million vaccines’; 50 million doses of the stockpile will be for use in ‘affected countries, according to public health risk and need, to assist in containing the first outbreak or outbreaks of an emerging pandemic’ and ‘100 million for distribution...to developing countries that have no or inadequate access to...influenza vaccines, on a per capita basis that can be distributed to affected and at risk developing states during a pandemic.’

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116 WHA, 'Resolution WHA60.28: Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits' (2007)
117 The VDI was a department within the WHO charged with managing and coordinating the global donation of 2009-H1N1 vaccines, and the resources needed to deploy them, and was created specifically to manage the distribution of vaccines for 2009-H1N1.
118 For a discussion of the ad-hoc nature in which vaccine were donated to the Vaccine Deployment Initiative during 2009-H1N1, and the impact this had on developing states being able to meet their vaccination target levels see: Chapter III Vaccine Procurement.
119 Standard Material Transfer Agreements is the method by which the WHO enters into agreements with entities outside the WHO GISRS, such as pharmaceutical companies that manufacture pandemic influenza related products such as vaccines or antivirals. SMTA2’s have provisions related to benefit sharing included within them.
121 PIP Framework, Article 6.9.2
The Framework is to be examined in order to determine to what extent it can enable developing states to achieve sufficient access to pandemic influenza vaccines. In respect of the Framework doing so, two issues will be considered: 1) If the WHO had a full stockpile of 150 million doses, what impact would this have on procurement by developing states during the next influenza pandemic?, and 2) How many vaccination doses are currently in the WHO PIP Stockpile, and what impact would this ‘true’ stockpile have on the procurement of pandemic influenza vaccines by developing states?

1.6.2 – The TRIPS Agreement

The World Trade Organisation (henceforward WTO) has been a key actor in the international debate regarding the link between intellectual property standards and access to medicines. Most notable in this regard is The Agreement on Trade-Related Aspects of Intellectual Property (TRIPS), which was enacted in 1994. TRIPS is concerned with prescribing the minimum standards of intellectual property protection which parties to the Agreement must incorporate into their domestic legislation. The Agreement takes the form of binding international obligations upon all Members of the World Trade Organisation, although with a staggered implementation period for developing and least developed states. One of the most controversial minimum standards that TRIPS imposes upon its signatories is that they must provide patent protection on pharmaceutical products, including drugs and vaccines. This requirement is controversial as traditionally many developing states offered little or no patent protection on pharmaceutical products as a matter of public health policy, as this would allow generic competition amongst pharmaceutical manufacturers to flourish, and drive down prices on products.

\[\text{122 TRIPS, Article 1}\]
\[\text{123 Ibid.}\]
\[\text{124 Ibid, Article 65(3)}\]
Despite the fact that it is largely concerned with prescribing minimum standards for intellectual property protection, incorporating provisions of the TRIPS Agreement may enhance the procurement of patented PIVs by developing states. TRIPS provides three mechanisms which can allow states to take action in order to counteract the undesirable impact of granting patents on pharmaceutical products. Firstly, states may implement provisions in their domestic law that allow them to manufacture or import products that are subject to patent production in their territory.\(^{126}\) Secondly, states may potentially make provision that could prevent elements of a drug or vaccine from being patented in their territory.\(^{127}\) Thirdly, states may implement more broad policies and legal mechanisms that are necessary in order to protect public health while maintaining access to the markets and benefits that come with WTO membership.\(^{128}\) Such mechanisms, known as the ‘TRIPS Flexibilities’, provide states with the opportunity to circumvent patent protection and introduce generic drugs to increase competition and reduce the prices\(^{129}\) or take measures to ensure products that are crucial to public order or morality are not able to be commercially exploited via a patent.\(^{130}\) In theory, this means that the product will be more accessible to the public. The applicability of these provisions has been considered in relation to the procurement of oral solid drugs, and the evidence suggests that they can be effective tools in order to enhance developing states procurement of patented drugs.\(^{131}\)

\(^{126}\) TRIPS, Article 31
\(^{127}\) TRIPS, Article 27.3(b)
\(^{129}\) TRIPS, Article 31
\(^{130}\) TRIPS, Article 27(2)
This research seeks to answer a number of questions regarding intellectual property and procurement of pandemic influenza vaccines. 1) Is the maintenance of a patent regime that includes pharmaceutical products necessary in order to incentivise the creation of pandemic influenza vaccines in the first place? 2) Does a patent regime that includes pharmaceutical products create a system whereby developing states are prohibited, or restricted from effectively procuring sufficient levels of pandemic influenza vaccines? 3) Could making use of the full range of TRIPS flexibilities enhance the procurement of pandemic influenza vaccines by developing states?

1.7 – Structure of the thesis
Chapter 1 presents the literature review for this thesis, highlighting the gaps in the current knowledge this research seeks to fill. Chapter 2 considers the traditional procurement methods used by states to obtain PIV during an influenza pandemic, with focus on 2009-H1N1. This chapter argues that the traditional methods of vaccine procurement are ineffective for developing states as procurement is dominated by developed states, particularly those with Advance Purchase Agreements in place, guaranteeing them priority access to PIV. I conclude that the right-to-health cannot be realised by developing states by attempting to procure pandemic influenza vaccines through the traditional procurement methods.

I argue in Chapter 3 that the provisions within the example Standard Material Transfer Agreement (henceforward SMTA) provided at the annex to the PIP Framework fail to maximise benefit sharing for developing states, largely due to the overly flexible benefit sharing obligations secured in the PIP Framework, and too few of the pandemic influenza vaccine manufacturers currently active within the market have committed to share benefits with the WHO via an SMTA. In addition, the viability of the PIP Stockpile as a procurement method is further reduced when the terms that have been secured with the three manufacturers that are party to a SMTA are evaluated, which are weak and fail to maximise benefits on behalf of developing states.
I argue in Chapter 4 that it does not appear that patents incentivise innovation in the field of PIV: the unique characteristics of the market do this without the need for patenting. I also argue that while the patents could be a barrier to procurement, as they could prevent generic manufacturers from entering the market, because the majority of developing states have the means to overcome these patent barriers in their domestic patent legislation, this offsets any barrier to generic entry which the patent landscape may pose. Despite this, the patent related flexibilities outlined in the TRIPS Agreement, and presented in the literature as suitable tools to enhance the procurement of drugs in developing states, lack utility in the procurement of pandemic influenza vaccines, because the knowledge required to manufacture the vaccines is not available outside of the established manufacturers. I conclude that the right-to-health cannot be realised by developing states making use of patent flexibilities, or even by denying the patentability of pandemic influenza vaccines.

Chapter 5 summarises the argument to this point and I advance the argument that reform of the Pandemic Influenza Preparedness Framework is the most viable reform that could lead to the right-to-health being realised in respect of pandemic influenza vaccines. This chapter also outlines a model that I argue is able to ensure that developing states are able to obtain ‘appropriate access’ to influenza vaccines during an influenza pandemic, while ensuring that an appropriate balance can be struck between access to medicines as a manifestation of the right-to-health. I argue that this can be achieved through the creation of a ‘knowledge and information Clearing House for pandemic influenza vaccines’. The Conclusion draws together the arguments made, outlines the original contribution to knowledge made in this thesis and identifies areas of future research.

1.8 - Conclusion
Influenza pandemics are particularly difficult to address. They have the potential to spread rapidly across borders, in a very short time frame, and require novel PIV to provide immunity, due to strain mutation. In order for states to minimise the mortality and morbidity from pandemic influenza they must undertake a vaccination campaign ensuring that at least 33% of their population is vaccinated as early on in the pandemic
as possible, in order to establish community immunity. A failure to do so is clearly a breach of a state’s right-to-health obligations outlined at The Committee on Economic, Social and Cultural Rights General Comment No. 14. Despite this, the maximum global production capacity for PIV is significantly lower than the required number of doses. Furthermore, it is unlikely that the global production capacity will ever be able to effectively meet demand due to the significant costs in increasing production capacity,\textsuperscript{132} coupled with the relatively low financial returns that are associated with vaccine manufacture.\textsuperscript{133}

The amount of PIV that can be procured by a state, and when that vaccine is procured, are key factors regarding how effectively a state can respond to an influenza pandemic. This determines the extent to which a state can be said to have discharged its right-to-health obligations during a pandemic. Developing states lack sufficient access to PIV during a pandemic, impeding the extent to which they can make an effective response to the virus, and discharge their right-to-health obligations.

\textsuperscript{132} It is estimated that the WHO planned capacity increase from 2007 – 2017 will cost $2,993 million at Table 3 (appendix) WHO, (n33)

CHAPTER II - LITERATURE REVIEW

This chapter critically evaluates the literature that has been generated regarding the Pandemic Influenza Preparedness Framework and the TRIP Agreement relevant to this thesis, and outlines why this body of literature has not sufficiently answered the questions this research is addressing. This chapter also outlines why the literature that has been generated regarding patents, access and the right-to-health, that considers these topics from a general ‘medicines’ or solid dose drugs perspective are not generalisable to access to pandemic influenza vaccines. In doing so, the original contribution of this research is contextualised within the literature.

A significant amount of literature can be identified which addresses access to medicines as a component of the right-to-health.¹ Some of this literature also specifically addressed the intersection of intellectual property, the right-to-health and access to medicine.² However, none of the literature identified specifically considers

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the Pandemic Influenza Preparedness Framework through a right-to-health lens. This literature is particularly helpful to this research, as it provides a foundation to access to medicine as a component of the right-to-health, and advances some theories regarding how intellectual property rights on medicines interact with the human right-to-health in this context. However, this literature is limited because none of it explicitly addresses access to vaccine as a component of the right, or discusses intellectual property and access to medicines in a general sense. It does not therefore reflect the unique characteristics and challenges of access to vaccine, which are outlined at 2.5 of this review.

The rest of this review is dedicated to giving an in-depth consideration to the literature that has been generated on the Pandemic Influenza Preparedness Framework, and the TRIPS Agreement. These are the two mechanisms which this research focusses on that could be used by developing states in order to improve the procurement of PIV, and in doing so, discharge their right-to-health obligations regarding access to pandemic influenza vaccines.

2.1 - The Pandemic Influenza Preparedness Framework

Given that the Framework was only passed in 2011, and has not yet been used during an influenza pandemic, there is a relatively small body of literature available regarding its provisions and their application, particularly when compared with the relevant literature on the TRIPS Agreement.³ Within the literature, The Framework has been
hailed as an innovative mechanism for guaranteeing access to vaccines and affordable life-saving drugs during an influenza pandemic.4

The fact that provisions within PIP that require vaccine manufacturers donate vaccines to the WHO’s stockpile in return for accessing viral samples was met by a good deal of support in the literature, on the assumption that it would improve access in developing states.5 However, concern was expressed by Kamradt-Scott and Lee that this may actually have the unintended consequence of forcing vaccine manufacturers out of the market, and thereby reducing global vaccine capacity:

The imposition of what effectively equates to user fees for pharmaceutical companies that access GISRS data and samples, either through directly funding the network or via commitments to provide at least 10 per cent of vaccines and diagnostics at reduced prices, raises the possibility that some manufacturers will exit what has traditionally been a low-profit industry.6

Further, a number of commentators including Vezzani and Kamradt-Scott and Lee have expressed concerns that the benefit sharing requirements of the Framework will not result in significant improvements in access for developing states. A number of theories have been presented as to why this is. It is claimed that the Framework has only imposed minimal changes on the existing market-based political economy surrounding influenza vaccine production and procurement.7 Vezzani has further claimed that philanthropic initiatives like PIP already been implemented on voluntary

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7 Kamradt-Scott and Lee, (ibid)
bases, without significantly improving access. While Vezzani is correct in stating that philanthropic initiatives such as the ones prescribed in the PIP Framework have not been successful in improving access to medicines or vaccines in developing states, on this point Vezzani does not consider that the Framework does give rise to legal obligations upon vaccine manufacturers to share benefits when they conclude an SMTA2, the impact this may have on pandemic preparedness in developing states, or that the extent to which the Framework has the potential to make the sharing of benefits a norm within the vaccine manufacturing industry.

The idea that the benefit-sharing system in the PIP Framework appears to be insufficient to rectify inequities in access to vaccines during a pandemic has also been addressed by Rhodes, who noted that the vaccine stockpile would, even if a single dose regime was viable, cover approximately 1.8% of the populations of developing states. This is concerning for a number of reasons. First, in all likelihood a two dose vaccination strategy will be required to provide full-immunity to a pandemic influenza virus, meaning that Rhodes’s estimation of vaccine coverage from PIP donated materials should be halved to give a more realistic idea of the Frameworks’ impact in this area. Second, Rhodes’s estimate was based on the 100 million doses it was envisaged PIP would procure for distribution to developing states - as I note at 4.5, the WHO has actually procured significantly less vaccine than envisaged when this estimate was made, further reducing the vaccination coverage PIP could ensure in developing states.

On the issue of benefit sharing, while praising the Framework for requiring vaccine manufacturers to contribute to the running costs of GISRS, and to provide long-term

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8 Ibid.  
10 Catherine Rhodes, 'Sovereign Wrongs: Ethics in the Governance of Pathogenic Genetic Resources' (2015) 3 Ethics in Biology, Engineering and Medicine 97  
benefits to developing states by increasing access to technologies and capacity-building resources.\textsuperscript{12} Gostin and Fidler were critical of the Framework for appearing to be a weak compromise on a number of key issues, including intellectual property rights over PIP biological material, and vaccine contributions by developing states.\textsuperscript{13} Academics such as Kate and Sampath have claimed that an access and benefit sharing system allows a developing state with a genetic resource, a stronger position in negotiations,\textsuperscript{14} thereby making them more likely to obtain an agreement beneficial to their national interests, such as increasing access to PIV. This position has been countered with the claim that developing states have no bargaining position because their participation in the production of these products is not valued as they are ‘just’ natural resources\textsuperscript{15}; on the other hand, the industrialized states' contributions are highly valued because they are involve technology and knowledge to which developing states do not have access.\textsuperscript{16}

\textit{2.1.1 - Developed and Developing States: Balancing the Division}

The extent to which the Pandemic Influenza Preparedness Framework has rebalanced the division between developing and developed states on access to vaccines is one of the key themes identified through analysis of the literature. In the wake of 2005-H5N1\textsuperscript{17} and 2009-H1N1, several commentators expressed serious concerns that many

\begin{itemize}
\item \textsuperscript{12} Fidler and Gostin, (n4)
\item \textsuperscript{13} Ibid.
\item \textsuperscript{14} Kerry ten Kate, \textit{The Commercial Use of Biodiversity: Access to Genetic Resources and Benefit Sharing} (Earthscan Publications 1999); Padmashree Gehl Sampath, \textit{Regulating Bioprospecting: Institutions for drug research, access, and benefit sharing} (United Nations University Press 2005)
\item \textsuperscript{15} Stephan Elbe, ‘Haggling over viruses: the downside risks of securitizing infectious disease’ (2010) 25(6) Health Policy and Planning 476
\item \textsuperscript{16} ER Sedyaningsih and others, ‘Towards mutual trust, transparency and equity in virus sharing mechanism: The avian influenza case of Indonesia’ (2008) 37(6) Annals of the Academy of Medicine, Singapore. 482; For a more theoretical discussion of the negotiation relationships between developing and developed states see: Alan Wertheimer, \textit{Exploitation} (Princeton University Press 1999)
\item \textsuperscript{17} Although not technically a pandemic, many of the experiences of developing states in terms of vaccine procurement are applicable in this case.
\end{itemize}
states that were in real danger from the pandemic were unable to access the vaccine. This was one of major impetuses for creating the PIP Framework.

On this point, the Framework has been praised on the basis that it ‘recognises that there is an ethical dimension to pandemic planning’, however, Fidler and Gostin have expressed some doubt that such a rebalance can be fully achieved by the Framework in its current guise. They note that the Framework’s most glaring omission is the absence of even ‘soft’ norms encouraging developed states to make specific equity-enhancing contributions to developing states, such as donating portions of purchased vaccine. Although, they do, more positively, highlight that because the Framework requires industry, predominantly in developed states, to contribute to GISRS’ operating costs and through benefits provided under the SMTA2, this is a major boost for rebalancing the division between developed and developing states in pandemic preparedness.

However, the extent to which such intangible benefits can be said to have any real impact on the aims of the PIP Framework, and close the gap between developing and developed states, is questionable, particularly as the Framework does little to alter the balance of power between developing states and industry. Furthermore, developing states have not seemed to gain as much in the way of improved access to

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21 Fidler and Gostin, (n4)

22 Fidler and Gostin (n4)

23 Ibid.
vaccines or technical assistance, or even commitments for improved access in the future, as they were thought to when the Framework was being drafted.  

Particular praise for the access to vaccine provisions of the Framework has come from Jefferies, who states that it will ensure sustainable increases in pandemic vaccine production, which means access for both developed and developing states.  

More specifically, Jefferies praises the benefit-sharing provisions of the Framework because the SMTA2 is significant as a tool to solve the challenges of sharing on an equal footing between contributors of viruses and manufacturers of influenza vaccines, and allows developing states when entering into contractual agreements to rebalance the disproportionate burden of risk and benefits associated with pandemic influenza viruses and vaccines which currently exists between developed and developing states.  

The major limitation regarding the literature identified above is that the majority of it was generated prior to any manufacturers signing an SMTA with the WHO for the supply of vaccine to the PIP stockpile. Therefore the evaluations made regarding how effective the Framework would be in improving access top vaccine in developing states was largely based on speculation as to terms and uptake by pandemic influenza vaccine manufacturers. However, it is necessary to note the low take-up of these agreements amongst PIV manufacturers, which limits the effectiveness of the Framework. This literature is also limited as it was generated prior to the terms of the SMTAs with pandemic influenza vaccine manufacturers being made public, therefore authors assumed that the WHO would secure terms similar to those outlined at the standardised SMTA provided in the Framework, but, as I make clear below at 4.5, the WHO has secured terms very different from those in the standardised SMTA. This therefore, significantly changes the effectiveness of the Framework as a procurement method by developing states. This research considers the utility of the Framework as

24 Kamradt-Scott and Lee (n6); Vezzani (n5)  
25 Jefferies (n5)  
26 Ibid.  
27 The impact of this is discussed in more detail at 4.4  
28 PIP Framework, Annex 2, SMTA2, Article 4.1.A.1
a procurement method by developing states having taken into account the terms of the SMTAs which have been signed with pandemic influenza vaccine manufacturers.

2.3 - The Agreement on Trade-Related Aspects of Intellectual Property

There is a considerable amount of literature discussing intellectual property, TRIPS and access to medicine. Literature addressing the patent standards of the TRIPS Agreement and access to medicines in the developing world is particularly helpful for providing an understanding of the impact patent protection provisions have on access, such as documented by Abbott, Correa and Reichmann, as well as reports drafted by NGOs with interest in this field. The general consensus appears to be that absolute patent protection on pharmaceutical products diminishes developing states’ abilities to access medicines, and flexibilities allowing the circumvention of such rights can minimise the impact such patents have on access. Most notably, some commentators have gone as far as to claim that the current HIV/AIDS epidemic in the

29 See 1.6.2 – The TRIPS Agreement for a brief descriptive account of what standards and flexibilities TRIPS prescribes. A More in-depth explanation and analysis of the standards is provided at 7.1 and the flexibilities at 7.2
developing world has been prolonged and exacerbated by patent rights inhibiting access, despite the flexibilities contained within the TRIPS Agreement. It is clear from this discussion that several non-patent factors affect access to essential medicines in sub-Saharan Africa. However, despite that, pharmaceutical patents also have negative impacts on access to essential medicines. And, attempts to use the TRIPS flexibilities to ameliorate the situation have been fraught with problems.

According to Correa, the main impact of developing states incorporating the TRIPS Agreement is the increased prices for patent protected products, including medicines. Indeed, an outcome of studies by the World Bank and International Monetary Fund in numerous developing states have shown an assumption that TRIPS will lead to increased prices for pharmaceuticals, which may consequently limit access to medicines.

Commentators such as Attaran & Gillespie-White and Li have claimed that blaming patent protection for the high price of medicines in the developing world is too simplistic, and that patent protection is merely one of the contributions causing high prices, and by no means the main one. They claim that weaknesses in domestic medical, financial and political infrastructures has a greater impact on access to

33 Sisule Musungu, Susan Villanueva, and Roxana Blasetti, 'Utilizing TRIPS Flexibilities for Public Health Protection Through South-South Regional Frameworks' (WHO 2016) <http://apps.who.int/medicinedocs/en/d/Js4968e/>
35 Adusei, (Ibid)
36 Correa (2000) (n31) 24
38 Correa (2000) (n31) 35
medicines than patent protection, and that in many developing states, access would be improved by political will and the commitment of new resources, rather than relaxing the level of patent protection on pharmaceutical products.

In summary, patents generally do not appear to be a substantial barrier to antiretroviral treatment access in Africa today. Activists, industry, physicians, and media who have so successfully raised public awareness of AIDS treatment issues are in a position to challenge the more important barriers.

This viewpoint appears to be supported by the largest empirical analysis on this topic. In a study of 53 developing states and 15 antiretroviral drugs for the treatment of HIV/AIDS, patent protection was only provided for in 21.6% of the states. At first glance this analysis would lend itself to the conclusion that patent protection is not a barrier to access to medicines in these states. This study, and commentators such as Li and Attaran & Gillespie-White, takes a narrow, jurisdictional approach to intellectual property rights in the global economy. This assumes that intellectual property rights only affect access to medicine in the jurisdiction in which they have been granted, which fails to address that patent protection in one state can have a drastic impact on access to medicines in another, particularly those states that lack their own manufacturing capabilities and are therefore reliant upon importing medicines in order to meet their public health needs. This is particularly relevant to the field of pandemic influenza vaccines, given that the manufacturing capacity for these products is concentrated in a small number of developed states.

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40 Attaran and Gillespie-White, (ibid.)
42 Attaran and Gillespie-White, (n39)
43 ibid
44 Prior to India becoming TRIPS compliant it was known as 'the pharmacy of the developing world' because it manufactured and exported such a high volume of generic medicines to developing states without manufacturing capacity. India becoming TRIPS compliant, and having to offer pharmaceutical patents, has clearly impacted upon access to medicines in a number of developing states, not just India. Timothy Bazzle, 'Pharmacy of the developing world: Reconciling intellectual property rights in India with the right-to-health:' (2011) 42 Georgetown Journal of International Law 785
45 Jeffrey Partridge and Marie Paule Kieny, 'Global production capacity of seasonal influenza vaccine in 2011' (2013) 31(5) Vaccine 728
The majority of these papers address access to medicines in general terms. However, a paper by Lawson and Hocking considers access to vaccines during a pandemic.\textsuperscript{46} Their paper concludes that ‘intellectual property is a central concern in developing effective responses to avian influenza and the likely resultant pandemic.’\textsuperscript{47} I address this point in Chapters 5, 6, and 7, determining if it is the case that intellectual property is a ‘central concern’ in responding to an influenza pandemic. In doing so, I examine if intellectual property incentivises the creation of pandemic influenza vaccines, if intellectual property poses a barrier to access to pandemic influenza vaccines, and if intellectual property flexibilities can improve access to pandemic influenza vaccines. Lawson and Hocking’s chapter is particularly helpful in terms of this research. However, it is not without its limitations. Lawson and Hocking have advanced the idea that developing states need to establish manufacturing capacity for pandemic influenza vaccines in their own territory, they do so on the presumption that it is intellectual property rights that prevent this from occurring:

The concern for countries of the South [developing] is that existing patents may prevent the use of a patented product, process or product of the process thereby tying up the technology necessary to develop efficient and effective vaccines. Enhancing the production capacity and efficacy of pandemic influenza vaccines almost certainly depends on technology accessed from patent holders in countries of the North [developed] together with the related know-how and regulatory submissions data. In short, intellectual property is a central concern in developing effective responses to avian influenza and the likely resultant pandemic.\textsuperscript{48}

Firstly, Lawson and Hocking only focus on the impact that patents on the genetic resources contained within the vaccine (the virus, or virus-like particles) will have on access, and do not consider the patents on the manufacturing processes for pandemic


\textsuperscript{47} Ibid. 300

\textsuperscript{48} Ibid. 331
influenza vaccines. Therefore a complete picture of patents and pandemic influenza vaccines is not provided by this chapter. Lawson and Hocking’s chapter also fails to engage with the issue of proprietary, non-patented knowledge, and as such does not fully engage with one of the predominant barriers to generic entry in the field of pandemic influenza vaccines in developing states. Engagement with barriers to generic entry, beyond intellectual property rights is necessary because, as highlighted later in this review\(^49\) and throughout this thesis, the presumption that intellectual property rights are the only thing preventing generic manufacturers in developing states from producing a pandemic influenza vaccine is misplaced.

2.4 - TRIPS Flexibilities

As well as prescribing the minimum standard of intellectual property protection which a party to the Agreement must incorporate into domestic legislation, TRIPS also provides for a number of flexibilities that states may also incorporate. TRIPS provides for a number of flexibilities regarding patents that allow states to balance their obligation to provide adequate patent protection on pharmaceutical products, with their desire to meet the pressing public health needs of their population by ensuring access to medicines. The relevant flexibilities are: The Principles\(^50\), Exclusions to Patentability\(^51\), and Use without Authorisation of the Right Holder\(^52\) provisions. More detailed explanations of how these flexibilities work, and what exactly TRIPS prescribes in respect of them, is provided at 7.2.

2.4.1- Principles

Much of the literature in respect of the Principles as a flexibility focusses on the Principles being a guiding, interpretive flexibility, which ought to inform states’ interpretation of all other provisions within TRIPS. To this end it has been argued that consistency with the TRIPS Agreement ‘should be assessed in the light of Article 7 and of the Preamble that is, taking the balance of rights and obligations and the social and

\(^{49}\) See discussion in 2.5 - The distinction between ‘medicines’ and vaccines

\(^{50}\) TRIPS, Articles 7 and 8

\(^{51}\) TRIPS, Article 27.3(b)

\(^{52}\) TRIPS, Article 31
economic welfare into account’. The utility of Article 8 for developing states has been noted as being important because it provides justifications for special exceptions that promote the public interest in sectors of vital importance to socioeconomic and technological development. More specifically, Correa has argued that

> Article 8.1 broadly recognizes Members’ rights ‘in formulating or amending their laws and regulations’. It does not only refer to laws and regulations on IPRs but to measures adopted in other fields, for instance, those that restrict the manufacture or commercialization of IPR-protected goods. Issues concerning the application of Article 8.1 may, hence, arise in two contexts, one fully within the IPR realm, and another one outside it, but with implications on the protection of IPRs.

However, there is little consensus within the literature as to a) how developing states might make use of the Principles in order to bring about meaningful reform related to public health within their domestic patent regimes, and b) how effective relying on the Principles to justify such reform as being TRIPS compliant is. This ongoing debate within the literature has been succinctly summarised by Correa:

> There are different possible interpretations for this paragraph. On the one hand, it may be viewed as a statement of fact rather than a rebalancing of the Agreement. On the other, it may be regarded as an indication that in cases where there is conflict, IPRs should not be an obstacle to the realisation of public health.

Much of the literature is divided on the utility of the Principles, and the extent to which developing states may actively rely upon Article 8 in order to make effective changes to their domestic patent regime while remaining TRIPS compliant. The contrasting interpretations regarding the impact the Principles of TRIPS can be seen in the comments made by Frankel and Cann on the impact of the Principles post-Doha.

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54 Peter Yu, ‘The objectives and principles of the TRIPS agreement’ (2009) 46 Houston Law Review 797

55 Correa, (n53) 104

56 Correa, (n53) 105
Using these articles to help interpret the object and purpose is only a starting point. There are inherent difficulties in that the articles seek to capture competing objectives and purposes, and they represent a compromise between the disparate views of those entering the agreement...Despite these difficulties it seems reasonable to expect that these objectives and principles have a bearing on any interpretation exercise. And that exercise ought, in as far as is possible, to balance those competing interests.57

The use of the term ‘necessary,’ as opposed to the language ‘it considers necessary’ employed in the Article 73 security exception, would seem to indicate that the imposition of these measures are not within the absolute discretion of the invoking Member, but are instead subject to potential WTO review in regard to their validity.58

Similar concerns to those outlined by Cann have been echoed by Gervais.59

Moreover, some commentators have argued that an interpretation which limits the utility of Article 8 would perpetuate the unfairness of the TRIPS Agreement and take away the member states’ needed discretion in developing its public policies, particularly in the field of public health,60 which would include drug procurement.

2.4.2- Exclusions to Patentability

57 Susy Frankel, ‘WTO application of ‘the customary rules of interpretation of public international law’ to intellectual property’ (2006) 46 Virginia Journal of International Law 365
TRIPS provides that Members may exclude inventions within their territory from being patented, where the prevention of commercial exploitation is necessary to protect *ordre public* or morality, explicitly stating exclusion may occur in order to protect health. However, as Sykes notes,

> [t]his confusingly worded exception might be read to create a general ‘public health’ exception to the requirement of patentability, but is not so interpreted. Rather, it is understood to refer to inventions that are themselves harmful to the *ordre public*, and that cannot be exploited under national law.

Much of the literature focused upon how *ordre public* or morality are to be interpreted and relied upon by developing states, as neither is defined within TRIPS. Given the lack of a definition, and the seemingly interconnected nature of the concepts of *ordre public* and morality, some academics have focused on clearly defining these concepts.

More specifically related to this research, the utility of Article 27(2) in the attempt to increase access to medicines has been discussed by Cann, in the context of the Article being used to deny the patentability of HIV/AIDS drugs and thereby enhance procurement though the introduction of generic medicines:

> [I]f a nation takes the position that the prevention and treatment of the HIV/AIDS epidemic is necessary to protect the *ordre public*,...[TRIPS] would

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61 TRIPS, Article 27(2). The most well-known example of a state refusing to recognise patent protection on pharmaceutical products is India, who did not recognise patent protection pharmaceutical products from 1971 (S.3(b) The Patents Act 1970 excluded patent protection from ‘inventions that are immoral or injurious to public health’) to 2005 when, in line with its obligations under the TRIPS Agreement, India allowed patenting of all suitable products and inventions, including pharmaceutical products (The Patents (Amendment) Act 2005).


apparently allow that nation to deny patent protection to relevant pharmaceuticals and then distribute those products, assuming they are attainable, on a non-profit, non-commercial basis. Since there could be no discrimination between the rights of foreign and domestic producers, as neither would be allowed to engage in commercial exploitation, such a strategy would appear consistent with the terms of...[TRIPS].

This is a particularly interesting proposition for access to medicines, as much of the literature focusses on the compulsory licensing of a product once it is patented, rather than merely denying its patentability in the first place. No existing literature addresses whether this potential solution has utility for establishing generic pandemic influenza manufacturing capacity in a developing state.

2.4.3 - Use without Authorisation

Use without Authorisation of the Right Holder provisions encompass Crown use licenses, and compulsory licenses. Both of these are non-voluntary licenses which are granted by the government that authorises a generic manufacturer to use a patented invention without the authorisation of the patent holder. These provisions are widely implemented in most national laws, including in developing states, and have been successfully used in order to procure medicines during public health emergencies. The World Bank’s technical guide on procuring antiretroviral drugs in

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65 Cann, (n58)
66 As outlined at 2.4.3.
67 TRIPS, Article 31(b)
developing states refers to these provisions are ‘the principle means of enabling procurement authorities to overcome patent barriers’.  

There is no literature in this field that deals specifically with the use of these provisions to procure vaccines during an influenza pandemic. A paper by Van Zimmermann does consider the successful use of Crown use provisions to procure and then negotiate long-term price reductions on an antiviral to treat influenza infections during a pandemic. However, the extent to which these benefits, including those concerning the procurement of medicines during an influenza pandemic, are replicable to procure pandemic influenza vaccines for developing states during a pandemic is questionable. This is because in order to make effective use of Crown use provisions a State would require domestic production capacity, and very few developing states possess the necessary technical infrastructure to manufacture pandemic vaccine.

While the literature acknowledges that these provisions can increase access to medicines in the short term, one of the key benefits which commentators focus upon is that they ultimately lead to price-reductions on patents products in the long term, and therefore improve access to these medicines in the long term. This is a tactic that has been used by developing states, and has been threatened by the United States in the wake of the 2001 Anthrax attacks, which ultimately led to a price reduction from the patent holder. In the context of pandemic influenza vaccines, as each vaccine only provides protection for the specific virus strains currently in

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71 Esther van Zimmeren and Gilles Requena, 'Ex-officio Licensing in the Medical Sector: The French Model' in Geerttrui van Overwalle (ed), Gene patents and public health (Bruylant 2007)
72 Abbott and Reichman, (n32); Flynn (n69); Reichmann (2009), (n34)
73 Abbott and Reichman, (n32); van Zimmeren and Requena, (n71) lists agreements with major pharmaceutical companies that were initiated via a Government authorisation in Malaysia (2004), Indonesia (2004), Brazil (2003 and 2007), Zambia (2004), Zimbabwe (2004), and Mozambique (2004).
74 Flynn (n69); Wibulpolprasert et al (n69); Yamabhai et al (n69)
circulation, which mutates and changes annually, the need for long-term price reductions is negligible, as each vaccine is only needed on a short-term basis. Therefore, this research will disregard any arguments which consider long-term price reductions as irrelevant to the questions this research is seeking to answer.

A number of commentators have shown support for use without authorisation provisions on the basis that developing states have the ability to use, or threaten to use these provisions, has ultimately led to voluntary agreements between governments and patent owners, such as occurred in Brazil and Thailand, regarding treatments for HIV/AIDS. This is because if a developing state threatens to invoke a compulsory license then this gives the state far greater power in negotiations, ultimately leading to voluntary licenses being granted by the patent owner. This is an interesting claim, but it is difficult to determine to what extent it is actually true. Furthermore this position does not seem to be justifiable in the face of a recent evaluation of compulsory licensing trends, which found only twenty-four instances of a Government official proposing a compulsory license since 1994, with the number falling dramatically since 2008. This may be a result of Governments no longer needing to publically ‘propose’ a compulsory license as a threat to the patent holders in order to for them to issue a voluntary license, but there is no evidence to suggest that this is the case.

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77 Ho (n69); Lybecker and Fowler, (n69); Outterson, (n69); Reichman (2009), (n32); Randall Kuhn and Reed F Beall, 'The time for pharmaceutical compulsory licensing has expired' (2012) 18(8) Nature Medicine 1168
78 Ibid.
79 Kuhn and Beall, (n77)
A distinct area of focus within the literature is the Doha Declaration,\(^{80}\) and the extent to which the ‘Paragraph Six System’ adequately addressed the problem addressed at Paragraph Six of the Declaration.\(^{81}\) The Paragraph Six System is a waiver that allows generic medicines to be manufactured under compulsory license exclusively for export to states that cannot manufacture the medicines themselves. This in effect removes the limit in Article 31(f) of TRIPS which limits the amount of medicine a state can export under a compulsory license to states that lack access, and manufacturing capacity. The System has only been used once,\(^{82}\) therefore much of the literature presents theories as to why the System is so underused. The literature is generally highly polarised in this area between those, such as Greenbaum\(^{83}\) and the Commission on Intellectual Property Rights and Innovation,\(^{84}\) who emphasise that there is little incentive for developing states and generic manufacturers to participate in compulsory licenses because of remuneration costs to the patent holder having to be paid by the exporting state, and those who claim that it is developing states that are disincentivised from participating in the Paragraph Six waiver because it is overly complex and time consuming,\(^{85}\) and the effects of past sanctions for engaging in such

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\(^{80}\) WTO (Doha Round), ‘The Doha Declaration on the TRIPS Agreement and Public Health’ (2001a) WT/MIN(01)/DEC/2; - this Declaration was approved by the WTO Ministers at the Doha Ministerial Conference. In the Declaration ministers stressed the importance of implementing and interpreting of the TRIPS Agreement in a way that supports public health, making explicit mention of the fact that ‘The TRIPS Agreement does not and should not prevent Members from taking measures to protect public health’, and reaffirming that the Agreement does not prevent members from granting compulsory licenses, or engaging in parallel importation of patented drugs, in order to improve access.

\(^{81}\) Paragraph Six states ‘we recognize that WTO members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002.’


\(^{85}\) Correa (2000) (n31); WTO, WIPO & WHO, Promoting access to medical technologies and innovation: Intersections between public health, intellectual property and trade (WTO Publishing 2013) 216; Reichmann (2009), (n32)
practices has lingering effects which make developing state reluctant to seek out exporting states.\textsuperscript{86}

Despite this polarization, the literature is useful as it provides indications that the Paragraph Six waiver is failing to deliver on its intended goal of increasing access to medicines in developing states that lack manufacturing capacity, even if there is no consensus as to the cause. When we consider that developing states have been reluctant to use the System to tackle long standing public health problems in their states such as HIV/AIDS, there is no reason to believe that they would be any more likely to use the System in order to procure pandemic influenza vaccines. A parallel can be drawn here with the general critique of the Paragraph Six system provided by Owoeye:

The Doha Paragraph 6 System allowing countries without manufacturing capacity to import through the use of compulsory licensing is inevitably highly cumbersome as it involves protracted processes that can result in significant delay and expenses. While the Doha Paragraph 6 System remains relevant to the access to medicines conundrum, it does not provide a liberal framework for making medicines available to countries lacking pharmaceutical manufacturing capacity.\textsuperscript{87}

To this end, the utility of the System is further limited when one considers the particular challenges in procuring pandemic influenza vaccines, in that there is a limited worldwide manufacturing capacity, well below the capacity which would be required in order to fulfil demand, and that pandemic influenza vaccines are in very high demand by developed and developing states. Therefore, the requirement to find a state with vaccine manufacturer capacity based in their territory willing to issue a

\textsuperscript{86} Vanessa Kerry and Kelley Lee, ‘TRIPS, the Doha declaration and paragraph 6 decision: What are the remaining steps for protecting access to medicines?’ (2007) 3(1) Globalization and Health 3; Abbott and Reichman, (n34)

compulsory license to one of these manufacturers during a pandemic in order to fulfil the Paragraph Six contract will be extremely difficult.\textsuperscript{88}

Much of the above literature discusses access to medicines in a general sense,\textsuperscript{89} though some of the literature does apply specifically to particular diseases, mainly HIV/AIDS\textsuperscript{90} and neglected tropical diseases;\textsuperscript{91} one book chapter considers intellectual property and pandemic influenza vaccines.\textsuperscript{92} Therefore, the majority of papers in this field fail to differentiate between vaccines and drugs, and the separate analyses they require.\textsuperscript{93} That there is so little literature on the TRIPS flexibilities and procurement of pandemic influenza vaccines may be because influenza pandemics are sporadic in nature, or may not be considered as pressing a public health issue to developing states. It may also be the case that many commentators in this field do not perceive a difference between using the TRIPS provisions to access oral solid oral drugs or ‘medicine’, and vaccines for pandemic influenza; as explained later in this review such an assumption is misplaced.

\textbf{2.5 - The distinction between ‘medicines’ and vaccines}

A considerable amount of the academic literature on access to health goods has grouped together ideas of access to solid dose drugs, and access to vaccine under

\textsuperscript{88} As noted at 4.5.1 concern has been expressed that during an influenza pandemic, member states with domestic pandemic influenza production within their territory would place restrictions upon exports of vaccine until domestic demand had been fulfilled. Therefore the likelihood of a compulsory license being issued under these circumstances is particularly remote.  
\textsuperscript{89} Nicol and Neilson, (n34); Peter Drahos and Ruth Mayne (eds), Global intellectual property rights: Knowledge, access and development (Palgrave Macmillan 2002); Carlos Correa, ‘Bilateralism in intellectual property: Defeating the WTO system for access to medicines’ (2015) 36(1) Case Western Reserve Journal of International Law; Carlos Correa, (2006), (n31); Abbott and Reichman, (n32)  
\textsuperscript{92} Lawson and Hocking, (n46)  
\textsuperscript{93} This is outlined at 2.5 - The distinction between ‘medicines’ and vaccine
the umbrella term ‘medicine’. This is succinctly demonstrated by Marks and Benedict, who wrote

[w]hile the literature has historically focused primarily on access to medicines, many of the considerations for access to vaccines and medical technologies are similar...this chapter will therefore assume a degree of commonality among these categories in extrapolating lessons from access to medicines to the broader category of health goods.94

Such an assumption is misplaced and unhelpful. While there may be some overlap between these categories in the sphere of access to health goods,95 the reasons for a lack of access, and the solutions regarding how to improve access to each of these health goods, are actually quite distinct. To assume commonality of characteristics in this way automatically leads us to assume commonality of solutions, as this research goes on to argue, this commonality of solutions does not apply to pandemic influenza vaccines.

A solid dose drug is a product that has been ‘manufactured through chemical synthesis, meaning that it is made by combining specific chemical ingredients in an ordered process.’96 These products are rather simple chemical combinations, and as such they can be easily copied by reverse engineering by generic drug manufacturers. Reverse engineering is essentially a way of working out the ‘recipe’ for a drug, without any of the official information from the patent owner. It involves breaking the original product down into its basic chemical components, and with the assistance of the patent application and market authorisation information, allowing a generic drugs manufacturer to accurately identify and quantify all of the ingredients in the drug

94 Stephen Marks and Adriana Benedict, ‘Access to Medical Products, Vaccines and Medical Technologies’ in Jose M. Zuniga, Stephen P. Marks, and Lawrence O. Gostin (eds), Advancing the human right-to-health (Oxford University Press 2013) 305
95 Marks and Benedict identify some of these such as: ‘affordable prices; government commitment through a well-conceived and implemented national medicines policy; adequate, sustainable and equitable public sector financing; generic substitution; transparent and widely disseminated consumer information; efficient distribution; control of taxes, duties and other markups; and careful selection and monitoring’ at ibid.
formulation\textsuperscript{97}, allowing them to create a bioequivalent, generic product. The only thing that prevents this from happening on a widespread scale around the world is the exclusive rights of the drug creator, typically in the form of a patent.\textsuperscript{98}

As generic bioequivalent drugs are in essence direct copies of the original product, in most jurisdictions there is an abbreviated regulatory process for bringing the drug to market.\textsuperscript{99} This is because the generic drug manufacturer can provide the results of clinical trials that were used to originally approve the patented pharmaceutical product, in order to prove the safety and efficacy of the bioequivalent generic product.\textsuperscript{100} This is particularly beneficial from a public health perspective as it means that during a public health emergency when a generic producer has been licensed to produce a patented product (either by the patent holder, or the national Government), the drug can be licensed, brought to market and distributed in a much shorter time frame than if it were a patented product being licensed for the first time. The benefits of generic drug manufacturers reverse engineering drugs to introduce generic versions are two-fold. First, when procuring drugs, the ability to introduce generic drugs can have a substantial impact on a developing state’s ability to procure sufficient levels of a drug, as generics are traditionally priced significantly lower than their brand-named counterparts.\textsuperscript{101} Second, merely the threat of allowing a generic manufacturer to enter the market could been regarded as an effective public health


\textsuperscript{98} Carlos Correa, (2006), (n31); Ruth Lopert and Deborah Gleeson, 'The high price of ‘Free’ trade: U.S. Trade agreements and access to medicines' (2013) 41(1) The Journal of Law, Medicine & Ethics 199 for information on the growing trend for 'Data Exclusivity' provisions in FTAs, which prevent generic manufacturers relying on the test data generated by the innovator, even when a compulsory license has been issued. This has the effect of essentially providing the innovator with a monopoly over the drug, beyond that which is provided by the patent.


tool, as this has been successfully used to encourage a number of patent holders to reduce the price of their patented product.\textsuperscript{102}

However, rather than being classed as a drug, a vaccine is technically a biologic, meaning that it is manufactured in a living system, typically a microorganism, or animal cells.\textsuperscript{103} Due to the complex structure and manufacturing processes associated with biologics, it is impossible for generic manufacturers to prove that their version a bioequivalent of the original biologic.\textsuperscript{104} This means that any vaccine which purports to be a bioequivalent\textsuperscript{105} of a currently licensed product must go through the same clinical trial and licensing procedures as the original product, and is not able to use the safety and efficacy data generated by the innovator of the original product in the way generic manufacturers of oral solid oral drugs can.\textsuperscript{106}

This significantly curtails the extent to which generic manufacturers are able to reverse engineer a vaccine and rely on the safety and efficacy data generated by an innovator in order to bring a cheaper generic version to market. This fact has been noted by Crager:

Strategies to improve access to medicines have thus coalesced around the goal of enabling generic production. This has led many of these efforts to focus on patent protection as a key barrier to the availability of affordable generic medicines. A crucial assumption that underlies this strategy is that it is fairly straightforward to reverse engineer a given drug; in concept, the problem is not that generic drug manufacturers would be unable to exactly replicate a drug, it is that they are prohibited from doing so by patent law. Although this is generally the case for small molecule drugs, this basic assumption does not hold true for biologics, including vaccines.\textsuperscript{107}

\textsuperscript{102} Flynn, (n69); Lybecker and Fowler, (n69); Wibulpolprasert, (n69); Yamabhai and Smith, (n69)
\textsuperscript{103} ibid.
\textsuperscript{104} ibid
\textsuperscript{105} Note: in this instance we are using the term bioequivalent to mean the vaccine in question obtain the same result as an already licensed product, not a direct carbon-copy of the product.
\textsuperscript{106} More details on the licensing procedure for pandemic influenza vaccines, and the impact this has on generic competition are provided at Chapter IV
While Crager’s paper is helpful for highlighting this distinction, it is limited in that it does not give a detailed analysis of why this basic assumption does not hold true for vaccines. Crager’s paper also fails to engage with how this distinction between drugs and vaccines affects the utility of the patent flexibilities, which are presented in the literature as appropriate tools for increasing access to patented ‘medicines’ (including vaccines).

2.6 - Contribution of the research to the literature

As stated above, there is very little specific literature on procurement of PIV. This research adds value to the current literature in terms of its comprehensiveness and analysis. I will consider not only the role procurement processes play in developing states accessing PIV during a pandemic, but also establish whether the tools to enhance procurement outlined above can be used to enhance any of the traditional procurement methods used by developing states in order to enable them meet their right-to-health obligations.

Much of the literature regarding the PIP Framework being used to enhance WHO’s collection and distribution of donated PIV to developing states was completed when the Framework was published, prior to any Standard Material Transfer Agreements being completed, and is therefore largely theoretical. My research adds to this literature by considering the content of the Standard Material Transfer Agreements currently in force, and providing insight into the working of the PIP Framework in practice. It also provides a comparative analysis of the ‘company obligations’ set out in the PIP Framework and the Standard Material Transfer Agreements that have been completed so far. This research also introduces a right-to-health dimension to the literature on the PIP Framework, providing an evaluation of the Framework, and the extent to which it can be relied upon by developing states in order to discharge their international obligations in this regard during an influenza pandemic.

A clear gap in the literature concerning the TRIPS flexibilities and the procurement of pandemic influenza vaccines is that the literature does not adequately differentiate between oral solid oral drugs and vaccines. Instead, it largely relies upon the all-
encompassing (and unhelpful) terms ‘medicines’ or ‘drugs’. One argument I advance is that a more clear differentiation between oral solid oral drugs and vaccines is needed when discussing ‘access to medicines’ in the context of intellectual property: there are significant differences between drugs and biologics, and the manner in which intellectual property law can impact upon oral solid oral drugs and biologics. As the current literature does not adequately convey the differences between oral solid oral drugs and vaccines, an assumption appears to have been made that solutions that have been used to great effect to introduce generic competition are equally applicable to products such as pandemic influenza vaccines. I seek to correct this assumption.
In this chapter I argue that the traditional manner by which states procure pandemic influenza vaccines for their population are not suitable for enabling developing states to achieve sufficient access to pandemic influenza vaccines. Therefore, developing states are unable to use these procurement methods in order to discharge their right-to-health obligations during an influenza pandemic. This chapter also argues that one of the main reasons for the traditional methods of vaccine procurement not being suitable to enable developing states to achieve sufficient vaccine is the role the Advance Purchase Agreements held by developing states have in allowing them to dominate procurement in the early stages of a pandemic. A case study of pandemic influenza vaccine procurement during 2009-H1N1 is used to demonstrate these points.

Unlike solid oral drugs, a vaccine is a biologic, meaning that it is manufactured in a living system, typically microorganisms or animal cells. In the case of pandemic influenza vaccines, the majority of the vaccines are manufactured using embryonated chicken eggs. Pandemic Influenza vaccines, like most biologics, are very large, complex molecules or mixtures of molecules, and there are currently only twenty-four manufacturers worldwide with the technological capacity, knowledge and infrastructure required in order to manufacture pandemic influenza vaccines. As a result of this, as noted at 1.3, worldwide manufacturing capacity of pandemic influenza vaccines is ‘insufficient to allow all developing states to procure sufficient

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1 Klaus Stöhr, 'Influenza vaccine production' in Robert Webster and others (eds), Textbook of Influenza (2nd edn, Wiley-Blackwell 2013) 352
2 ibid; Catherine Gerdil, 'The annual production cycle for influenza vaccine' (2003) 21(16) Vaccine 1776
3 Jeffrey Partridge and Marie Paule Kieny, 'Global production capacity of seasonal influenza vaccine in 2011' (2013) 31(5) Vaccine 728
levels of pandemic influenza vaccine in a timely manner', and falls short of the capacity required by approximately one billion doses per annum. Problems in vaccine procurement arise when a vaccine is in high demand by many states at the same time, and there is insufficient capacity to meet the demand. This is the case with pandemic influenza. In order to better understand which states gain access to pandemic influenza vaccines, and when they do so, it is necessary to first understand the methods by which states traditionally procure vaccines. From this, it is possible to determine if these methods are appropriate for ensuring that states can obtain sufficient access to pandemic influenza vaccines, in order to discharge their right-to-health obligations during a pandemic.

3.1 - The Traditional Methods of Vaccine Procurement

For the most part, vaccines are purchased by the central government of a state, typically their Department of Health. Indeed, 71% of all vaccination funding worldwide is provided by national governments. There are a number of reasons why vaccines for public health programmes are procured by the central government. First, it allows for the monitoring of vaccine administration within a population. This is particularly important when a vaccine immunises against a communicable disease which could spread rapidly amongst an unvaccinated population. Second, it allows for vaccines to be distributed to priority groups in the first instance, rather than just to those who are able to finance the vaccine. Finally, when a state is self-procuring vaccine, centralised procurement provides a state with a stronger ‘bulk buying’ negotiating position in order to achieve potential price reductions.

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4 WHO, 'Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative' (2011) <http://www.who.int/influenza_vaccines_plan/resources/h1n1_vaccine_deployment_initiative_moll.pdf>

5 WHO, 'global pandemic influenza action plan to increase vaccine supply' (WHO 2006) <http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf> 2.2.1


7 Janet Bumpers, 'Study on Comparative Efficiencies in Vaccine Procurement Mechanisms' (The World Bank 2008)
Vaccines are obtained by governments for populations using four procurement methods: self-procurement directly by the state; donations from an international organisation; procurement and administration by an international organisation; and/or procurement from other sources.

3.2.1 - Self-procurement

Self-procurement, the process of vaccines being purchased directly by governments, represents the majority of vaccines - 79%\(^8\) - procured worldwide. Self-procurement typically uses a competitive tendering process with relevant manufacturers bidding to fulfil the contract.\(^9\)

Self-procurement has a number of distinct benefits for governments, the most important of which is flexibility, allowing for the independent selection of manufacturer (which may result in the negotiation of a lower unit price, or allow for more favourable contract terms, particularly if the manufacturer is based in the state). This allows for increased responsiveness to individual health needs within a state. Such benefits may not be replicable to states who procure via donations, as they are reliant on the vaccine selection and procurement methods of the donor organisation.\(^10\)

If a government wishes to self-procure vaccines, technical elements of the procurement process, such as pre-qualification or product licensing,\(^11\) preparation of

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\(^8\) WHO-UNICEF, (n6)
\(^10\) Bumpers, (n7)
\(^11\) Vaccine manufacturers must demonstrate that their vaccines are safe and effective for human use, that they can be manufactured in a consistent manner and that they are stable. This involves the gathering of clinical data on the safety and immunogenicity of the vaccine in initial small studies, then larger human studies to further demonstrate the safety and efficacy of the vaccine. Inspection of the vaccine production facility must also occur. Each of these steps must be satisfactorily completed proving that the benefits of the vaccines outweigh its risks. – for more information see: WHO, 'guidelines on regulatory preparedness for human pandemic influenza vaccines (adopted 2007)' (2012)
bidding documents and realisation of the tender, selection of supplier, financial arrangements, and contract and quality monitoring, must be managed by the state (as opposed to the procurement agent). This requires technical knowledge in the fields of medicine and law as well as an appropriate cold-chain infrastructure to store the vaccines, the financial resources to purchase the vaccines, and an appropriate certification process for licensing biologics efficacy and safety. Such advanced infrastructure, knowledge and technical ability is beyond the capacity of many developing states, with the African Region of the WHO being considered to have the weakest infrastructure in terms of legislative framework and financing, preparedness, and public health emergency response. (If least developed states


12 Once the vaccine is licensed, post-marketing safety and efficacy studies occur once the vaccine has been administered to the human population, this measures benefits and side-effects to ensure the vaccine continues to meet the parameters established during product development, and that no further adverse side-effects have been identified in the human population: For more information on the technical elements of the influenza vaccine procurement process see: WHO, (n9) 7-9

13 "The ‘cold chain' is a term used to describe the cold temperature conditions in which certain products need to be kept during storage and distribution.....Maintaining the cold chain ensures that vaccines are transported and stored according to the manufacturer’s recommended temperature range....[a failure to store vaccines at the correct temperature]... causes deterioration of vaccines and may give rise to a loss of potency and an increase in reactogenicity" - Department of Health, 'Storage, distribution and disposal of vaccines ('The Green Book')' (HM Government 2013)


14 Alan R. Hinman, 'Perspectives on sustainable vaccine introduction' (2013) 31(3) Vaccine C8


16 Figure 5, WHO, 'Summary of the 2013 State Parties Report on the IHR Core Capacity Implementation (International Health Regulations 2005)' (2014)

<http://apps.who.int/iris/bitstream/10665/145084/1/WHO_HSE_GCR_2014.10_eng.pdf?ua=1>

17 Defined as: ‘the identification of available resources, the development of appropriate national stockpiles of resources and the capacity to support operations at the intermediate and local community/primary response levels during a public health emergency’ WHO, (ibid) 3.2.2

18 Defined as: ‘....including mapping of potential hazards and hazard sites, the identification of available resources, the development of appropriate national stockpiles of resources and the capacity to support operations at the intermediate and local community/primary response levels during a public health emergency.’ WHO, (n16) 26

19 Defined as: ‘Mechanisms for command, communications and control operations are required to coordinate and manage outbreak operations and other public health events effectively. Multidisciplinary, multisectoral Rapid Response Teams (RRT) should be established and be available 24 hours a day, 7 days a week. Appropriate case management, infection control and decontamination are key components of this capacity that need to be developed, strengthened or maintained.’ WHO, (n16) 22
are using the international organisation as a procurement agent, some degree of technical assistance may be available for such matters in some instances.\textsuperscript{20} Such technical assistance is primarily available through the GAVI Alliance, who do not provide funding or technical assistance for pandemic influenza vaccines.

3.2.2 - Donations via international organisations

As the traditional method of self-procuring vaccines on the open market from manufacturers is beyond the healthcare budgets or technical ability of many developing states,\textsuperscript{21} a number of non-governmental, and inter-governmental organisations provide vaccines to governments, such as the GAVI Alliance,\textsuperscript{22} World Health Organisation,\textsuperscript{23} and UNICEF.\textsuperscript{24} International organisations acquire vaccines through a number of routes: donations from manufacturers\textsuperscript{25} or states,\textsuperscript{26} purchasing directly from the manufacturers;\textsuperscript{27} or by acting as procurement agents\textsuperscript{28} using

\begin{itemize}
\item WHO, (n4)
\item WHO, (n4) At 8-19 which outlines the donations made by Australia, the USA, UK, Norway, Canada Germany and Japan during 2009-H1N1
\item For a breakdown of vaccine purchases made by UNICEF see UNICEF, (n24)
\item A procurement agent is an organisation that purchase vaccines on behalf of a state or group of states using finances provided by the state on a pooled procurement process. A procurement agent may also be involved in identifying the appropriate manufacturer, licensing, and storage and delivery of the vaccine – The World Bank, Procurement of health sector goods (Pharmaceuticals, Vaccines, and Condoms) (3rd edn, World Bank Publications 2006) 27
\end{itemize}
finances provided by the states on whose behalf they are procuring.\textsuperscript{29} Vaccines are then provided to developing states that lack the capacity to self-procure.

A key benefit of international organisations procuring vaccines is that they are able to place orders on behalf of several states, or entire regions, purchasing a much larger number of doses than individual states. This generally results in increased negotiating leverage, leading to a reduced price per unit.\textsuperscript{30} However, states that are reliant upon international organisations to procure vaccines on their behalf may be at a disadvantage when compared to self-procuring states, given that their ability to immunise their population is directly linked to the ability of international organisations to procure vaccines. This hinders such states’ abilities to fulfil their priorities and targets for immunisation in their territory. While procurement via international organisations may be very useful for states in relation to many vaccines, this will not necessarily be the case during influenza pandemics.

Traditionally during a pandemic, international organisations have been heavily reliant upon the goodwill of states with excess vaccine or manufacturers for donations of vaccines. However, during a pandemic that has the potential to affect all states, those states that have received vaccine may be reluctant to donate or sell them, because they wish to reserve them for their own populations.\textsuperscript{31}

3.2.3 - Procured and administered by international organisations

In some instances, international organisations procure the vaccines and administer them to populations directly.\textsuperscript{32} This predominantly occurs when a state lacks the

\textsuperscript{29}See for example the use of The Pan American Health Organisation (PAHO) EPI Revolving Fund to purchase vaccines for 35 developing states in Latin America and the Caribbean outlined in: Denise DeRoeck and others, 'Regional group purchasing of vaccines: Review of the pan American health Organisation EPI revolving fund and the gulf cooperation council group purchasing program' (2006) 21(1) The International Journal of Health Planning and Management 23

\textsuperscript{30}Heinz-J Schmitt and others, 'Child vaccination policies in Europe: a report from the Summits of Independent European Vaccination Experts' (2003) 3(2) The Lancet Infectious Diseases 103; Denise DeRoeck and others (ibid)

\textsuperscript{31}See 3.4.1 for a discussion of this during 2009-H1N1

necessary infrastructure to administer the vaccines, such as cold chain storage, which would prevent them from being able to safely or effectively transport and store the vaccines at required temperatures.

In these cases the procurement methods of an international organisation are used in the same manner as outlined above, but rather than providing vaccines to a government for administration, representatives of the international organisation coordinate, manage and administer the vaccines to the population.

3.2.4 - Procured via other sources

Vaccines are predominantly acquired via government self-procurement or donations from international organisations. Some vaccines are acquired by other methods, such as inter-state donations and inter-state purchasing. Inter-state donations are made directly from one state to another, without using an international organisation as a procurement agent. Inter-state sales of vaccines are quite rare, although they did occur during the 2009-H1N1 influenza pandemic. During 2009-H1N1 28% of vaccines were procured via other sources, although it should be noted that this figure is not broadly representative of influenza vaccine procurement methods, as the majority of states did not use this as a procurement method. Despite this, over 80% of the 193 million doses procured in the Western Pacific Region were procured using this

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33 Dipika M Matthias and others, 'Freezing temperatures in the vaccine cold chain: A systematic literature review' (2007) 25 Vaccine 3980
34 For example, see report on MSF’s Cholera vaccination campaign in Guinea: Iza Ciglenecki and others, ‘Feasibility of Mass Vaccination Campaign with Oral Cholera Vaccines in Response to an Outbreak in Guinea’ (2013) 10(9) PLoS Medicine
35 During the 2009-H1N1 outbreak approximately 28% of all doses were procured via ‘other sources’;
36 The WHO Western Pacific Region has 27 member states, for more information on membership see: WHO, 'Regional office for the western pacific' (12 January 2016) <http://www.who.int/about-regions/wpro/en/>
method, while the African, European, and South East Asian states procured between 0-0.4% of their vaccines from other sources.

Germany, France, and the Netherlands each had Advance Purchase Agreements in place for the supply of PIV, and received large quantities of the vaccine in October 2009. In November 2009 the Netherlands announced the sale of fifty-five per cent of the vaccines for 2009-H1N1 that they had procured via their Advanced Purchase Agreement; the following month Germany placed just over forty per cent of their APA allocation on the open market; and in January 2010 France announced that ‘part’ of their allocation would be sold to other states. 2009-H1N1 was not as severe as initially anticipated, vaccine uptake was low in these states, and only a one-dose vaccination strategy was required to provide immunity; as a result there were excess vaccine doses in several states who had procured vaccine early on in the pandemic. Such factors clearly eased governments’ decision to sell, or donate, purchased vaccines. In the event of a more severe pandemic in the future with higher mortality rates, or one that requires a two-dose strategy, demand could easily outstrip supply of vaccines, leaving states unwilling to sell or donate vaccine.

This strong position which developed states were in during 2009-H1N1, of having excess vaccine to sell or donate in the early part of the pandemic, was created by the Advance Purchase Agreements these states had with the manufacturers of pandemic influenza vaccines. The next section considers these Agreements in more detail,

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37 The WHO Africa Region has 47 member states, for more information on membership see: WHO, Regional Office of the African region (20 March 2008) <http://www.afro.who.int/en/countries.html>
38 The WHO European Region has 53 member states, for more information on membership see: WHO, Regional Office of the European Region (17 March 2016) <http://www.euro.who.int/en/countries>
39 The WHO South East Asia Region has 11 member states, for more information on membership see: WHO, Regional Office of the South-East Asian Region (9 March 2016) <http://www.searo.who.int/en/countries/en/>
40 WHO, (n35)
41 See 3.3 for an explanation of what Advance purchase Agreements are, how they work, and the impact they have on procurement of pandemic influenza vaccines.
42 BBC, ‘France sells off surplus swine flu vaccine’ BBC Health (3 January 2010) <http://news.bbc.co.uk/1/hi/health/8438663.stm>
43 Ibid.
44 Ibid.
analysing which states have them; what terms these Agreements have; and what impact these Agreements have on procurement of influenza vaccines by developing states during a pandemic.

3.3 - Advance Purchase Agreements and Vaccine Procurement
APAs provide an alternative to standard procurement methods for governments. APAs for vaccine procurement take the form of ‘sleeping contracts’; that is, a contract between two parties (in this case, a vaccine manufacturer and a government) which lays dormant and unenforceable until triggered by a pre-determined event, at which stage it becomes legally binding.46 APAs allow governments to reserve doses of vaccine to treat a disease sub-type which may not have yet come into existence.

3.3.1 - Traditional Advance Purchase Agreements
Typically APAs do not reserve or guarantee an in-demand medicine; APAs are more commonly used to stimulate research and development for a drug to combat neglected diseases.47 When consumers, be they national governments or individuals, are unable to afford to purchase medicines, very little commercial research is focused on developing medicines for these communities. Such is the case regarding tropical diseases, or diseases prevalent in developing states; due to the lack of economic incentives for drug manufacturers.48 Between 2000 and 2009, of the 221 new drug compounds which were licensed worldwide, only twenty three were for the treatment of tropical diseases.49 APAs attempt to counter this trend as the sponsor of the agreement commits to fully or partially funding purchases of a product, providing it meets specified conditions. For example, the Center [sic] for Global Development has committed to purchase US$3billion worth of any new vaccine that can be developed

47 Michael Kremer and Rachel Glennerster, (ibid)
49 Joshua Cohen, Maria Staroselsky Dibner, and Andrew Wilson, 'Development of and access to products for neglected diseases' (2010) 5(5) PLoS ONE e10610
that immunises against malaria.\textsuperscript{50} The sponsor makes a commitment to purchase a set number of doses at a set price, stimulating the research and development into a product which would not usually warrant research from a commercial perspective, due to the limited market for the end product.

3.3.2 - \textit{Advance Purchase Agreements for Pandemic Influenza}

APAs for PIVs allow states to guarantee priority access to a vaccine, before it has been manufactured. For example, the United Kingdom entered into a number of APAs in 2007 for the supply of vaccines to protect against pandemic influenza if a pandemic were to occur in the future; these contracts were not activated until May 2009.\textsuperscript{51} The APAs that the UK had in place before the 2009-H1N1 pandemic allowed the government to purchase between 30 million and 132 million doses.\textsuperscript{52} The minimum number of vaccines procured via an APA appears to have some degree of flexibility. When it became apparent that the 2009-H1N1 pandemic was not as severe as anticipated, a number of states with APAs in place attempted to reduce the quantity of vaccine guaranteed by their APA. Of the eleven that attempted to reduce their allocation, all but two were allowed to do so by the manufacturer.\textsuperscript{53}

Advance Purchase Agreements for PIVs appear to be widespread amongst developed states; during 2009-H1N1 twenty states had APAs in place. Within the European Union alone, sixteen states had an APA in place prior to start of the outbreak; eleven of these states had an APA with one manufacturer, four had APAs with two manufacturers and one state had agreements with three manufacturers.\textsuperscript{54} Outside of the European Union


\textsuperscript{52} Parliamentary Office for Science and Technology, ‘Post note; H1N1 ‘Swine Flu’ Vaccine: number 331’ <http://www.parliament.uk/briefing-papers/POST-PN-331.pdf>


\textsuperscript{54} Ibid.
APAs were activated by Canada, Switzerland, America, and New Zealand during 2009-H1N1. After 2009-H1N1 further developed states have entered into Advance Purchase Agreements for the supply of influenza vaccine during a future pandemic.

In terms of pandemic preparedness and response, such a degree of flexibility was clearly highly beneficial to states with Agreements in place during 2009-H1N1, allowing a number of states to guarantee the delivery of the maximum number of doses during a particularly severe pandemic, and to reduce their number of guaranteed doses during a less severe pandemic.

3.3.3 - Maintaining Advance Purchase Agreements

Advance Purchase Agreements for the supply of PIVs are signed on a risk mitigation basis. States seek to alleviate or minimise the impact from a disease which is not yet present in the territory of the government signing the Agreement. Such Agreements are signed months or years before the contract might need to be fulfilled by the manufacturer. During this time the Agreement is dormant, until such time as an influenza virus circulating in the human population is declared to be a pandemic, by the WHO declaring the virus to be Phase Six. This Phase Six declaration activates the Agreement.

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59 Sam Halabi, ‘the Uncertain Future Of Vaccine Development And Deployment For Influenza Pandemics (Briefing Paper No. 8)’ (Georgetown University 2014) <https://www.law.georgetown.edu/oneillinstitute/resources/documents/Briefing8HalabiRevised4162014.pdf>
60 More information on Phase Six declarations, and the activation of Advance Purchase Agreement is provided at Figure 1. below.
The maintenance and activation of the UK’s APAs for PIVs became the subject of scrutiny in the House of Lords Science and Technology Committee report into the UK pandemic preparedness plans. During the Committee’s hearings the then Minister of State for Health Services, Rosie Winterton MP, discussed APAs in the context of pandemic preparedness for the UK. At the time of giving evidence, the Agreements were not yet in place, although negotiations were in their final stages.

It was confirmed that while the vaccines for pandemic influenza reserved via an APA are paid for at the point of purchase during a pandemic, during the dormant phase the Agreements are maintained by the government paying ‘Pandemic Preparedness Fees’ to maintain the contract. At the time of giving evidence it was ‘rather difficult to give exact figures’ as to the cost of the Pandemic Preparedness Fee associated with maintaining the UK’s APA, as negotiations were ‘still ongoing’. For the purposes of this research, a Freedom of Information request made to the Department of Health to determine the cost of the Pandemic Preparedness Fee was refused on the basis that making such information available could ‘potentially limit the contractor’s negotiating position with other customers if this information was put in the public domain’.

APAs for pandemic influenza vaccines are always a contract between a national government and a manufacturer. While the exact costs of maintaining an APA by way of a Pandemic Preparedness Fee are not publicly available, a system whereby states are required to pay to maintain contracts for vaccines that may not be required over the course of the contract’s life may be financially prohibitive for many developing states. Equally, spending on a Pandemic Preparedness Fee may not be considered a priority for developing states with limited healthcare budgets. Despite the fact that the WHO has encouraged use of APAs by developing states in order to ‘increase equity

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62 Rt Hon Rosie Winterton MP, ibid 88-89
63 Ibid, Q225 & Q231
64 Ibid, Q231
in supply and delivery of pandemic vaccines’, and commitments have been made from pharmaceutical companies such as GlaxoSmithKline that they ‘would supply [vaccines via an APA] at tiered prices, based on the gross national income of the nation’, it appears unrealistic to expect states with limited healthcare budgets (a fact noted by GlaxoSmithKline) to spend a large proportion of that budget on maintaining a contract that guarantees vaccines for a pandemic which may not occur in the next five, ten, or even twenty years. This is particularly notable given that the per capita government expenditure on healthcare is an average of $12USD in least-developed states, $56.8USD in low-middle income (developing) states, $275USD in upper-middle income (developing) states and $2,186USD in developed states.

3.3.4 - Activation of Advance Purchase Agreements

The process by which Advance Purchase Agreements are activated during a pandemic is directly linked to the pandemic’s status. As part of their surveillance and response mechanisms for influenza pandemics the WHO provides phases of pandemic alert between one and six with Phase One being the least severe and Six being the most severe. Within the pandemic period itself, there are three phases of pandemic activity, Phase Six pandemic activity, Post-Peak Period and Post-Pandemic Period.

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68 Memorandum By GlaxoSmithKline, ibid, 3
69 Whether the alternative methods of vaccine procurement adequately provide developing states with access is discussed in Chapters Five and Six respectively.
### Fig 1. Phases of an influenza pandemic

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>No viruses circulating among animals have been reported to cause infections in humans.</td>
</tr>
<tr>
<td>Phase 2</td>
<td>An animal influenza virus circulating among domesticated or wild animals is known to have caused infection in humans, and is therefore considered a potential pandemic threat.</td>
</tr>
<tr>
<td>Phase 3</td>
<td>An animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks. Limited human-to-human transmission may occur under some circumstances.</td>
</tr>
<tr>
<td>Phase 4</td>
<td>Verified human-to-human transmission of an animal or human-animal influenza reassortant virus able to cause ‘community-level outbreaks’. The ability to cause sustained disease outbreaks in a community marks a significant upwards shift in the risk of a pandemic</td>
</tr>
<tr>
<td>Phase 5</td>
<td>Human-to-human spread of the virus into at least two countries in one WHO region. While most countries will not be affected at this stage, the declaration of Phase 5 is a strong signal that a pandemic is imminent and that the time to finalize the Organisation, communication, and implementation of the planned mitigation measures is short.</td>
</tr>
<tr>
<td>Phase 6</td>
<td>Community level outbreaks in at least one other country in a different WHO region in addition to the criteria defined in Phase 5. Designation of this phase will indicate that a global pandemic is under way.</td>
</tr>
<tr>
<td>Post Peak Period</td>
<td>Pandemic disease levels in most countries with adequate surveillance will have dropped below peak observed levels. The post-peak period signifies that pandemic activity appears to be decreasing; however, it is uncertain if additional waves will occur and countries will need to be prepared for a second wave.</td>
</tr>
<tr>
<td>Post Pandemic Period</td>
<td>Influenza disease activity will have returned to levels normally seen for seasonal influenza. It is expected that the pandemic virus will behave as a seasonal influenza A virus.</td>
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</tbody>
</table>


Advance Purchase Agreements cannot be activated by governments until after the WHO has declared that the circulating virus has become a pandemic, having entered ‘Phase Six’, although the government is of course free to enter into further contracts prior to the Phase Six declaration. It is worth noting however, that because of the heavy time delay in manufacturing pandemic influenza vaccines it is unlikely. However, once Phase Six has been declared APA orders are completed prior to any other orders in the early stages of a pandemic, therefore this contract term does little to prevent states with APAs in place from dominating procurement of the vaccine in the early stages of a pandemic.

While states with APAs in place obtain priority access to vaccines during Phase Six of an influenza pandemic, they do not gain priority over other states with APAs. As was noted by the Parliamentary Office for Science and Technology,

> [t]he first doses produced will be shared out amongst all countries with sleeping contracts, in proportion to the number of doses which each has reserved. It will take approximately one year for the UK to obtain all of its reserved doses.

A 2009 survey by the World Health Organisation of PIV manufacturers asked whether these manufacturers would be willing to reserve 10% of real-time production for purchase by United Nations agencies. Many producers were unable to meet the request to set aside 10% of their production capacity, because they were constrained by meeting the volume of vaccines reserved by APAs.

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73 Rt. Hon Alan Johnson, ibid.

74 Rt. Hon Alan Johnson, ibid.

75 Nicolas Collin and Xavier de Radiguès, 'Vaccine production capacity for seasonal and pandemic (H1N1) 2009 influenza' (2009) 27(38) Vaccine 5184
It is worth reiterating that within the context of the right-to-health, two of the ‘core obligations’ of General Comment 14 of the ICESCR states are relevant to access to pandemic influenza vaccines:

States must ensure provision of health care, including immunization programmes against the major infectious diseases.\textsuperscript{76}

The creation of conditions which would assure to all medical service and medical attention in the event of sickness...includes the provision of equal and timely access to basic preventive, curative, rehabilitative health services and...the provision of essential drugs.\textsuperscript{77}

In order to have been considered to have discharged these obligations, states must achieve sufficient access to pandemic influenza vaccines, which is based on two interlocking factors: vaccination levels and vaccination timings.

Advance Purchase Agreements for pandemic influenza vaccine appear to put the developing states that have such agreements in a position whereby they are able to meet their right-to-health obligations in respect of pandemic influenza vaccines. On the point of appropriate levels of pandemic influenza vaccines, the APAs which the UK has in place allows them to reserve up to two doses for 100\% of their population - which is clearly sufficient to meet the 33\% community immunity level required in order to discharge the vaccination level element of the right-to-health obligation. While data is not available on the number of doses reserved by other APAs held by developing states, it is reasonable to assume that these agreements secure sufficient vaccine to meet the 33\% target required in order to discharge the duty. Moreover, as APAs guarantee priority access to vaccine during an influenza pandemic clearly satisfies the vaccination timings requirements.

Conversely, it is clear that the APAs held by developed states diminish developing states’ ability to achieve sufficient access to influenza vaccines during a pandemic, and thereby limit the opportunities that developing states have to discharge their right-

\textsuperscript{76} para. 36, General Comment 14
\textsuperscript{77} para. 17, General Comment 14
to health obligations during a pandemic. This negative impact is manifested in two ways. First, because APA orders must be fulfilled prior to any other contracts, this means that there is a significant time delay in developing states procuring pandemic influenza vaccines. The ‘vaccination timings’ element of the sufficient access criterion is not being met by developing states as a direct result of the APAs held by developed states. Second, the number of doses that developing states are able to procure is greatly limited by the terms of the Advance Purchase Agreements, which reduces the vaccination levels developing states can hope to achieve during an influenza pandemic - particularly in the early stages.

The case study of vaccine procurement during 2009-H1N1 below outlines the levels of vaccine that states were able to procure during 2009-H1N1 and at what point during the pandemic the vaccine was procured. Using this data, I argue that no developing states were able to meet their right-to-health obligations during 2009-H1N1, failing to meet the sufficient levels, and in sufficient time components of the obligation.

3.4 – Vaccine Procurement During 2009-H1N1

During an influenza pandemic, states are significantly more likely to obtain vaccines, and obtain them earlier in the pandemic, if they self-procure: four times as much vaccine was self-procured than was donated during 2009-H1N1, with donated vaccine arriving in states at least four months after self-procuring states. The fundamental problem facing many developing states reliant upon international organisations for vaccine donations is that the majority of this finite amount of PIVs that can be manufactured in the first year is already reserved and guaranteed through Advance Purchase Agreements held by many developed states. This leaves

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78 WHO, (n35)
79 Jeffrey Partridge and Marie Paule Kieny, (n3)
80 Germaine Hanquet and others, ‘Lessons learnt from pandemic A(H1N1) 2009 influenza vaccination. Highlights of a European workshop in Brussels (22 March 2010)’ (2011) 29(3) Vaccine 370; David Fidler, (n45); Marcel Verweij, ‘Health Inequities in Times of a Pandemic’ (2009) 2(3) Public Health Ethics 207
developing states and international organisations reliant upon donations from vaccine manufacturers or states with excess vaccines.

During 2009-H1N1, many Advance Purchase Agreements held by developed states were triggered, providing them with guaranteed priority access to vaccines, and these states also bought vaccine to cover a large proportion of their population in the early stage of the 2009-H1N1 influenza pandemic. Vaccine manufacturers were unable to take or complete orders from many developing states, or international organisations on behalf of developing states, in the early stages of manufacturing. It was estimated that it would take approximately one year for vaccine manufacturers to complete all APA orders, if no states reduce their APA allocation, because APA orders dominate the limited manufacturing capacity. This means that while the first vaccination was administered in a developed state six months after the pandemic was announced, no developing state was able to procure vaccine for a further four months.

Australia, Canada, USA, the UK, Japan, France and the Netherlands were some of the first states to receive vaccine during 2009-H1N1, and in an attempt to increase access to vaccines for developing states the WHO requested these states donate a proportion of the vaccine to them to distribute to developing nations at risk of the outbreak. However, it was noted that ‘WHO and developing countries had little leverage to influence developed countries other than rhetoric about equity, justice, and solidarity’. Furthermore, the pledges which were made by manufacturers during

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81 Collin and de Radiguès, (n74)
82 Parliamentary Office for Science and Technology, (n51)
83 Ibid.
84 Pernille Jorgensen and others, 'Unequal access to vaccines in the WHO European Region during the A(H1N1) influenza pandemic in 2009' (2013) 31(38) Vaccine 4060 discusses the manner in which states within Europe with APAs in place dominated the production capacity in the early stages of the 2009-H1N1 pandemic
85 Jane Parry, 'China gears up for swine flu vaccination as virus spreads inland' (2009) 339(sep14 2) BMJ
86 Jeffrey Partridge and Marie Paule Kieny, (n3)
87 Marcel Verweij, (n80)
88 WHO, (n35) at v
89 David Fidler, (n45)
the 2009-H1N1 outbreak were made without specifying a delivery date or timeframe, despite the fact that manufacturers were already producing and shipping vaccine to self-procuring states when the pledge to donate was made.\(^90\) This resulted in the donated vaccines arriving at least four months later during the post-peak pandemic phase, when the vaccine has reduced impact on a population due to the number of people already exposed to the outbreak.\(^91\)

Despite the fact that nearly 120 million doses were pledged to the WHO by the USA, Australia, Brazil,\(^92\) France, Italy, New Zealand, Norway, Switzerland, and the UK,\(^93\) they only began shipping doses after it became apparent that a one-dose regime would suffice to immunise adults, which effectively doubled the amount of vaccine available,\(^94\) and data revealed that the threat posed by the 2009-H1N1 was not as severe as first thought.\(^95\) The outcome of the two major studies considering the efficacy of a one-dose strategy was made available on 17\(^{th}\) December 2009,\(^96\) and the first shipments of donated vaccine arrived in recipient states in late January 2010,\(^97\) despite the fact that it had been available in developed states, in large quantities, since

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\(^90\) WHO, (n35)


\(^92\) It is worth noting that Brazil is something of an anomaly in this regard. Firstly, Brazil is not a developed state, it did not have an APA with an established manufacturer, and yet it received sufficient access to pandemic influenza vaccine very early on during 2009-H1N1. This is because Brazil is the only developing state that has a nationalised pharmaceutical manufacturer that has the capacity to manufacturer pandemic influenza vaccines. This enabled Brazil to respond quickly to an emerging influenza pandemic. For more information see: 7.1.1

\(^93\) WHO, (n35)

\(^94\) WHO, (n35)


\(^96\) Michael E. Greenberg and others, (ibid) & Tristan W. Clark and others, (ibid)

October 2009. It appears as if the move to a one dose strategy, giving some developed states excess doses of the vaccine, was key in the decision making process of some donor states: US Health and Human Services Secretary Kathleen Sebelius told the Associated Press that ‘as the US is flush enough [with vaccines, now that a one-dose strategy will suffice] the long-promised donation of 25 million doses to developing countries is ready to ship.’

Fig 2. Distribution and sources for pandemic A(H1N1) 2009 vaccine doses, by region†

<table>
<thead>
<tr>
<th>Region</th>
<th>Total no. of doses received from all sources</th>
<th>% of vaccine received as deployment from WHO</th>
<th>% of vaccine procured through government purchases</th>
<th>% of vaccine procured from other sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>33,955,078</td>
<td>94.5%</td>
<td>6.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>AMR</td>
<td>143,968,840</td>
<td>7.0%</td>
<td>70.9%</td>
<td>14.0%</td>
</tr>
<tr>
<td>EMR</td>
<td>10,784,000</td>
<td>40.3%</td>
<td>42.9%</td>
<td>16.8%</td>
</tr>
<tr>
<td>EUR †</td>
<td>230,715,990</td>
<td>0.8%</td>
<td>98.8%</td>
<td>0.4%</td>
</tr>
<tr>
<td>SEAR</td>
<td>23,110,200</td>
<td>91.2%</td>
<td>8.7%</td>
<td>0.1%</td>
</tr>
<tr>
<td>WPR</td>
<td>193,089,000</td>
<td>4.5%</td>
<td>15.1%</td>
<td>80.4%</td>
</tr>
<tr>
<td>Total</td>
<td>634,702,320</td>
<td>12.3%</td>
<td>59.4%</td>
<td>28.3%</td>
</tr>
</tbody>
</table>

† Only countries that participated in the 2010 WHO H1N1 Survey are tallied here. In total, 1.1 billion doses of vaccine were acquired by countries.
† Total number of doses received from all sources represents donations to countries in all regions eligible to receive WHO-donated vaccines combined with vaccine donations from other sources and vaccines procured through government purchases.

Table reproduced from: World Health Organisation, ‘Global Survey on National Vaccine Deployment and Vaccination Plans for Pandemic A(H1N1) 2009 Vaccine’ (2010)

AFR – African Region; AMR - Region of the Americas; EMR – Eastern Mediterranean Region; EUR – European Region; SEAR – South- East Asian Region; WRP – Western Pacific Region

As can be seen from the table above, during the 2009-H1N1 pandemic over 634 million doses of vaccine were procured. The majority of the vaccines obtained by states were from central government purchases (59.4%), with 28.3% vaccines being procured from other sources (inter-state sale donations), and 12.3% of vaccines

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100 Table replicated from: WHO, (n35)
deployed internationally being donated via the WHO’s Vaccine Deployment Initiative. The VDI was a department within the WHO charged with managing and coordinating the global donation of 2009-H1N1 vaccines, and the resources needed to deploy them, and was created specifically to manage the distribution of vaccines for 2009-H1N1.\textsuperscript{101} During the 2009-H1N1 outbreak the WHO distributed 78 million doses of PIV, however over 30 million of these doses were delivered to developing states in the ‘post-pandemic phase’; when the virus’ transmission levels and intensity is considered more akin to a seasonal influenza outbreak than that of a pandemic.\textsuperscript{102} During these three months, a further 7000 deaths were recorded from 2009-H1N1 by the World Health Organisation, predominantly in developing states.\textsuperscript{103} While this is a relatively low figure when compared with the population of developing states, it is worth bearing in mind that 2009-H1N1 was a particularly mild pandemic,\textsuperscript{104} and during a more severe pandemic the number of deaths during this period would certainly be higher.

Although only 12.3% of vaccines procured worldwide were donated by the WHO, donations accounted for 94.5% of the African Regions’ vaccines, 91.2% of vaccines used in the South-East Asia Region, but only 4.5% in the Western Pacific region and 0.8% in Europe. Although all regions acquired some vaccines via self-procurement, this ranged from 98.8% in Europe, to only 6.5% in Africa.

The differing procurement methods used by developing and developed states appears problematic when we consider the relative successes of states reliant upon these

\begin{footnotesize}
\item[101] More information on the VDI and its working during 2009-H1N1 can be found at: WHO, (n35)
\item[104] having a mortality to infection rate of 0.03% - WHO, ‘Pandemic (H1N1) 2009 - update 100’ (World Health Organisation, 14 May 2010) <http://www.who.int/csr/don/2010_05_14/en/> which is relatively low when compared to <0.1% for Hong Kong Flu <0.1% for Asian Flu and >2.6% for Spanish Flu Edwin D. Kilbourne, ‘Influenza Pandemics of the 20th Century’ (2006) 12(1) Emerging Infectious Diseases 9; Jeffery K. Taubenberger and David M. Morens, ’1918 Influenza: the Mother of All Pandemics’ (2006) 12(1) Emerging Infectious Diseases 15; Bruno Lina, ‘History of Influenza Pandemics’ in Didier Raoult and Michel Drancourt (eds), Paleomicrobiology: Past human infections (Springer 2008) 486
\end{footnotesize}
methods to procure vaccines during an influenza pandemic. Self-procurement dominated the supply of vaccines during 2009-H1N1, particularly in the early stages of the pandemic, and a state was much more likely to obtain vaccines if they self-procured than if they were reliant upon donations. This can be demonstrated by considering the European and African Regions’ experience during 2009-H1N1 who at the time of the outbreak had fairly similar populations of around 800 million people. The procurement methods used by the states within these regions differed significantly, and with it the likelihood of states achieving sufficient access to pandemic influenza vaccines, in order to discharge their right-to-health obligations.

The European Region of the WHO consists entirely of developed states. These states procured 98.8% of their vaccines via the self-procurement method. Conversely, the African Region of the WHO consists just of developing states, and 6.5% of vaccines were self-procured; in Africa 93.5% of the vaccines used were donated by the WHO. There appears to be a correlation between the procurement method used by states, and the vaccination coverage achieved. While overall vaccination coverage in both of these regions was lower than the 33% target, states within the European Region procured enough to immunise 27.5% of their population on a one-dose strategy, whereas in the African Region, only 3.9% of the population was immunised, significantly lower than the 33% threshold required to provide the benefits of community immunity and meet the vaccine level required in order to meet the access-to-medicine component of the right-to-health obligation during an influenza pandemic.

It is worth noting, however, that a number of states within the European Region reduced their order with the PIV manufacturers; therefore, it is likely that vaccination coverage would have been higher in states within the European Region had they not elected to reduce their allocation. Moreover, as over 90% of the vaccines procured by

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106 WHO, (n35), 15
107 Ibid, 15
states in the African Region were donated by the WHO VDI, there was a significant time delay in these states receiving their vaccine, with no vaccine being distributed by the WHO VDI until at least four months after it was available in developed states. This again has implications for the extent to which developing states can be said to have discharged their right-to-health obligations, because the vaccine is not being made available in developing states in the same timeframe as it is in developed neighbours, and therefore the ‘sufficient time’ component has not been met.

3.4.1 – Limitations

As this section only considers vaccine procurement during 2009-H1N1, it may have limited predictive power. Global manufacturing capacity has expanded since 2009; the most recent survey of vaccine manufacturers shows capacity grew from nearly 800 million doses per annum in 2009,\(^{108}\) to 1420 million doses per annum at the most recent estimation in 2011.\(^{109}\) In addition, as 2009-H1N1 was not as severe as anticipated, this increased the number of vaccines available for developing states via the VDI (although there is no guarantee that developed states will behave in this manner should the next pandemic be more severe: developed states may be less likely to donate vaccine). Further, the policy environment for donation of pandemic influenza vaccines by manufacturers to the WHO has changed since 2009-H1N1, predominantly due to Standard Material Transfer Agreements introduced by the Pandemic Influenza Preparedness Framework. These SMTAs have been presented in the literature as representing a fundamental shift in the ability of the WHO to procure vaccine on behalf of developing states,\(^{110}\) though this research has found that it is unlikely the PIP Framework represents such a fundamental shift in procurement of pandemic influenza vaccines for developing states, due to the limited impact the

\(^{108}\) Jeffrey Partridge and Marie Paule Kieny, ‘Global production of seasonal and pandemic (H1N1) influenza vaccines in 2009–2010 and comparison with previous estimates and global action plan targets’ (2010) 28(30) Vaccine 4709

\(^{109}\) Jeffrey Partridge and Marie Paule Kieny, (n3)

\(^{110}\) See 2.2 for an analysis of this literature.
Framework stockpile will have on future procurement by developing states, as I argue in 4.3-4.6.\textsuperscript{111}

However, some generalisations from vaccine procurement during 2009-H1N1 may be justified. First, while manufacturing capacity has grown since 2009, 75\% of this capacity is dedicated to meeting the needs of the ‘Northern Hemisphere’,\textsuperscript{112} which is predominantly made up of developed states. Second, while there have been changes to the policy environment for vaccine procurement since 2009, arguably these will have limited impact overall,\textsuperscript{113} meaning procurement during the next pandemic will occur in a similar manner to 2009-H1N1. Third, while influenza vaccine manufacturing capacity may have grown by 440 million doses between 2009 and 2011, human population grew by 170 million people from 6.81\textsuperscript{114} billion to 6.98 billion\textsuperscript{115} in the same period, with population growth predominantly occurring in least-developed states.\textsuperscript{116} These factors combined mean that, when the next influenza pandemic occurs, demand will once again outstrip supply amongst developing nations, in much the same way as occurred during 2009-H1N1.

3.5 - Conclusion

During the 2009-H1N1 pandemic influenza outbreak, there were significant disparities in vaccination coverage between those developed states that self-procure their vaccines, and those developing states that were reliant upon donations from international organisations. In short, developed states that self-procure, particularly those with Advance Purchase Agreements, are able to obtain sufficient access to

\textsuperscript{111} The use of SMTAs to procure vaccine on behalf of developing states, is considered in more depth at ‘Chapter Five: The Pandemic Influenza Preparedness Framework’.
\textsuperscript{112} Jeffrey Partridge and Marie Paule Kieny, (n3), at table 2
\textsuperscript{113} The impact of Standard Material Transfer Agreements to procure vaccine on behalf of developing states, is considered in more depth at ‘Chapter Six: The Pandemic Influenza Preparedness Framework’; for general comments on this point see: Nicole Jefferies, ‘Levelling the playing field? Sharing of influenza viruses and access to vaccines and other benefits’ (2012) 20(1) Journal of law and medicine 59; Catherine Rhodes, ‘Sovereign Wrongs: Ethics in the Governance of Pathogenic Genetic Resources’ (2015) 3 Ethics in Biology, Engineering and Medicine 97
\textsuperscript{116} Population Reference Bureau, (n114) 6
pandemic influenza vaccines (in both levels and timings) in order to discharge their right-to-health obligations, whereas developing states are not. Using the traditional methods of pandemic influenza procurement, developing states do not procure enough vaccines to meet the ‘vaccination levels’ requirement of ‘sufficient access’, and that vaccine which they do procure is procured too late in the pandemic to meet the ‘vaccination timings’ element of sufficient access. This means that developing states are failing to discharge their core right-to-health obligations under the ICESCR by failing to provide an ‘immunization programme against major infectious diseases’117, and failing to ‘provide essential drugs’118 for their population during an influenza pandemic.

The following chapters consider how developing states may make use of two mechanisms that could potentially improve the procurement of PIV by developing states, and in doing so, would enable these states to meet their right-to-health obligations regarding access to pandemic influenza vaccines. The two mechanisms to be examined are the PIP Framework,119 which has been a major development in procurement of pandemic influenza vaccines post-2009-H1N1, and the TRIPS Agreement, the flexibilities of which have been presented as potential solutions to the problems in access to medicines in the developing world. These instruments are examined in order to determine whether the provisions of these international agreements can be used by developing states to improve their procurement of influenza vaccine during a pandemic, beyond that which they can be expected to achieve when using the traditional procurement methods outlined in this chapter. Particular focus is given to whether either of these mechanisms could be used by developing states to enable them to meet the ‘sufficient access’ requirements outlined at the introduction, which, for the purpose of this research, would be considered sufficient to enable developing states to have discharged their right-to-health obligations.

117 para. 33, General Comment 14
118 para. 36, General Comment 14
119 WHO, ‘Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits’ (2012)
CHAPTER IV –
THE PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK

This chapter argues that the PIP Framework is unlikely to have a significant impact on procurement of PIV by developing states during the next pandemic and the extent to which developing states are able to meet the requirements in order to discharge their right-to-health obligations. I argue this on the basis that the vaccine stockpile that the Framework has created is not sufficiently large to meet the demand from developing states. I also argue that because so few pandemic influenza vaccine manufacturers have committed, via an SMTA2, to supply the PIP stockpile, and those that have, have given commitments lower than those initially proposed by the WHO in the Framework, this implies that the overall impact the PIP stockpile will have on procurement of PIV is even lower than initially anticipated within the literature.

The PIP Framework was enacted by the WHO in 2011. The PIP Framework was passed in accordance with Article 23 of the Constitution of the World Health Organisation¹, meaning it takes the form of ‘soft law’ recommendations to member states², as opposed to being binding international law³. ‘Soft law’ recommendations are fairly typical for law made via the WHO: obligations are rarely provided by way of binding conventions.⁴ While the effectiveness of the WHO relying upon soft law recommendations rather than binding international law has been criticised on the basis that states tend to be more compliant with treaty obligations than soft law norms,⁵ a purported benefit of such soft law obligations is that they ‘may involve

² Article 23, ibid.
³ Legally binding obligations are approved pursuant to Article 21 of the Constitution.
greater participation of non-state stakeholders in the creation of international norms, which will correspondingly increase compliance’. This purported benefit may be translatable to the PIP Framework, which includes non-state actors within its provisions.

The Framework provides obligations and recommendations in two areas: first, the timely sharing of influenza viral samples with human pandemic potential between member States of the WHO Global Influenza Surveillance and Response System\(^7\) (GISRS); and second, the sharing of viral samples with entities that operate outside of GISRS, such as pharmaceutical and vaccine manufacturers, in return for these external entities sharing benefits with the WHO and its members.\(^8\) A major impetus for reform in the area of access to viral samples and the vaccines resulting from them was the Indonesia virus sharing incident during 2005-H5N1.

4.1 - Indonesia H5N1

In order to manufacture a PIV, the vaccine preparation must contain an element of the inactivated virus against which the vaccine inoculates.\(^9\) It is a widely held belief, at both the international and domestic level, that prompt access to viral samples from which to develop vaccines is crucial to an effective global response to pandemic

\(^6\) Dinah Shelton, 'Law, non-law and the problem of 'soft law'’ in Dinah Shelton (ed), Commitment and Compliance: The Role of Non-Binding Norms in the International Legal System (Oxford University Press, USA 2000) 4

\(^7\) GISRS means the international network of influenza laboratories, coordinated by WHO, that conduct year-round surveillance of influenza, assessing the risk of pandemic influenza and assisting in preparedness measures. The WHO GISRS comprises National Influenza Centres, WHO Collaborating Centres on Influenza, WHO H5 Reference Laboratories and Essential Regulatory Laboratories’ – definition provided at 4.3, WHO, Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits (2011) (henceforward ‘PIP Framework’)

\(^8\) Article 1(9), ibid. these benefits, are considered in more detail at Part II of this Chapter.

\(^9\) Catherine Gerdil, 'The annual production cycle for influenza vaccine' (2003) 21(16) Vaccine 1776
strains of influenza.\textsuperscript{10} The viral strains that are used in vaccine preparations are likely to have originated in a developing state, as influenza viruses tend to originate in states that are developing.\textsuperscript{11} Traditionally, when a state identifies an influenza virus of human pandemic potential, they provide samples to GISRS,\textsuperscript{12} which then identifies and characterises influenza viruses and creates and distributes virus seed strains to influenza vaccine manufacturers. These viral seed strains can then be used to develop and manufacture a vaccine.\textsuperscript{13} The virus-sharing mechanisms of GISON have been traditionally managed via practice and custom, and it has been noted that ‘[t]he norm of unconditionally sharing virus samples stood more or less uncontested for more than fifty years, until Indonesia defected from GISON\textsuperscript{14}’.

At the time of the Indonesian virus sharing incident, the most recent WHO Guidance document on virus sharing (issued in 2005) provided a list of viruses/specimens should be shipped to WHO Reference laboratories as a matter of urgency, including

\begin{quote}
[a]ll viruses that could not be typed/subtyped by the most recently updated WHO diagnostic reagents; all viruses from human cases infected by animal influenza and selected viruses from animals in areas affected by animal
\end{quote}

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\textsuperscript{12} See WHO, ‘interim global epidemiological surveillance standards for influenza’ (WHO 2012) <http://www.who.int/influenza/resources/documents/INFSURVMANUAL.pdf> for an overview of the history and work of GISRS – details relevant to this PhD are provided at Chapter V
\end{flushright}

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\textsuperscript{13} GISRS do not manufacture vaccines as their aims are to: ‘to monitor changes in antigenicity of influenza viruses; to guide the selection of strains for the annual influenza vaccine; and to provide virus samples for use in vaccine production’ – ibid at 1.1
\end{flushright}

\begin{flushright}
\textsuperscript{14} WHO: GISON is the Global Influenza Surveillance Network, the previous name for WHO-GISRS; Frank Smith, 'Insights into surveillance from the influenza virus and benefit sharing controversy' (2012) 24(1) Global Change, Peace & Security 71
\end{flushright}
influenza outbreaks; and newly isolated animal influenza viruses with a record of causing human infection and disease.  

The Guidance gave assurances that

[t]he designated WHO Reference Laboratories will seek permission from the originating country/laboratory to co-author and/or publish results obtained from the analyses of relevant viruses/samples; and, there will be no further distribution of viruses/specimens outside the network of WHO Reference Laboratories without permission from the originating country/laboratory.

In 2006, in response to the threat posed by 2005-H5N1, the World Health Assembly passed Resolution WHA59.2, which called upon member states to ‘[d]isseminate to the WHO collaborating centres information and relevant biological materials related to highly pathogenic avian influenza and other novel influenza strains in a timely and consistent manner’. While 2005-H5N1 did not actually result in a pandemic, it was at the time an ‘unprecedented [outbreak of a] highly pathogenic influenza virus that cause[d] many human fatalities and pose[d] an increasing pandemic threat’. At the time, Indonesia had the highest number of infections and deaths from 2005-H5N1. Despite this, and the established norm of viral sharing, Indonesia’s sharing of viral samples with GISRS fluctuated between openly sharing samples in the traditional manner, and refusing to share viral samples, claiming that the samples were the sovereign property of the State of Indonesia, and they were under no obligation to


16 Ibid.


19 Table A 2003-2009, WHO, ‘Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2015’ (WHO 2015) <http://www.who.int/influenza/human_animal_interface/EN_GIP_20150106CumulativeNumberH5N1cases_corrected.pdf?ua=1>
share them with the wider international community. In claiming that the viral samples were the State’s sovereign property, Indonesia sought to rely upon the UN Convention on Biological Diversity, which states that ‘access to genetic resources shall be subject to prior informed consent of the Contracting Party providing such resources,’ and any access granted ‘shall be on mutually agreed terms,’ although the legal basis for such claims in relation to viral samples has been contested.

The Indonesian Government cited an unfair lack of correlation between sharing samples with GISRS and the benefits obtained in return as the primary reason for refusing to share samples. Indonesia’s then Health Minister Siti Fadilah Supari claimed that WHO passed the samples Indonesia provided on to pharmaceutical companies to develop PIVs, who then patented the vaccine and its components, which

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21 United Nations. Convention on Biological Diversity. UN Treaty Series. 1760;143 (1993); moreover, it is also worth noting that viral samples of influenza with human pandemic potential were likely obtained by the developing state from samples taken from individual citizens. This therefore gives rise to a discussion regarding property in the body itself - and the monopolisation of tissue originating in the human body. Erin and Harris (Charles A Erin and John Harris, ‘An ethical market in human organs’ (2003) 29(3) Journal of Medical Ethics 137) have proposed what they consider to be a ‘strictly regulated and highly ethical market in live donor organs and tissue’ which would have the following characteristics: the market would be confined to a self-governing geopolitical area; Only citizens resident within the union or state could sell into the system and they and their families would be equally eligible to receive organs; There would be only one purchaser, which would buy all organs and distribute according to some fair conception of medical priority; There would be no direct sales or purchases, no exploitation of low income countries and their populations; Such a system could, if applied to pandemic influenza, lead to a scenario whereby an individual in a developing state could sell the viral samples of pandemic influenza which were extracted from them on to a vaccine manufacturer, in return for access to the resulting vaccine. Thereby guaranteeing their own right-to-health, rather than relying upon the state to do so. However, such a market would create a desert based model of allocation of vaccine - where those that have already been infected by the virus received the benefit (in this case the vaccine), or receive priority access to the benefit. This desert based model is undesirable, firstly from an ethical perspective, as I go on to argue at 8.4, but also because vaccine is only beneficial to those that have not yet been infected. It provides no immunity or benefit to those that have already been infected with the viral strain, and survived. Therefore, there is no benefit accrued under this model for the individual infected with the virus.
22 Article 15.5, ibid.
23 Article 15.4, ibid.
24 For a critical overview of Indonesia’s claim in relation to the CBD see: David Fidler, ‘Influenza Virus Samples, International Law, and Global Health Diplomacy’ (2008) 14(1) Emerging Infectious Diseases 88
developing countries are not able to afford when attempting to procure PIV for their populations.  

The basis of this claim was subsequently shown to be correct, when it was discovered that viral samples were being passed from GISRS to pharmaceutical manufacturers without consultation with, or the permission of, the originating country. 27 In Indonesia’s case, the WHO listed that H5N1 viral samples provided by Indonesia were available for transfer from GISRS to ‘institutions, companies and others interested in pandemic vaccine development’ 28. The notification stated that ‘[a]n H5N1 recombinant vaccine strain developed from A/Indonesia/5/2005, by the WHOCC in Centers for Disease Control and Prevention, Atlanta USA, is available for distribution, under a Material Transfer Agreement (MTA)’ 29. No obligations were placed on the receiving company to provide benefits to Indonesia or the WHO in return for accessing the viral sample. Vaccines to protect against A/Indonesia/5/2005 were subsequently developed by both GSK and Sanofi-Pasteur based on the samples provided by Indonesia. 30

Elbe described the change in global health diplomacy which occurred when Indonesia first claimed viral-sovereignty pandemic influenza viruses thus:

[T]hose viruses now became transformed from mere biological materials to key political ‘bargaining chips’ in the diplomatic arsenal of the Indonesian state, which it would use to further its own national interest on the international stage. 31

27 Colin McInnes and Kelley Lee, Global Health and International Relations (John Wiley & Sons 2012) 193
30 WHO, ‘Use of licensed H5N1 influenza vaccines in the interpandemic period report of the H5N1 SAGE working group to the April 2009 meeting of the strategic advisory group of experts’ (WHO 2009)<http://www.who.int/immunization/sage/SAGE_H5N1_26Mayb.pdf> 11
31 ibid.
It is quite apparent that this was also the thinking of Minister Supari when it was reported to her that the H5N1 virus in Indonesia was a novel and more virulent species of H5N1 (and thus of immense interest to those tracking the evolution of the virus and making vaccines). She described in her memoirs that ‘Supari [sic] actually felt happy because for Indonesia that now meant ‘bargaining power!’’

During a period of not sharing samples with GISRS, the Indonesian government entered into negotiations with Baxter International to develop a vaccine based on samples provided by Indonesia. The parties reached a Memorandum of Understanding that ‘provide[d] a framework for future discussions and negotiations related to any formal collaboration or supply agreements for pandemic vaccine’. These discussions eventually broke down, and Indonesia returned to consistently sharing viral samples with GISRS in mid-2007, when a joint statement issued by the WHO and the Ministry of Health of Indonesia concluded that ‘The Minister agrees that the responsible, free and rapid sharing of influenza viruses with WHO, including H5N1, is necessary for global public health security and will resume sharing viruses for this purpose.’

The Indonesian virus sharing incident provided a clear impetus for the resulting negotiations of the PIP Framework; indeed, Indonesia’s concerns regarding access to viral samples and the resulting technology was brought to the fore during the negotiations of the PIP Framework. At the interdisciplinary working group on PIP, Indonesia submitted that

[a] framework of benefit sharing is to be developed through agreed terms and conditions to ensure a global stockpile of pre-pandemic and pandemic

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32 Siti Fadilah Supari, It’s time for the world to change: In the spirit of dignity, equity, and transparency: Divine hand behind avian influenza (English translation) (Sulaksana Watinsa Indonesia 2008)
33 Baxter is an international pharmaceutical company that undertakes research, development and manufacturing in the influenza vaccine sector.
vaccines, accessibility of vaccine at an affordable price, access to and transfer of technology and know-how for production of vaccines and empowerment and capacity building of vaccine manufacturing in developing countries.\textsuperscript{36}

While Indonesia’s refusal to share viral samples was undoubtedly controversial in the global health arena, their actions did bring attention to the blatant inequalities in the virus-sharing obligations of developing states and the fact that many of them are unable to procure the resulting vaccines during an influenza pandemic. The Pandemic Influenza Preparedness Framework was intended to reduce this inequality in vaccine procurement, and to ensure that engagement with international virus sharing obligations resulted in benefits for developing states. However (as I will argue), it does not appear as if the purported benefits, which were designed to reduce the inequalities between developed and developing states in the procurement of PIV, will have any real impact on their procurement of vaccine during an influenza pandemic. To this end, the purported benefits will not actually go any way towards effectively reducing the inequality between developed and developing states which the Indonesia virus sharing incident highlighted so clearly.

4.2 - Negotiating PIP

The process of enacting what eventually became the PIP Framework began in 2007,\textsuperscript{37} with the passing of Resolution WHA 60.28 by the World Health Assembly. In this Resolution the Assembly required that the WHO Director-General formulate mechanisms and guidelines, in close consultation with Member States, aimed at ensuring fair and equitable distribution of pandemic-influenza vaccines at affordable prices in the event of a pandemic, in order to ensure timely availability of such vaccines to Member States in need.\textsuperscript{38}


\textsuperscript{37} WHO, ‘Resolution WHA 60.28, Sixtieth World Health Assembly, Seventh Plenary Meeting’, (2007).

\textsuperscript{38} Ibid, 2(3)
In addition, the Resolution called upon the Director-General to ‘devise oversight mechanisms, formulate draft standard terms and conditions for sharing viruses between originating countries and WHO collaborating centres, and between the latter and third parties’.

Resolution WHA 60.28 made specific references to the access to and benefit sharing of viruses from which vaccines could be made to provide immunity against avian and other pandemic influenza viruses. In drafting this part of the Resolution the World Health Assembly linked together two of the most pressing concerns in pandemic influenza vaccine development and procurement: access to specimens of viruses with human pandemic potential, and procurement of the resulting vaccines which those viral specimens were used to create. While the Assembly, in having set out to reach an agreement regarding two of the most contentious issues in global health at the time, may appear at first glance to have been overly ambitious, the linkage is entirely sensible. As noted above, in order to manufacture a pandemic influenza vaccine, manufacturers require access to specimens of the virus against which the vaccine immunises, which were most likely provided by developing states, where influenza viruses typically originate. However, these same states are amongst the least likely to procure sufficient amounts of the resulting vaccine, and to suffer the greatest

39 Ibid, 2(5)
40 Ibid, 2(5)
41 Ibid, 2(1)-2(2)
43 Cox and Subbarao, (n11)
effects from the pandemic. Neither of these problems could be adequately addressed in isolation.

Prior to the Framework being enacted, a considerable amount of discussion on access to PIV had centred on the fact that samples of the virus used to produce a vaccine were likely to have been supplied by developing states, which then struggled to afford the resulting vaccine. At this time, the influenza virus sharing obligations of states were determined by practice, custom and WHO Guidance Documents, which formed ‘soft law’ recommendations to states. There were no binding international legal obligations governing influenza virus sharing until the passing of the 2005 International Health Regulations, which came into force in 2007. It was acknowledged by the WHO Intergovernmental Meeting on Pandemic Influenza Preparedness that the pre-PIP system did not deliver fairness, transparency or equity to developing states, and disproportionately benefited developed states with their own vaccine manufacturing base, by allowing easy access to viral samples with which

47 WHO, 'WHO guidance on public health measures in countries experiencing their first outbreaks of H5N1 avian influenza' (WHO, 2005)
48 The extent to which states are legally obligated to share physical specimens of pandemic influenza viruses as part of the ‘information sharing’ obligations of the IHR is contested. For a summary of these arguments see: Fidler, (n24)
49 WHO, 'Interim statement of the intergovernmental meeting on pandemic influenza preparedness: Sharing of influenza viruses and access to vaccine and other benefits' (WHO)

to develop a vaccine with no clear obligations to share the benefits. As a result, the WHO and developing states that were unable to procure PIV had ‘little leverage to influence developed countries other than rhetoric about equity, justice, and solidarity.’

Concerns regarding the inequality between developed and developing states when procuring pandemic influenza vaccines were again raised at the Interdisciplinary Working Group convened by the Director-General following Resolution 60.28. The Working Group failed to reach a consensus on how information and viruses shared by developing states should be linked to the procurement of the resulting vaccines. It did however note that the ‘overriding concern expressed by members…was that neither intellectual property rights, nor prior informed consent requirements, if any, should stand in the way of developing and producing a pandemic influenza vaccine’. It also concluded that a range of benefit sharing options should be considered in return for access to viral samples including cash, transfer of technology and know-how, and vaccines. The work of the Interdisciplinary Group fed into the subsequent intergovernmental meetings of the WHA, which took the development of the PIP Framework forward.

While there was consensus at the Intergovernmental meeting on what The Pandemic Influenza Preparedness Framework ought to achieve, consensus on how best to

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50 David Fidler, ‘Negotiating Equitable Access to Influenza Vaccines: Global Health Diplomacy and the Controversies Surrounding Avian Influenza H5N1 and Pandemic Influenza H1N1’ (2010) 7(5) PLoS Medicine
52 Ibid, Annex 11
53 Ibid, Annex 3
create a system that allowed for the ‘timely sharing of surveillance information and
highly pathogenic avian influenza viruses, as well as ensuring equitable access to
effective vaccinations, medicines and related technology’ was less forthcoming.
Throughout the negotiations, developing states argued that clearly defined compulsory benefit-sharing obligations should be placed on PIV manufacturers that received viral samples through GISRS, through the use of Standard Material Transfer Agreements. Developed states opposed this approach in the negotiations, and were reluctant to commit domestic manufacturers within their territory to compulsory benefit-sharing obligations, preferring an approach based on voluntary, flexible commitments being negotiated by individual manufacturers. As outlined below, the resulting Framework appears to reflect the views advanced by developing states in the Framework negotiations.

4.2.1 - PIP Commitments

It should first be noted that firm commitments were secured in regard to manufacturers making financial contributions towards the operational costs of GISRS. All vaccine, diagnostic and pharmaceutical manufacturers that use the WHO-GISRS system are under an obligation to make an annual partnership contribution to WHO contributing an amount equivalent to 50% of the operational costs of GISRS, which in 2012 amounted to $56.6million. While securing commitments regarding running costs for the WHO-GISRS is clearly beneficial for the WHO, the focus of this research are the provisions of the PIP Framework which will impact upon the procurement of pandemic influenza vaccines by developing states. To this end, pandemic influenza vaccine manufacturers who wish to receive PIP biological materials by way of a

55 Ibid.
56 See: Articles 6.1-6.4, Annex, (WHO (2009), (n54); 2.1a & 2.2 ibid (WHO (2008), (n54); Two types of Standard Material Transfer Agreement are provided for in the PIP Framework. SMTA1 is used to cover all transfers of PIP biological materials between laboratories and research centres that form WHO GISRS; SMTA2 is used by the WHO to enter into agreements with entities outside the WHO GISRS, such as pharmaceutical companies that manufacture pandemic influenza related products such as vaccines or antivirals. SMTA2’s have provisions related to benefit sharing included within them.
57 See: ‘Submission from USA’ Annex 6, WHO (2008), (n54)
58 6.14.3, PIP Framework
Standard Material Transfer Agreement with the WHO must commit to at least two of the following options:

A1. Donate at least 10% of real time pandemic vaccine production to WHO.
A2. Reserve at least 10% of real time pandemic vaccine production at affordable prices to WHO.
A3. Donate at least X treatment courses of needed antiviral medicine for the pandemic to WHO.
A4. Reserve at least X treatment courses of needed antiviral medicine for the pandemic at affordable prices.
A5. Grant to manufacturers in developing countries licenses on mutually agreed terms that should be fair and reasonable including in respect of affordable royalties, taking into account development levels in the country of end use of the products, on technology, know-how, products and processes for which it holds IPR for the production of (i) influenza vaccines, (ii) adjuvants, (iii) antivirals and/or (iv) diagnostics.
A6. Grant royalty-free licenses to manufacturers in developing countries or grant to WHO royalty-free, non-exclusive licenses on IPR, which can be sublicensed, for the production of pandemic influenza vaccines, adjuvants, antivirals products and diagnostics needed in a pandemic. WHO may sublicense these licenses to manufacturers in developing countries on appropriate terms and conditions and in accordance with sound public health principles.60

Particular praise for these benefit sharing provisions of the Framework has come from Nicole Jefferies, who states that it will ensure sustainable increases in pandemic vaccine production, which means access for both developed and developing states.61 Jefferies bases this support on the fact that

[t]he SMTA2 is significant as a tool to solve the challenges of sharing on an equal footing between contributors of viruses and manufacturers of influenza

60 Annex 2, SMTA2, Article 4.4.1.A, PIP Framework
vaccines, and allows developing states when entering into contractual agreements to rebalance the disproportionate burden of risk and benefits associated with pandemic influenza viruses and vaccines which currently exists between developed and developing states.\textsuperscript{62}

Paragraphs 4.1.A.1 and 4.1.A.2 appear to commit manufacturers to provide \textit{at least} 10\% of their real time production to the WHO. However, the above provision has an accompanying footnote '[r]ecognizing that flexibility is important in negotiating with all manufacturers, in a range of 5–20\%.\textsuperscript{63} Moreover, as outlined at 4.4, each manufacturer that has signed an SMTA2 with the WHO has made use of this inbuilt flexibility and has committed to provide under 10\% of their real time production, which would undermine the argument advanced by Jefferies that the SMTAs signed by pandemic influenza vaccine manufacturers will be ‘significant as a tool to solve the challenges of sharing on an equal footing between contributors of viruses and manufacturers of influenza vaccines’. As argued at 4.5, it is unlikely that the PIP Framework Stockpile will lead to developing states being able to procure more vaccine that they did from the VDI during 2009-H1N1. It actually appears as if the stockpile will have fewer vaccines to distribute than the VDI.

Despite the fact that the Chair of the PIP negotiations envisioned that SMTAs would be ‘standardised, universal and globally applicable to all transfers of PIP biological materials and not subject to further negotiation’\textsuperscript{64}, there does appear to be a significant amount of flexibility within the SMTA2 provided in the Framework. These flexible terms afford PIV manufacturers scope to negotiate terms regarding the donation of vaccines, antivirals, granting licenses, and transfer of technology. For instance, paragraphs 4.1.A.1 and 4.1.A.2 of the SMTA2 state that manufacturers of vaccines and/or antivirals in receipt of viral samples from WHO GISRS may commit to ‘[d]onate at least 10\% of real time pandemic vaccine production to WHO\textsuperscript{65} ‘and

\textsuperscript{62} Ibid.
\textsuperscript{63} Footnote 1, Annex 2, SMTA2, Article 4.1.A PIP Framework
\textsuperscript{65} Annex 2, SMTA2, Article 4.1.A.1, PIP Framework
and the SMTA2 ‘reserve at least 10% of real time pandemic vaccine production at affordable prices to the WHO’\textsuperscript{66}. 

In addition, a significant amount of the content of the SMTA2 provided in the Framework remains unstandardised, and subject to negotiation by the Parties to the Agreement. The relevant articles on liability and indemnities, warranties, duration and termination of contracts, governing law, and dispute resolution are not standardised within the Framework and remain simply ‘to be agreed by the parties’\textsuperscript{67}. This is concerning for a number of reasons. First, as so many terms within the SMTA2 need to be agreed upon by the parties, it is likely to elongate the negotiation process\textsuperscript{68} and given that influenza pandemics are sporadic in nature, it is not entirely clear to what extent such a delay in the negotiations (and therefore PIV manufacturers committing to supply the PIP stockpile) will impact on procurement from the stockpile during an influenza pandemic. Second, if it is not possible to reach a consensus on all the flexible terms, the negotiations will fail, and the SMTA2 will not enter into force, thereby leading to fewer vaccines being available for the PIP vaccine stockpile. Moreover, as so much of the SMTA2 is flexible and subject to negotiation, it will likely provide the manufacturer with a stronger negotiating position than the WHO, as the manufacturer will be one of a very limited number of providers of a product that is in very high demand, and the WHO will be one of a number of potential purchasers of such products.

\textsuperscript{66} Annex 2, SMTA2, Article 4.1.A.2, PIP Framework 
\textsuperscript{67} Articles 5, 6, and 9-13, Annex 2, SMTA2, PIP Framework 
\textsuperscript{68} ‘The complex and time-consuming work to negotiate and conclude SMTA-2s as well as the lack of resources – both human and financial – to scale up the pace of negotiations’ was noted by the Pandemic Influenza Preparedness Framework Advisory Group, in May 2013. At this time One SMTA2 has been concluded with GSK, and negotiations were underway with Baxter, China National Biotec Group and the Serum Institute of India, and pre-negotiation discussions were on-going with Sanofi and Novartis. Currently only two of these negotiations and pre-negotiations have led to an SMTA2 being concluded (Sanofi and the Serum Institute) WHO, ’Pandemic Influenza Preparedness: Sharing Of Influenza Viruses And Access To Vaccines And Other Benefits Report Of The Meeting Of The Pandemic Influenza Preparedness Framework Advisory Group Report by the Director-General’ (WHO 2013) <http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_17-en.pdf> Add.1
On the point of such flexible terms included within the SMTA2, and so much of the SMTA2 content remaining to be negotiated between the parties, Wilke has expressed the view that having WHO lead on such negotiations may actually lead to a more equitable and effective outcome for developing states:

Unlike before the PIP Framework, when negotiations were conducted on a bilateral basis (often involving developing countries), it is the WHO that negotiates the final SMTA which introduce further checks and balances, thereby increasing the effectiveness, and more importantly, the equity.69

The extent to which these compromises in the wording of the standardised SMTA2, along with flexibilities in the donations of vaccines provisions in the PIP Framework, will have on procurement of PIV by developing states is explored more fully below. It is also important to contextualise the development and negotiating history of the PIP Framework within the wider debates regarding intellectual property, viral sovereignty and drug procurement that were happening at the WHO at the time. During the PIP negotiations the WHO was conducting a wider ‘analysis of intellectual property rights, innovation, and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries’70. These negotiations were focused on overarching principles and objectives, rather than the specific mechanisms of the PIP negotiations, but they were equally contentious between developing and developed states. For example, the statements ‘the right-to-health takes precedence over commercial interests’71 and ‘avoid the incorporation of TRIPS-Plus measures in any trade agreements and in national legislation that may have a

negative impact on access to health products or treatments in developing countries were not included in the final text of the document. Moreover, the phrase ‘promote transfer of technology and production of health products in developing countries through investment and capacity building, including by providing guidance on appropriate technologies,’ was replaced with the wording ‘promote transfer of technology and production of health products in developing countries through investment and capacity building’. Therefore, it would appear that the compromises that developing countries acceded to within the PIP Framework negotiations are reflective of the wider compromises they acceded to at a fundamental policy level at the Working Group on Public Health, Innovation and Intellectual Property negotiations.

4.3 – PIP and Vaccine Procurement
The idea of a centrally-managed stockpile of pandemic influenza vaccines being used as an aid to developing states’ procurement of PIV had been considered by the WHO in the years leading up to the creation of the PIP Framework. In May 2007, the World Health Assembly recommended that a highly pathogenic avian influenza A H5N1 vaccine stockpile be established for emergency response to an impending H5N1 pandemic. That November, the WHO Strategic Advisory Group recommended that this stockpile should contain at least 150 million doses of H5N1 vaccine for use in pandemic response. As a result, vaccine manufacturers agreed to donate approximately 110 million doses of H5N1 vaccine to a WHO stockpile, with doses to be held at vaccine manufacturer sites. During the 2009-H1N1 pandemic, the WHO sought further donations of PIV from vaccine manufacturers, as those committed to

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72 Ibid, 36
73 Ibid, 34(b)
75 WHA, ‘Resolution 60.28 - Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits. Sixtieth World Health Assembly’ (2007)
the H5N1 stockpile had no impact on the 2009-H1N1 strain. Fortunately PIV manufacturers that had already pledged donations to the H5N1 stockpile agreed to replace this pledge with 2009-H1N1 vaccines, although with no fixed timescales for delivery.78 This incident clearly demonstrated the difficulties of pre-selecting strains of PIV for a stockpile. While the problem of the wrong strain being stockpiled was easily resolved on this occasion by pharmaceutical manufacturers, it is not apparent that such an easy solution would be forthcoming in the event of a future, more virulent strain of pandemic influenza, when there would be a much greater demand for PIVs.

Subsequently, the WHO decided that, because of the ‘relatively stable influenza A H5N1 epidemiology and with the risk of poor antigen or strain match between an actual pandemic virus and stockpiled influenza A H5N1 vaccine’, they should not re-establish a stockpile of H5N1 vaccine.79 A clear impetus in this decision was that the Pandemic Influenza Preparedness Framework had recently been passed, which would allow the WHO real-time access to manufactured pandemic influenza vaccines, thus removing the need to pre-select strains prior to their becoming pandemic.80

The next major milestone in the development of PIV stockpiling at the international level was the passing of the PIP Framework in 2011. The PIP Framework enables the WHO to manage a stockpile of approximately 150 million doses of pandemic influenza vaccines. This stockpile is created by requiring vaccine manufacturers who receive pandemic influenza virus samples from the WHO for vaccine development to contribute to the stockpile as one of the terms in an SMTA2. In the event of an influenza pandemic, the WHO will then distribute PIV from the stockpile. The Framework provides that

79 WHO, ‘Meeting of the Strategic Advisory Group of Experts on immunization, November 2013—conclusions and recommendations’ (2014) 89 Wkly Epidemiol Rec 1
80 ibid
50 million doses of the stockpile will be for use in ‘affected countries, according to public health risk and need, to assist in containing the first outbreak or outbreaks of an emerging pandemic and 100 million for distribution...to developing countries that have no or inadequate access to....influenza vaccines, on a per capita basis that can be distributed to affected and at risk developing states during a pandemic.81

The stockpile created by the Framework could be used by developing states in order to enhance their procurement process, as it creates a more structured process of collection and distribution of donated vaccine by the WHO. Within the context of PIV procurement, the PIP Framework can be framed as an enhancement to the ‘Donations via international organizations’ procurement method outlined at 3.2.2.82 The fact that a stockpile will already be established at the outset of the pandemic, with real-time commitments from PIV manufacturers in place to donate to the stockpile, should eliminate the delay in pledges being fulfilled by donor agencies that were noted during the 2009-H1N1 outbreak.83 Of particular note in this regard is that the obligation that PIV manufacturers have to contribute vaccine to the PIP stockpile is to be fulfilled at the same time as manufacturers’ contractual commitments to self-procuring states, including those with APAs in place. This means that those developing states that will be in receipt of pandemic influenza vaccine from the PIP stockpile will receive their vaccine allocation in the same timeframe as self-procuring states, thereby ensuring that developing states can vaccinate members of their population earlier in the pandemic, which is crucial in reducing disease transmission, and preventing mortality and morbidity from a pandemic influenza virus.84

81 6.9.2, PIP Framework
82 It is important to note at this stage that the creation of the PIP stockpile does not prevent the WHO (through the Vaccine Deployment Initiative) seeking further donations from vaccine manufacturers and developed states with excess vaccine, in the same way they did during 2009-H1N1.
83 See Chapter III Procurement of PIV for more details
84 WHO, ‘Guidance on development and implementation of a national deployment and vaccination plan for pandemic influenza vaccines’ (WHO 2012)
<http://apps.who.int/iris/bitstream/10665/75246/1/9789241503990_eng.pdf?ua=1> 3
The creation of a fixed stockpile is beneficial to recipient states, and donor manufacturers. In the review of the operational successes and failures of the WHO Vaccine Deployment Initiative during 2009-H1N1, it was noted that PIV manufacturers had stated that ‘support for the WHO Deployment Initiative may have disrupted business in other areas and reduced their competitive strength.’ Therefore, pre-arranged commitments being made for stockpile donations via an SMTA2 provides for certainty and consistency on both sides of the arrangement.

The Pandemic Influenza Preparedness Framework can rightly be described as a ‘milestone for global health’ solely because is the first international agreement that has sought to address inequalities in virus sharing by developing states, and procurement of medical technologies stemming from such viruses. However, because there has not been an influenza pandemic since the PIP Framework was created, the impact the Framework will actually have on procurement of PIV by developing states is difficult to ascertain at this stage.

4.3.1 – Standard Material Transfer Agreements: Company Obligations
A number of papers have considered the PIP Framework, and attempted to determine the impact the stockpile it manages will have on procurement. In summary, much of the literature expresses concern that the Framework is unable to make any real changes to vaccine allocation due to its inability to close the gap between developed and developing states where procurement of PIV is concerned and that the Framework lacks sufficient legal powers in order to instigate positive changes to the manner in which developing states procure PIV. These papers considered the benefit sharing provisions of the Standard Material Transfer Agreements, as they were

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85 WHO, 'Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative' (2011) <http://www.who.int/influenza_vaccines_plan/resources/h1n1_vaccine_deployment_initiative_moll.pdf>
86 David Fidler and Lawrence Gostin, 'The WHO pandemic influenza preparedness framework: A milestone in global governance for health' (2011) 306(2) JAMA 200
88 Jefferies, (n61); Fidler DP & Gostin LO, (86); Smith, (n14); Vezzani, ibid.
presented in the Appendix of the PIP Framework, as at the time, no SMTAs had been concluded with PIV manufacturers.

In regard to the utility of the Framework being reliant upon PIV manufacturers to voluntarily make commitments to the stockpile Vezzani claimed that

[p]hilanthropic initiatives of this type have already been implemented on a voluntary basis, without significantly improving the situation of poor countries. Although meritorious and very welcomed [sic], they should not be relied on as the sole tool to achieve the ambitious aims of the envisaged framework.\[^{89}\]

Rhodes noted that the stockpile which the Framework creates and manages appears to be wholly insufficient to enable developing states to procure sufficient levels of PIV during a pandemic:

In terms of a simple calculation, the 100 million doses from the stockpile that will be allocated to developing countries on a per capita basis, would, even if a single dose regime was viable, cover approximately 1.8% of their populations.\[^{90}\]

The major development since these articles were written is that three SMTAs have been concluded between the WHO and pandemic influenza vaccine manufacturers. The WHO concluded an SMTA2 with GlaxoSmithKline in December 2012\[^{91}\], the Serum Institute of India in October 2013\[^{92}\], and Sanofi Pasteur in February 2014\[^{93}\]. Each of these agreements outlines ‘Obligations of the Company’, and it is the content of these obligations which gives a clear indication of the true practical impact the PIP stockpile will have on procurement of PIV during the next influenza pandemic.

\[^{89}\] Vezzani, (n87)
\[^{90}\] Catherine Rhodes, ‘Sovereign Wrongs: Ethics in the Governance of Pathogenic Genetic Resources’ (2012) 3(1-3) Ethics in Biology, Engineering and Medicine 97
\[^{91}\] GSK-WHO SMTA2: A copy of the Agreement can be found at: http://www.who.int/influenza/pip/benefit_sharing/gsk_smta2_dec_2012.pdf?ua=1
\[^{92}\] Serum Institute of India-WHO SMTA2: A copy of the Agreement can be found at: http://www.who.int/influenza/pip/benefit_sharing/sii_smta2_oct_2013.pdf?ua=1
\[^{93}\] Sanofi-WHO SMTA2: A copy of the Agreement can be found at: http://www.who.int/influenza/pip/benefit_sharing/sanofi_smta2_feb_2014.pdf?ua=1
Prior to considering the content of the SMTAs that have been concluded between the WHO and PIV manufacturers, it is necessary to note the low take-up of these agreements amongst PIV manufacturers, as the number of manufacturers with an SMTA2 will clearly impact upon the effectiveness of the PIP stockpile as a procurement method for developing states.

4.4 - SMTA uptake Amongst PIV manufacturers

In the most recent review of PIV manufacturing capacity, Partridge & Kieny (on behalf of the WHO) identified twenty-four manufacturers that are active in manufacturing pandemic influenza vaccines. In addition to this categorisation of influenza manufacturers, the WHO, when calculating partnership contributions for the running costs of GISRS, identifies those influenza vaccine manufacturers using the WHO GISRS, in order for them to contribute to the running costs. Of those manufacturers identified by Partridge & Kieny, eighteen also make partnership contributions to the WHO, on the basis that they use the WHO-GISRS. Use of GISRS is understood to include receipt of physical materials, or use of data and/or information, some of which may not be routinely provided to the general public. Yet, despite the fact that eighteen active PIV manufacturers have been identified as having benefited from the work of GISRS, only three of these manufacturers have an SMTA2 in place.

Prior to the implementation of the PIP Framework Kamradt-Scott & Lee expressed concern that requiring PIV manufacturers to make partnership contributions for the running costs of GISRS could have the unintended consequence of forcing vaccine

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95 6.14.3, PIP Framework
96 This figure was reached by cross-referencing the list provided in Partridge and Kieny (n94) at Footnote.1 and WHO, '2013 PIP Partnership Contribution (PC) Collection: Results as of 1 August 2014’ (WHO 2014) <http://www.who.int/influenza/pip/benefit_sharing/2013_pc_collection_results_1aug2014.pdf?ua=1>
97 WHO, (n59)
manufacturers out of the market, and thereby reducing the overall global vaccine capacity:

The imposition of what effectively equates to user fees for pharmaceutical companies that access GISRS data and samples, either through directly funding the network or via commitments to provide at least 10 per cent of vaccines and diagnostics at reduced prices, raises the possibility that some manufacturers will exit what has traditionally been a low-profit industry.\(^98\)

While it does not appear that manufacturers are actively leaving the market in order to avoid making contributions to GISRS as Kamradt-Scott & Lee feared, because so few PIV manufacturers have concluded an SMTA2 appears to suggest that the majority believe they can continue PIV production while operating outside of the PIP Framework, and GISRS. Presumably this would be achieved by concluding bilateral agreements with states that have relevant viral samples in their territory, in a similar fashion to the Indonesia-Baxter agreement. Indeed, nothing within the PIP Framework prevents states from transferring viral samples to GISRS via an SMTA, and concluding a bilateral agreement with a PIV manufacturer that operates outside of GISRS.

It has further been noted that ‘A few manufacturers are using genetic sequence data to make vaccines and other influenza related products\(^99\), a trend that allows manufacturers to make use of data generated via the WHO-GISRS network\(^100\) but not require access to the viral samples which would allow them to easily operate within the PIV market without being party to an SMTA. This trend is ‘anticipated to increase\(^101\) amongst PIV manufacturers, due to the anticipated increase in the use of genetic sequence data in pandemic influenza research and development. Both of these factors are particularly concerning from a procurement of PIV perspective as manufacturers, by avoiding the need to conclude an SMTA2 in order to gain viral

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\(^100\) Ibid, 4
\(^101\) Ibid, 4
samples, also avoid any obligations to contribute to the stockpile that PIP manages, which will reduce as a direct consequence.

With regard to the PIV manufacturers that have concluded an SMTA2, the WHO uses a formula based upon the average annual influenza product sales per manufacturer, for the three past years, plus the most recent pandemic year when determining contributions towards the running costs of GISRS.\textsuperscript{102} On this basis, Sanofi Pasteur and GSK are the two largest PIV manufacturers in the world by sales value\textsuperscript{103}, and the Serum Institute of India is the tenth largest, out of the eighteen PIV manufacturers that contribute to GISRS.

Had these three manufacturers committed to donate 10\% of their production capacity to the stockpile, (as the standardised SMTA2 provided at Annex 2) based on the company’s most recent estimates of production capacity for pandemic influenza vaccines\textsuperscript{104}, this would amount to donations to the stockpile of 63.4 million doses of PIV, which is under half the amount of vaccine that the Framework was intended to raise. Moreover, considering that two-thirds of this amount is to be allocated to developing countries on a per capita basis, this pledge would have covered approximately 1.4\% of affected developing state’s populations, if a one-dose regime would suffice.\textsuperscript{105} In the event of a two-dose regime being necessary, population coverage from PIP donations within developing states would have dropped to 0.7\%.

\textsuperscript{102} Ibid, 4
\textsuperscript{103} WHO, (n96) Table: 1
\textsuperscript{105} This figure is reached based on the fact that Rhodes estimates that 100 million doses would cover 1.8\% of the population of developing states that lack access, in Rhodes, (n90)
4.5 - SMTA2 Commitments by Industry

However, despite the standardised SMTA2 providing at Annex 2 that manufacturers of vaccines in receipt of viral samples from WHO-GISRS should donate at least 10% of real time pandemic vaccine production to WHO\textsuperscript{106}, those SMTA2s that have been concluded have industry commitments lower than this 10%. GSK has committed to ‘donate 7.5% of real-time pandemic influenza vaccines to the WHO’ and ‘reserve 2.5%....at an affordable price to WHO’\textsuperscript{107}. Sanofi has committed to donate 7.5% to WHO, and reserve an additional 7.5% at an affordable price for purchase by WHO, and the Serum institute of India has committed to donate 8% of real-time production, and reserve 2% for purchase by the WHO. As the table below demonstrates, this means that the three manufacturers have committed to donate just under 48 million doses to the stockpile - a 25% decrease on the commitments provided in the example SMTA2 in the Framework, and over 100 million doses fewer than the Framework was intended to manage. The WHO has the option to purchase an additional 28 million doses at ‘affordable prices’.

\textit{Table 1. Comparison of Commitments provided in example SMTA2, with those provided in the signed Agreements}

<table>
<thead>
<tr>
<th></th>
<th>Example SMTA2: Donations</th>
<th>SMTA2 Commitments: Donations</th>
<th>SMTA2 Commitments: Purchase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi</td>
<td>25</td>
<td>18.75</td>
<td>18.75</td>
</tr>
<tr>
<td>GSK</td>
<td>34</td>
<td>25</td>
<td>8.35</td>
</tr>
<tr>
<td>Serum</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Total (million)</td>
<td>64</td>
<td>47.75</td>
<td>28.1</td>
</tr>
</tbody>
</table>

\textsuperscript{106} PIP Framework, Annex 2, SMTA2, Article 4.1.A.1
\textsuperscript{107} ‘Recognizing that flexibility is important in negotiating with all manufacturers, in a range of 5–20%.’
Such reductions in the obligations placed upon manufacturers that have SMTAs with the WHO significantly reduces the vaccination coverage within developing states using the stockpile as a procurement method. Based on the current production capacity of those manufacturers with an SMTA2, 0.8% of the population of developing states could be vaccinated from the PIP Stockpile, based on the donation commitments contained within the enforceable SMTAs. This represents a 24% reduction in vaccination coverage when compared with the example commitments provided within the PIP Framework SMTA2. Vaccination coverage increases to 1.26% if the WHO purchases all those vaccines which are reserved by the manufacturers for purchase by the WHO\textsuperscript{108}.

The suitability of procurement via donations (making use of the PIP Framework) as a viable procurement method for developing states has actually reduced since the use of the VDI during 2009-H1N1, due to the low number of doses secured on behalf of the PIP stockpile. The stockpile the WHO managed during 2009-H1N1 distributed 78 million doses to the ninety-seven developing states that lacked domestic vaccine production and lacked the ability to purchase vaccine on the commercial market\textsuperscript{109}, whereas the PIP stockpile has firm commitments to receive donations of 47.75 million donations, and the option to purchase an additional 28 million doses. However, not all of this stockpile is reserved specifically for developing states that are unable to procure PIV on the open market. If the WHO maintains the proportions at which it intended to distribute the donated vaccine with

One-third ‘for use in affected countries, according to public health risk and need, to assist in containing the first outbreak or outbreaks of an emerging pandemic’, two-thirds to ‘developing countries that have no or inadequate access to H5N1 influenza vaccines, on a per capita basis, with use to be determined by those countries.’\textsuperscript{110}

\textsuperscript{108} These vaccination coverage figures assume that that a one-dose strategy will suffice. If a two-dose vaccination strategy is required, vaccination coverage levels will halve.

\textsuperscript{109} WHO, 'Report of the WHO pandemic influenza A(H1N1) vaccine deployment initiative' (WHO 2012) <http://www.who.int/influenza_vaccines_plan/resources/h1n1_deployment_report.pdf> 3.1

\textsuperscript{110} PIP Framework, 6.9.2
Only 31.8 million of those doses will be available to be procured by developing countries that have no or inadequate access.

4.5.1 – vaccination coverage and the PIP Stockpile

The shortcomings of the PIP stockpile as a procurement method for developing states are more clearly demonstrated with reference to vaccination coverage within developing states. The current PIP stockpile has 46 million doses committed to it, giving coverage of 0.76% on a one-dose strategy, and 0.38% on a two-dose, which is well below the vaccination coverage the VDI donations managed during 2009-H1N1, and significantly below the target of 33% needed to establish herd immunity within a population. While the PIP Stockpile was not explicitly created with the 33% vaccination target in mind (nowhere in the drafting or the final text was a vaccination coverage target set) the herd immunity level of 33% is well established within the literature as the most vaccination coverage target. In relation to this target, clearly, the commitments provided in the example SMTA2 do not make procurement from the PIP stockpile a particularly attractive procurement option for developing states, particularly if a developing state is seeking to procure sufficient vaccine in order to establish herd immunity levels within their territory in order to discharge their right-to-health obligations.

When comparing procurement of PIV from the PIP stockpile with the procurement of PIV from the Vaccine Deployment Initiative stockpile the WHO created during 2009-H1N1, it is clear that the one major benefit of the PIP stockpile is the removal of the time delay of donated vaccine being committed to the WHO\textsuperscript{111}. Despite this apparent benefit, concern has been expressed by the industry that during an influenza pandemic, member states with domestic PIV production within their territory would place restrictions upon exports of PIV that have been committed to the PIP stockpile, until domestic demand had been fulfilled\textsuperscript{112}. This concern appears to be well founded.

\textsuperscript{111} As was noted in the Vaccine Procurement chapter vaccine committed to the VDI stockpile by industry and developed states arrived in recipient developing states at least four months later than in self-procuring states.

\textsuperscript{112} WHO, (n109) 20
As 3.4.1 demonstrated, many developing states procured less vaccine, and procured it later, than their developed neighbours during 2009-H1N1. One reason noted for this was that governments of developed states with domestic manufacturing capacity (that would have benefited from virus sharing by developing states) restricted exports to other territories until domestic demand had been fulfilled.\(^{113}\) As Fidler noted, Canada awarded its vaccine contract to a Canadian company because it feared that foreign governments might restrict exports to Canada because of vaccine shortages within their territories. The Australian government made it clear to the Australian manufacturer CSL that it must fulfil the government’s domestic needs before exporting vaccine to the United States. The United States [stated that the US] would not donate H1N1 vaccine as promised until all at risk Americans had access, because production problems had created shortages in the United States.\(^ {114}\)

While the WHO Director-General is seeking periodic assurances from Member States that they would enable companies to fulfil their SMTA2 commitments to supply pandemic vaccine to WHO on a real-time basis\(^ {115}\), it is not yet apparent if these assurances will be given by Member States, or even if they are given, whether they will be honoured during a future pandemic. However, the Director-General appears keen to obtain such assurances as the problem of governments of developed states with domestic manufacturing capacity being able to prevent the export of PIVs to the WHO or developing states until domestic demand has been satisfied has not been resolved by the PIP Framework. Article 14 of the SMTAs signed with PIV manufacturers states that ‘no Party shall be liable for any delay in the performance of or failure to perform its obligations under this Agreement, where such a delay or failure is caused by Force Majeure’,\(^ {116}\) and the definition provided for ‘Force Majeure’ includes

\(^{113}\) Ibid; Fidler, (n50); Sam F Halabi, ‘Multipolarity, intellectual property, and the internationalization of public health law’ (2014) 35 Michigan Journal of International Law 714

\(^{114}\) Fidler, (n50)


\(^{116}\) See Article 14 of GSK-WHO SMTA2, (n91); Serum Institute of India-WHO SMTA2 (n92); Sanofi-WHO SMTA2 (n93)
‘...embargo or requisition’ and ‘acts of government’\(^\text{117}\), meaning that the PIP Framework does not prevent the nationalisation of pandemic influenza vaccination manufacturing, or the embargo or requisition of vaccinations by states with domestic manufacturing in their territory. Such an embargo or requisition occurring could have a significant impact on the viability of the PIP Stockpile by reducing the number of vaccines the Stockpile has to distribute, or by causing a significant delay in the delivery of the vaccines to the Stockpile, and onward transfer to recipient states. This suggests that it is unlikely the PIP Framework will have, in practice, a significant positive impact on the procurement of PIVs by developing states, or that the Framework has done anything to change the status quo that exists between developed and developing states during an influenza pandemic.

The low uptake of SMTAs amongst PIV manufacturers, combined with the reduced commitments being given by PIV manufacturers in those SMTAs that have been concluded, make the PIP stockpile a particularly undesirable procurement method for developing states. Moreover, even when all of the vaccine that has been committed to the WHO via SMTAs has been delivered, it is likely that the WHO will need to seek donations from PIV manufacturers (outside of SMTA2 commitments) and developed states, in order to be able to fulfil the procurement needs of developing states, in much the same way they did during 2009-H1N1. This is a particularly undesirable scenario because, when making appeals for donated vaccine the WHO will again have ‘little leverage to influence developed countries [and PIV manufacturers] other than rhetoric about equity, justice, and solidarity’\(^\text{118}\). If the WHO must again make appeals to equity and justice in order to procure vaccine to donate to developing states, as appears likely, it will highlight the significant shortcomings in the PIP Framework, which was designed specifically to minimise such a scenario during a pandemic.

This part of the chapter has demonstrated that direct procurement from the PIP stockpile is not a viable option for developing states seeking to increase their access

\(^{117}\) See Article 3 of GSK-WHO SMTA2 (n91); Serum Institute of India-WHO SMTA2 (n92); Sanofi-WHO SMTA2 (n93)

\(^{118}\) Fidler, (n50)
to pandemic influenza vaccines. In the context of the right-to-health the PIP Framework does satisfy one element of the ‘sufficient access’ requirement set out at the Introduction - if developing states were to procure vaccines from the PIP Stockpile, then these vaccines would be distributed within the same timeframe as developed states.\textsuperscript{119} While this is a clear benefit over procurement of the VDI during 2009-H1N1, procurement from the PIP Stockpile merely satisfies one element of the two-part test this research is utilising, in order to determine when sufficient access has been achieved to the extent to which the right-to-health obligations can be discharged. However, the second element of the two-part test, procuring sufficient levels of vaccine to immunise at least 33\% of their population, cannot be satisfied by procurement via the PIP Framework. Therefore, a developing state cannot fulfil and discharge their right-to-health obligations in respect of pandemic influenza vaccines by relying upon procurement from the PIP Framework. On the point of vaccination levels, it would appear that procurement from the PIP Framework will lead to lower vaccination levels in developing states, than procurement from the VDI did, unless the WHO can procure significantly more vaccines for onward donation to developing states by making use of ‘rhetoric about equity, justice, and solidarity’ in order to request donations from developed states and influenza manufacturers.

In addition to creating a stockpile for direct procurement, the PIP Framework also attempts to increase transfer of technology from established PIV manufacturers in developed states, to new manufacturers in developing states. Transfer of technology, if properly managed, can also improve the procurement of pandemic influenza vaccines by developing states. Transfer of technology can create a situation whereby developing states are able to contract with pandemic influenza vaccine manufacturers based in their own territory (possibly by way of an Advance Purchase Agreement), as opposed to being reliant upon the established manufacturers based in developed states. This would allow developing states to have rapid access to pandemic influenza vaccines, and would eliminate the risk of developed states with pandemic influenza

\textsuperscript{119} Providing none of the developed states in whose territory the manufacturing facilities are based place restrictions on the exports of pandemic influenza vaccines until domestic demands have been fulfilled. As 4.5.1 noted, this is a very real possibility in the event of a severe pandemic.
vaccine manufacturers based in their territory restricting exports of vaccines until domestic demand has been fulfilled during a pandemic.

4.6 – Transfer of Technology and Vaccine Procurement

The term transfer of technology does not have an unambiguous, universally applicable definition. Multiple authors have attempted to define what transfer of technology encompasses. For the purpose of this research the definition relied upon is provided by Sarfaraz and Emmamizadeh, who defined transfer of technology as being the process of transferring from one nation, typically a developed one, to another nation, typically developing, the know-how required to use a particular technology successfully. Given that, as I will argue in more detail at 6.4.2, developing states lack both access to the technology used in manufacturing pandemic influenza vaccines, and the knowhow required to make use of the technology, Sarfaraz and Emmamizadeh’s definition is particularly appropriate since it stresses both transfer of technology and knowhow, which many others definitions of transfer of technology do not.

The importance of developing states having some degree of self-sufficiency in pandemic influenza vaccine procurement, by contracting with pandemic influenza vaccine manufacturers based in their own territory, as opposed to being reliant upon the established manufacturers based in developed states, was highlighted in a paper by Friede and others, in which they noted that

[i]n 2006, 90% of influenza vaccine production was located in nine countries (largely in Europe and North America) that represented only 10% of the global population. Other countries, notably those in Africa, the Middle East and Asia, could witness a staggering death toll and a severe strain on their health

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120 See for example: Paul Lowe, The management of technology: Perception and opportunities (Chapman and Hall 1995); DJ Waddington, ‘Education, Industry and Technology’ (Pergamon, 1987);

121 Ahmad Sarfaraz and Bahram Emmamizadeh, 'Cost estimating for transfer of technology in developing countries' (1993) 5 Transactions of AACE International 6
services while waiting for producing countries and regions to have vaccinated their own populations.\footnote{122}

While pandemic influenza vaccine manufacturing capacity has increased since 2006, the proportions by which this capacity is divided between developing and developed states has remained largely the same, with capacity in developing states still being significantly lower than that which is required in order to adequately immunise the populations of developing states.\footnote{123} Therefore there is a clear need for developing states, either standing alone or as part of regional groups, to move towards self-sufficient procurement of pandemic influenza vaccines.

As I will argue in chapters six and seven, patents are not the sole barrier to effective self-sufficient procurement of pandemic influenza vaccines for developing states. I will argue that even if the patents over pandemic influenza vaccine related technology did not exist, or could be effectively circumvented by benefiting from compulsory license provisions in domestic patent legislation, specific technical knowledge that cannot be inferred from the patent, and is not available in the public domain, is needed in order to manufacture a pandemic influenza vaccine. Without access to such technical knowledge, in combination with the right to exploit patented technology that is key to the PIV manufacturing process, developing states, or manufacturers in developing states, are unable to manufacture their own PIV as a method of procurement. Even when there are no patent barriers in place, such as is the case with live attenuated influenza vaccines,\footnote{124} transfer of technology and information related

\footnote{122} M Friede and others, 'WHO initiative to increase global and equitable access to influenza vaccine in the event of a pandemic: Supporting developing country production capacity through technology transfer' (2011) 29 Vaccine

\footnote{123} Jeffrey Partridge and Marie Paule Kieny, 'Global Production of Seasonal and Pandemic (H1N1) Influenza Vaccines in 2009–2010 and Comparison with Previous Estimates and Global Action Plan Targets' (2010) 28 Vaccine 4709; Partridge and Kieny (n94)

to the manufacturing process and producers from an established manufacturer would be required in order to allow the new manufacturer to commence manufacturing in a cost-effective manner.

Most notably, transfer of technology would allow the new manufacturer to benefit from accessing the safety and efficacy data generated by the established manufacturer for use in a slightly reduced regulatory pathway for the resulting vaccine\textsuperscript{125}. Without transfer of technology from an established manufacturer, a new manufacturer would have significantly increased costs of development and production which could have one of two effects: a) it makes the sunk costs of research and development prohibitively high, and the manufacturer does not enter the market, or b) it makes the sunk costs of research and development high, and they are passed on to the end consumer in the form of higher prices, meaning there is little cost benefit for developing states seeking to procure pandemic influenza vaccines.

4.6.1 - Transfer of Technology for PIV Manufacturing and the WHO

To this end, at a policy level, the World Health Organisation has often encouraged transfer of technology from established manufacturers of pandemic influenza vaccines to new manufacturers in developing states, in order to improve pandemic preparedness within developing states.

In the wake of growing concerns over the H5N1 strain of pandemic influenza in late 2005, the World Health Assembly passed Resolution WHA58.5, which focused upon strengthening pandemic influenza preparedness and response\textsuperscript{126}. Resolution WHA58.5 required the Director-General to continue to develop WHO’s plans and capacity to respond to an influenza pandemic, to be able to provide technical support, capacity building and technology transfer related to H5N1 influenza vaccines and diagnostics to developing countries.\textsuperscript{127}

\textsuperscript{125} Friede and others, (n122)
\textsuperscript{126} World Health Assembly, ‘Resolution 58.5, Fifty-Eighth World Health Assembly’ (2005)
\textsuperscript{127} Ibid. at 2(7)
While not specifically related to pandemic influenza vaccines, the next major policy development at the WHO regarding transfer of technology in order to improve access to and the procurement of medicines was the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) in 2008. The GSPA-PHI was ‘designed to promote innovation, build capacity [and] improve access to medicines’\(^{128}\), and aimed to ‘promote new thinking on innovation and access to medicine’, as well as ‘provide a medium term framework for securing an enhanced and sustainable basis for needs driven essential health research and development relevant to diseases which disproportionally affect developing countries’.\(^{129}\)

GSPA-PHI aimed to promote transfer of technology and the production of health products in developing countries by

- (a) exploring ‘possible new mechanisms and make better use of existing mechanisms to facilitate transfer of technology and technical support to build and improve innovative capacity for health-related research and development, particularly in developing countries’;
- (b) promoting ‘transfer of technology and production of health products in developing countries through investment and capacity building’; and
- (c) promoting ‘transfer of technology and production of health products in developing countries through identification of best practices, and investment and capacity building provided by developed and developing countries where appropriate.’\(^{130}\)

In relation to pandemic influenza vaccines, this policy of promoting transfer of technology to developing state manufacturers was largely facilitated though the WHO Influenza Vaccine Technology Transfer Initiative, a collaborative project between the WHO, some developed states and PIV manufacturers. The Influenza Vaccine Technology Transfer Initiative aimed to create regionally based, independent, and


\(^{129}\) Ibid, Article 13.

\(^{130}\) Ibid, 34(4.1)
sustainable pandemic influenza vaccine production capacity in developing countries, through financial support and technology transfer to manufacturers in developing states. Transfer of technology through the Influenza Vaccine Technology Transfer Initiative was largely facilitated through the creation of a ‘hub’ for the transfer of influenza vaccine technology. The hub is a platform for transferring a complete manufacturing process at ‘pilot scale’ to a new manufacturer in a developing state by granting a non-exclusive license for use of the technology, along with providing information and training on using the technology, along with relevant safety and efficacy data, which allows the recipient to make use of a shortened regulatory pathway for licensing the PIV.

The WHO Hub was launched in 2007 and, to date, vaccine manufacturers in seventeen developing states have received financial grants, and technical knowledge and understanding from the hub, which has enabled them to produce pandemic influenza vaccine. Despite this success, it is reported that the WHO is concerned that ‘there is a great lack of interested technology providers’ wishing to contribute to the Hub, meaning that the Hub is limited in the amount, or level, of technology available to it to be transferred. The role of the technology provider is obviously key to the success of the hub model, as the ‘model can only be used with vaccines for which no intellectual property barriers exist in both the country hosting the hub and the country receiving the technology’. Therefore the active engagement of the technology holder to grant a license that effectively removes these barriers in host and reciprocal states, as well as providing the technology and know-how, is key to the success of the hub model. The result of this lack of interest from technology providers to provide

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131 For more information on the work of the WHO Influenza Vaccine Technology Transfer Initiative see: WHO, (n77) 2.2.2
132 Friede and others, (n122)
133 G Torelli, ‘WHO Technology Transfer Initiative: Progress Update (8th meeting with international partners on prospects for influenza vaccine technology transfer to developing country vaccine manufacturers)’ (WHO 2015) <http://www.who.int/phi/DAY1_02_Torelli_PM_SaoPaulo2015.pdf>
new and updated technology to the hub is that recipient manufacturers are unlikely to benefit from any of the scientific advances which occur in the field of pandemic influenza vaccines. The impact of this is that the pandemic influenza vaccines produced by recipient manufacturers will not be as effective, or produced in as efficient a manner, as the vaccine produced by established manufacturers in developed states.

4.6.2 - Transfer of Technology Provisions and the PIP Framework

One of the most notable omissions from the SMTAs that have been signed with PIV manufacturers is that none of the agreements currently in place have secured any commitments from manufacturers regarding transfer of technology.\textsuperscript{136} This is despite the fact that during the negotiations of the PIP Framework, the importance of transfer of technology for pandemic preparedness and procurement was stressed in the reports of the Advisory Group on Pandemic influenza at the WHO and the WHO Director-General, which were integral to the development of the Framework. The Director-General noted that: ‘Preparedness requires long-term investment, particularly when capacity building requires training and transfer of knowledge’\textsuperscript{137}, whereas the Group stressed the need to achieve the greatest impact by building capacity in countries where it is lowest and observed that preparedness requires long-term investment, particularly when capacity building requires training and transfer of knowledge\textsuperscript{138}.

Facilitating the transfer of technology from established PIV manufacturers to manufacturers in developing states is one of the clear aims of the PIP Framework. Paragraph 6.0.2(iv) states that ‘the PIP Benefit Sharing System will operate to: build capacity in receiving countries over time for and through technical assistance and transfer of technology, skills and know-how and expanded influenza vaccine

\textsuperscript{136} GSK-WHO SMTA2 (n91); Serum Institute of India-WHO SMTA2 (n92); Sanofi-WHO SMTA2 (n93)

\textsuperscript{137} WHO, ‘pandemic influenza preparedness: Sharing of influenza viruses and access to vaccines and other benefits: Report of the advisory group report by the director-general’ (WHO 2012)


\textsuperscript{138} ibid
production, tailored to their public health risk and needs. Further detail on the WHO’s vision for transfer of technology via PIP is provided at 4.6.1-4.6.2, which states that

The Director-General will continue to work closely with Member States and influenza vaccine manufacturers to implement the WHO Global Pandemic Influenza Action Plan to Increase Vaccine Supply, including its strategies to build new production facilities in developing and/or industrialized countries and through transfer of technology, skills and know-how.

Member States should urge influenza vaccine, diagnostic and pharmaceutical manufacturers to make specific efforts to transfer these technologies to other countries, particularly developing countries, as appropriate.

Influenza vaccine manufacturers who receive PIP biological materials may grant, subject to any existing licensing restrictions, on mutually agreed terms, a non-exclusive, royalty-free license to any influenza vaccine manufacturer from a developing country, to use its intellectual property and other protected substances, products, technology, know-how, information and knowledge used in the process of influenza vaccine development and production, in particular for pre-pandemic and pandemic vaccines for use in agreed developing countries.

This section has so far focused on demonstrating that the WHO views increasing transfer of technology as an integral part of the plan to increase access to pandemic influenza vaccines and reduce the inequality between developing and developed states on this issue. Following this, it is necessary to determine to what extent transfer of technology provisions have been incorporated into the PIP Framework. This is particularly relevant as the PIP Framework has been hailed as a ‘landmark in global governance for health, representing the first international agreement on influenza virus and benefit sharing’, it represents an ideal opportunity to increase transfer of technology to developing states manufacturers. However, despite the clear impetus

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139 PIP Framework, 6.0.2(IV)
140 6.13.1-4, PIP Framework
141 Fidler and Gostin, (n86)
within the WHO, both at a policy level, and in the development of the PIP Framework, the resulting obligations which were placed upon manufacturers in regard to transfer of technology via the PIP Framework appear particularly weak.

Within the ‘Obligations of the Company’ in the standardised SMTA2 provided in the Annex of the PIP Framework, the transfer of technology related provisions state that manufacturers of vaccines and/or antivirals can commit to

A5. Grant to manufacturers in developing countries licenses on mutually agreed terms that should be fair and reasonable including in respect of affordable royalties, taking into account development levels in the country of end use of the products, on technology, know-how, products and processes for which it holds IPR for the production of (i) influenza vaccines, (ii) adjuvants, (iii) antivirals and/or (iv) diagnostics\textsuperscript{142} and/or:

A6. Grant royalty-free licenses to manufacturers in developing countries or grant to WHO royalty-free, non-exclusive licenses on IPR, which can be sublicensed, for the production of pandemic influenza vaccines, adjuvants, antivirals products and diagnostics needed in a pandemic. WHO may sublicense these licenses to manufacturers in developing countries on appropriate terms and conditions and in accordance with sound public health principles.\textsuperscript{143}

It seems bizarre that the WHO at a policy level, and within the aims of the PIP Framework, stressed the importance of transfer of technology for pandemic preparedness and procurement, and yet the relevant provisions addressing transfer of technology within the SMTA2 are so weak. There are a number of elements concerned with transfer of technology within these SMTA2 that are particularly concerning. Firstly, it seems unusual that, in creating the Framework, the WHO has chosen not to expressly link together the work of the WHO Influenza Vaccine Hub, and the PIP Framework. While Paragraph A.6 does provide the technology holder with the

\textsuperscript{142} Annex 2, SMTA2, Article 4.4.1.A5, PIP Framework
\textsuperscript{143} Annex 2, SMTA2, Article 4.4.1.A6, ibid.
option to grant royalty-free, non-exclusive licenses on intellectual property rights to the WHO, who can then sublicense these rights to manufacturers in developing states, it makes no reference to the transfer of technical knowhow required to work the invention covered by these intellectual property rights also being transferred to the WHO. This is concerning because, as the previous chapter highlighted, it is not merely the intellectual property rights which pose a significant barrier to developing states being able to establish pandemic influenza vaccine manufacturing in their territory. While intellectual property rights can be a barrier to manufacturers in developing states establishing manufacturing capacity, it is the lack of technical knowhow amongst prospective manufacturers in developing states that has clearly been identified as the barrier to self-sufficient procurement of pandemic influenza vaccines by developing states.144

Instead, PIV manufacturers that choose to engage with transfer of technology as part of their ‘Company Obligations’ are compelled only to transfer technology to a non-specific number of manufacturers in developing states, meaning the knowledge will only be transferred to a limited number of entities, at the technology holder’s discretion. Technology transfer which occurs on a bilateral basis between an established manufacturer acting as donor to a new manufacturer in a developing state has been noted as being ‘not readily feasible in cases where there is limited financial benefit for donor’ in the context of pandemic influenza vaccines.145 Therefore it is particularly concerning that this is the only transfer of technology option which is available as an ‘Obligation of the Company’ within an SMTA2. Transfer of technology via the PIP Framework could have had significantly greater impact if the technology holder were compelled to transfer their knowledge to the WHO Influenza Vaccine Hub, along with the right for the hub to transfer this knowledge on again, to multiple relevant manufacturers in developing states. This would ensure maximum distribution of relevant technical knowledge, which in turn would help build pandemic preparedness by increasing vaccine manufacturing capacity in developing states.

145 Friede and others, (n122)
In addition to the above, the wording in each of the transfer of technology provisions in the SMTA2 provisions is too vague. As noted above, if transfer of technology is to occur on a bilateral basis from one manufacturer to another, this will only occur when it is financially viable for the donor. The wording of paragraph A.5 specifies neither the number of recipient manufacturers, nor the number of recipient developing states that are to receive transferred technology in order to comply with the obligation. This is seemingly left to the PIV manufacturer transferring the technology to decide. Moreover, the wording ‘terms that should be fair and reasonable’ is again particularly ambiguous, with both ‘fair’ and ‘reasonable’ not being defined within the Framework, again, leaving it open to the interpretation of donor manufacturers. The vague wording of the transfer of technology related provisions within the SMTAs, particularly in relation to key terms, will inevitably lead to inconsistencies in the amount of technology transfer that will occur, and the terms of the transfer. This may lead to donor manufacturers determining that ‘fair’ and ‘reasonable’ has a particularly low threshold, and therefore, that they are only obliged to undertake minimal transfer in order to meet this requirement. While it may be the case that some particularly benevolent manufacturer will transfer more technology than is deemed ‘fair’ or ‘reasonable’ to a state, this will lead to an inequitable situation whereby some developing states have benefited significantly more than other recipient states.

Transfer of technology from an established pandemic influenza vaccine manufacturer to a new manufacturer in a developing state has been encouraged by the WHO through its policy initiatives, on the basis that it is not patents, but access to knowledge that constitutes the most significant barrier for new manufacturers to begin pandemic influenza vaccine production. To this end, the WHO has seen some limited success in transferring technology related to the pandemic influenza vaccine manufacturing process from established manufacturers, to new ones. Despite this, and the PIP Framework representing a major opportunity for the WHO to strengthen the transfer of technology, it is clear that the WHO missed this opportunity.
None of the pandemic influenza vaccine manufacturers that have an SMTA2 in force have committed to transfer technology to the WHO as part of its company obligations. However, even if any manufacturer had committed to this, the transfer of technology related provisions contained within the Framework are too weak to have any real positive impact on the manner in which developing states can establish PIV manufacturing capacity within their territory, in order to achieve the sufficient access which is required in order to discharge their right-to-health obligation. This is a key failing of the Framework, as it is this ability to establish manufacturing capacity which looks to be the most suitable method to provide developing states with a sustainable and effective method of pandemic influenza vaccine procurement. Transfer of technology, along with the removal of intellectual property related barriers to production, is key to this being possible.

4.7 – Conclusion
While the relevant academic literature has praised the PIP Framework as being an innovative model mechanism for guaranteeing access to vaccines and affordable life-saving drugs,\(^\text{146}\) I argue that such praise appears to be misplaced. While, in the context of the right-to-health the PIP Framework does satisfy one element of the ‘sufficient access’ requirement set out at the Introduction, in that those developing states that procure vaccine from the PIP Framework procure them in the same timeframe as self-procuring developed states, it is clear that the Framework is not appropriate tool by which developing states could procure enough vaccines to meet the second element of the two-part ‘sufficient access’ test. With this in mind, it is reasonable to argue that the PIP Framework is not able to ensure that developing states are able make use of the Stockpile in order to discharge their core right-to-health obligations in respect of pandemic influenza vaccines, as mandated by General Comment 14.

Three predominant reasons for this can be identified. In the first instance, the provisions within the example Standard Material Transfer Agreement provided at the annex to the PIP Framework fail to maximise benefit sharing for developing states,

\(^{146}\) Jefferies, (n61); Fidler and Gostin, (n86); Vezzani, (n87);
largely due to the overly flexible benefit sharing obligations secured in the PIP Framework, and the lack of legal compulsion that requires relevant PIV manufacturers to commit to benefit sharing via a Standard Material Transfer Agreement. Secondly, the prospect of developing states using the PIP Stockpile as a procurement tool becomes even less viable when the SMTAs that pandemic influenza vaccine manufacturers have signed are taken into consideration. Too few of the pandemic influenza vaccine manufacturers currently active within the market have committed to share benefits with the WHO via an SMTA, with only 17% of manufacturers currently party to an SMTA. This clearly reduces the number of doses the PIP Stockpile has available to it for distribution to developing states that have been unable to procure vaccine via self-procurement methods. Thirdly, the viability of the PIP Stockpile as a procurement method is further reduced when the terms which have been secured with the three manufacturers that are party to a SMTA are evaluated.

In the next chapter, I shall examine the relationship between intellectual property rights and access to medicines, and present a patent landscape for pandemic influenza vaccines in order to determine if the existence of such rights have any impact on access to pandemic influenza vaccines in developing states.
In this chapter I argue that patents have the potential to limit the extent to which developing states can discharge their right-to-health obligations, by limiting developing states’ access to medicines. From this general critique of the role patents play in access to medicines and the right-to-health, I present a patent landscape outlining relevant patents in the field of pandemic influenza vaccines. From this, I argue that these patents have the potential to negatively impact upon developing states’ ability to discharge their right-to-health obligations, in respect of access to pandemic influenza vaccines. By creating barriers to entry for generic manufacturers, patents limit the number of manufacturers that can enter the market. This limits procurement options for developing states, and could contribute to the high price of pandemic influenza vaccines.

The academic literature concerning patents and pharmaceuticals can be rather crudely divided into two camps: those who argue that awarding patent rights over pharmaceutical products, even if they are life-saving, is justifiable, as without such patent rights pharmaceutical companies will lack the incentive necessary to invest time and money in drug creation in the first place; and those who argue that awarding patent rights over pharmaceutical products is unjustifiable, on the basis that awarding patents on pharmaceutical products diminishes access to these products,

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1 It is worth noting that no drug can truly claim to be ‘life-saving’, what we mean by this is ‘life-extending’, no drug can truly save one’s life, merely extend it. See: LB Tan and R Murphy, ‘Shifts in mortality curves: Saving or extending lives?’ (1999) 354(9187) The Lancet 1378 However, the language of ‘life-saving’ drugs permeates the literature, and therefore is used throughout this research for consistency.

with undesirable repercussions for the right-to-health. This argument is based on the fact that a patent will provide a pharmaceutical manufacturer a monopoly over a potentially life-saving product, and the patent affords the manufacturer the power to control production and distribution, and artificially inflate its price, should they choose to. It should be noted that arguments to justify the patent system sit along a spectrum, and the dichotomy highlighted above represents some of the more polarised opinions in the literature.

Given the intense criticism directed towards the role intellectual property rights play in the creation and subsequent procurement of pharmaceuticals, both by member states at the PIP negotiations and more generally in the academic literature, it is necessary to scrutinise these claims in the context of pandemic influenza vaccine procurement over the next three chapters.

5.1 Patents, Access to Medicine and the Right to Health

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4 WHO, ‘Sharing of Influenza Viruses and Access to Vaccines and Other Benefits: Interdisciplinary Working Group on Pandemic Preparedness: Report by the Director-General’ (A/PIP/IGM/4 2007) <http://apps.who.int/gb/pip/pdf_files/PIP_IGM_4-en.pdf> ‘the overriding concern expressed by members...was that neither intellectual property rights, nor prior informed consent requirements, if any, should stand in the way of developing and producing a pandemic influenza vaccine’ at Annex 11

As noted in the introduction, access to medicine, as a component of the right-to-health, was elaborated upon in The Committee on Economic, Social and Cultural Rights General Comment No. 14: the Right to the Highest Attainable Standard of Health. In the context of access to medicines, state parties to the Covenant are obliged to ensure

[t]he creation of conditions which would assure to all medical service and medical attention in the event of sickness...includes the provision of equal and timely access to basic preventive, curative, rehabilitative health services and...the provision of essential drugs

In the context of access to medicines, much has been written about the apparent conflict between granting intellectual property rights over pharmaceutical products, and the right-to-health. This debate has focused on the exclusionary rights granted to patent holders, which prevent third parties from making, using, offering for sale, selling or importing for these purposes that product, without the express consent of the patent holder. This prevents generic competition, which is the biggest

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7 para. 17, General Comment 14.
9 TRIPS, Article 28 (1)(a)
contributor to price reduction in pharmaceutical products.\(^{10}\) With price reductions 
eventually comes increased access, particularly in developing states.\(^{11}\) The debate 
regarding the extent to which these exclusionary rights can negatively impact upon 
the right-to-health largely stems from concerns over access to HIV/AIDS medicines in 
developing states,\(^{12}\) though it has subsequently been translated to other public health 
concerns, particularly in developing states.\(^{13}\)

As Cullet said, on the requirement of developing states to provide patents in the field of pharmaceuticals:

In most developing countries, the introduction of process and product patents 
on drugs is likely to influence access to drugs to a significant extent. There will 
be abrupt rises in price, impacts on local pharmaceutical industries and a 
greater emphasis on private sector research and development. Together, 
these are likely to create a situation where drugs become both less accessible 
and less affordable. There is therefore a direct link between patentability of 
drugs on one hand and, on the other, the availability of medicines, the 
realization of the right-to-health and ultimately of the right to life.\(^{14}\)

\(^{10}\) A Cameron and others, 'Medicine prices, availability, and affordability in 36 developing and middle-

\(^{11}\) Ruth Mayne, 'The Global Campaign on Patents and Access to Medicines: An Oxfam Perspective' in 
Peter Drahos and Ruth Mayne (eds), \textit{Global intellectual property rights: Knowledge, access and 
development} (Palgrave Macmillan 2002); Suerie Moon and others, 'A win-win solution? A critical 
analysis of tiered pricing to improve access to medicines in developing countries' (2011) 7(1) 
Globalization and Health 39

\(^{12}\) Bridget Sleap, 'The most debilitating discrimination of all: Civil society's campaign for access to 
Hogerzeil and others, 'Is access to essential medicines as part of the fulfilment of the right-to-health 
enforceable through the courts?' (2006) 368(9532) The Lancet 305; James Harrison, 'Trade 
agreements, intellectual property and access to essential medicines: What future role for the right-to-
health?' in Obijiofor Aginam, John Harrington, and Peter K. Yu (eds), \textit{The global governance of HIV/AIDs: 
Intellectual property and access to essential medicines} (Edward Elgar Publishing 2013); Godoy, (n8); 
Matthews, (n8)

\(^{13}\) Cullet, (n8); Alicia Ely Yemin, 'Not just a tragedy: Access to medications as a right under international 
law' (2003) 21 Boston University International Law Journal 352; Godoy, (n8); Diederik Lohman, Rebecca 
Schleifer, and Joseph J Amon, 'Access to pain treatment as a human right' (2010) 8(1) BMC Medicine 8; 
Chris Beyrer and others, 'Neglected diseases, civil conflicts, and the right-to-health' (2007) 370(9587) 
The Lancet 619; Phillipe Cullet, 'Human Rights and Intellectual Property Protection in the TRIPS Era' 
(2007) 27 Human Rights Quarterly 403

\(^{14}\) Cullet, (n8)
The negative impact that the exclusionary rights granted to a patent holder can have on access to medicine, and therefore on realising the right-to-health in developing states, is well established.\textsuperscript{15} Moreover, much literature has been generated by the academic community, and by civil society, on how to limit or eliminate this negative impact in developing states.\textsuperscript{16} However, it appears that the literature concerning the impact of patents on the right-to-health in the context of access to medicines considers only oral solid drugs – tablets, not vaccines – but does so under the umbrella term ‘medicines’. As noted previously, oral solid drugs and vaccines are very different products, and have different patentability components, even though they are both grouped together under the umbrella term ‘medicines’. This use of the umbrella term ‘medicine’ leads us to assume that the comments outlined above about the impact patents have on access to oral solid dose drugs for HIV/AIDS or tuberculosis are equally applicable to access to a vaccine for meningococcal B or influenza. However, this is not necessarily true, given the significant differences between drugs and vaccines.

To this end, the patentable elements of oral solid dose drugs are based on the product’s composition of matter, and its application within medicine. A novel\textsuperscript{17} compound with pharmaceutical properties is eligible for patent protection.\textsuperscript{18} Pharmaceutical patenting is limited because ‘a method of treatment of the human or animal body by surgery or therapy, or a method of diagnosis practiced on the human or animal body’\textsuperscript{19} is not eligible for patent protection. However, a patent may be

\textsuperscript{15} see (n10)
\textsuperscript{17} Novel in the sense that it does not form part of the current state of the art –S.2(1)-2(4) Patents Act 1977 (as amended 2004)
\textsuperscript{18} Providing it also meets the requirements of having an inventive step and industrial applicability, see S.1(1) PA1977
\textsuperscript{19} S.4A(1) PA1977
granted for a first medical indication when an inventor discovers that a compound, already part of the state of the art, has a pharmaceutical application that can be used to treat a specific medical indication. Second, medical indication patents can be granted for further, specific uses of known substances or compositions. Both first medical indication and second medical indication applications must be supported by sufficient evidence to prove likely efficacy.

This differs significantly from the patentability of pandemic influenza vaccines, whereby it is not just the compounds that comprise the vaccine that are patentable, but also the processes by which the vaccine is manufactured, the adjuvant, and in some instances, the inactive virus or genetic structures within the virus against which the vaccine protects. In order to determine any impact these patents have on access to pandemic influenza vaccines and the therefore the extent to which a state can discharge its right-to-health obligations during a pandemic, it is first necessary to describe the patent landscape of these same vaccines, components and processes.

5.2 - Patent Landscape

Three major reports regarding the pandemic influenza vaccine patent landscape can be identified. First, in 2006 a freedom to operate exercise was carried out by Krattinger and others in the field of pandemic influenza vaccines, in order to determine what, if any, intellectual property related barriers could prevent a manufacturer from achieving freedom to operate in the field. No patents regarding viral strains or components were included in this search. Second, a patent landscape report regarding pandemic influenza viruses 2005-H5N1 and 2009-H1N1 was

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20 S.4A(3) PA1977 – the boundaries between the exclusion of methods of treatment from patents and the patentability first medical indication has presented a considerable challenge to UK and international courts see: Bristol-Myers Squibb v Baker Norton Pharmaceuticals [2001] RPC 1; T 09/81 ASTA/Cytostatic combination OJIEPO [1983]; T 24/91 THOMPSON/Cornea OJIEPO [1995]

21 S.4A(4) PA1977

22 See: Prendergast’s Applications [2000] RPC 446; F. Hoffmann - La Roche’s Application BL O/192/04; Medsystems v Angiotech Pharmaceuticals [2008] RPC 28

23 See glossary for explanation of term.

published by the World Intellectual Property Organisation (WIPO) in 2011.\textsuperscript{25} This report specifically considered patents claiming inventions comprising the virus, a component, or a derivative of the virus, for diagnostic, therapeutic or prophylactic purposes, where the patent was applied for after the date at which it became clear that that strain of virus could be of pandemic potential.\textsuperscript{26} This report did not consider any manufacturing patents. Third, is the report by the Franklin Pierce Center for Intellectual Property, which in 2013 published the \textit{Patent Landscape of Influenza: A Prophylactic Vaccines and Related Technologies} report (henceforward “the Franklin Pierce report.”\textsuperscript{27} This report considered both the vaccine manufacturing patent landscape, and the viral strain patents, and is therefore the most relevant to this research.

The Franklin Pierce report reached a number of interesting conclusions about the patent landscape for pandemic influenza vaccines. Firstly

the number of patent documents related to influenza being published has been steadily increasing in the last decade…. Until the mid-1990s, there were only a few influenza patent documents being published each year. The number of publications increased noticeably when TRIPS took effect, resulting in publication of patent applications. However, since 2006 the number of vaccine publications has exploded. In each of 2011 and 2012, about 100 references disclosing influenza vaccine technologies were published\textsuperscript{28}

And

Influenza virus technologies appear to originate from a small set of countries, mostly the United States, Great Britain, France, China, Japan, Korea, and Russia. Protection for influenza vaccine intellectual property has been sought worldwide. However, except for Brazil coverage in South America is quite

\begin{footnotesize}
\begin{itemize}
\item[\textsuperscript{26}] Ibid, 3
\item[\textsuperscript{27}] Jon R Cavicchi and others, 'Patent landscape of influenza A virus Prophylactic vaccines and related technologies' (Franklin Pierce Center for Intellectual Property 2013) <http://scholars.unh.edu/cgi/viewcontent.cgi?article=1195&context=law_facpub>
\item[\textsuperscript{28}] Ibid, 6
\end{itemize}
\end{footnotesize}
minimal, and except for South Africa protection for these technologies is sparse in Africa.\textsuperscript{29}

In terms of the overall patent landscape for pandemic influenza vaccines the Franklin Pierce report concluded that there are

[approximately] 3,800 patent families [related to pandemic influenza vaccine manufacturing]. However, only about one-half of those patent documents will actually be specific for prophylactic influenza A vaccines\textsuperscript{30} or for technologies that are used in the manufacture of vaccines. Of those relevant documents, approximately 10-15\% are specifically related to pandemic influenza, although the remainder could probably be applied to pandemic strains.\textsuperscript{31}

When seeking freedom to operate in a field of technology, the number of patents is of course relevant, but so is the number of patent holders. The predominant barrier to freedom to operate that an anticommons creates is that there are numerous patent holders with whom a new manufacturer seeking to enter the market must successfully negotiate. While the Franklin Pierce report notes that ‘influenza vaccine technologies are disclosed in a fairly small set of patent documents,’\textsuperscript{32} it is also worth noting that these patents are held by a number of patentees, as the table below demonstrates. Large patent families, being held by multiple patent holders in this way, could reduce freedom to operate, or cause an anticommons in the pandemic influenza vaccine manufacturing field.\textsuperscript{33}

\textsuperscript{29} Ibid, 101
\textsuperscript{30} Although the authors of this report do not expressly define what ‘influenza A’ is, it is the substring of influenza that is most likely to lead to a pandemic strain circulating amongst the human population - CDC, ‘Avian influenza A virus infections in humans’ (11 December 2015) <http://www.cdc.gov/flu/avianflu/avian-in-humans.htm>
\textsuperscript{31} Cavicchi and others, 101
\textsuperscript{32} Cavicchi and others, 101
\textsuperscript{33} This issue is discussed in more detail at 6.4.4
Table 2: Patent Holders in Pandemic Influenza Vaccine, Virus and Manufacturing Technologies*

<table>
<thead>
<tr>
<th>Standardized Assignee</th>
<th>Number of Families</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novartis</td>
<td>33</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>25</td>
</tr>
<tr>
<td>Pfizer</td>
<td>25</td>
</tr>
<tr>
<td>Merck and Co. (Merck Sharpe &amp; Dohme)</td>
<td>23</td>
</tr>
<tr>
<td>Nauchno-issledovatelskij institut ehkperimental’noj meditsiny RAMN (Scientific Research Institute of Experimental Medicine, RAMS)</td>
<td>23</td>
</tr>
<tr>
<td>Sanofi</td>
<td>21</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>20</td>
</tr>
<tr>
<td>University of Wisconsin</td>
<td>18</td>
</tr>
<tr>
<td>US Department of Health</td>
<td>16</td>
</tr>
<tr>
<td>Baxter International</td>
<td>15</td>
</tr>
<tr>
<td>Saint Jude’s Hospital</td>
<td>15</td>
</tr>
<tr>
<td>Chinese Academy of Agricultural Sciences</td>
<td>14</td>
</tr>
<tr>
<td>Chinese Academy of Sciences</td>
<td>11</td>
</tr>
<tr>
<td>Kaketsuken</td>
<td>9</td>
</tr>
<tr>
<td>Institute of Medical Biology Chinese Academy of Medical Sciences</td>
<td>8</td>
</tr>
<tr>
<td>Ministry for Food Agriculture, Forestry and Fisheries (Korea)</td>
<td>8</td>
</tr>
<tr>
<td>Mount Sinai Hospital</td>
<td>8</td>
</tr>
<tr>
<td>Boehringer Ingelheim</td>
<td>7</td>
</tr>
<tr>
<td>Choong and Vaccine Laboratory</td>
<td>7</td>
</tr>
<tr>
<td>Ministry of Health, Labour and Welfare (Japan)</td>
<td>7</td>
</tr>
<tr>
<td>Vsesoyuznyj Nauchno-Issledovatskij Institut Grippa (Union Scientific Research Institute of Influenza)</td>
<td>7</td>
</tr>
</tbody>
</table>

*Table reproduced from The Franklin Pierce Report, (2013), 74

The patents identified in the field of pandemic influenza vaccines can be divided into two subcategories worthy of further consideration. Those patents which relate to, or make use of, pandemic influenza viruses, and those patents related to the pandemic influenza vaccine manufacturing process. Each of these subcategories of patents may have an impact on the extent to which developing states are able to obtain sufficient access to pandemic influenza vaccines in order to discharge their right-to-health obligations.
5.2.1 - Patents related to pandemic influenza viruses

Section Five of TRIPS provides that members shall grant patents in any field of technology, providing the grounds for patentability have been satisfied, and TRIPS exemptions to patentability have not been breached. TRIPS does not explicitly exclude any area of innovation from patentability – but does allow states to exclude inventions that offend *ordre public* or morality, including where it is necessary to protect human health, and diagnostic, therapeutic or surgical methods. Despite this flexibility, many states have chosen not to exclude viruses, or VLPs, from patentability, which has met a great deal of controversy.

A number of patents identified by the Franklin Pierce Report directly make use of, and refer to, a substrain of a pandemic influenza virus, including viruses which do not currently exist naturally but may begin circulating in the future. Such patents could limit freedom to operate, should the genetic material claimed then be required in order to manufacture a PIV for a circulating strain. The majority of patents relating to virus genetic material cover specific uses of the virus in a novel vaccine composition; therefore, such patents do not affect freedom to operate and ‘could not legitimately be used to constrain parallel development of alternative uses of the same genetic inputs’, provided the virus could be used in another novel vaccine composition, not

34 Article 27, TRIPS
35 Article 30, TRIPS
36 Article 27(2), TRIPS
37 Article 27(3)(a), TRIPS
38 See for example, the EU: Directive 98/44/EC (1998); *Australia: Cancer Voices Australia v Myriad Genetics* [2013] FCA 65; USA: *Diamond v. Chakrabarty* [1980] 447 U.S. 303
40 Freedom to operate is the ability to proceed with the commercialisation of a new product or process with a minimal risk of infringing on the intellectual property rights of others in the field.
covered by the original patent, or any other patent that claims use of the genetic material in this way.

Some patents granted have applicability to a number of influenza outbreaks, both seasonal and future pandemics. For example, WO/2010/148386, a patent that at first glance appears to cover a method of production for 2009-H1N1 vaccine, is not limited to the methods of production for 2009-H1N1 vaccines. It also encompasses the method of extracting and using VLPs in future pandemics. WO/2009/092038, a patent claiming use of multiple H5-subtypes in a DNA vaccine, and is applicable to any substrain of the H5 virus being used in a DNA vaccine manufacturing process, meaning it may have applicability beyond the pandemic for which it was developed.

If such patents remain enforceable at the time the virus begins to circulate naturally, they may hinder future research, development and manufacture of a vaccine. The existence of numerous patents, held by numerous patent holders, covering multiple substrains of the influenza virus may disincentivise future innovation in this field, because they cause an anticommoms and deny sufficient freedom to operate for manufacturers. As can be seen from the table above, at least twenty-one different entities hold multiple, relevant patents in this field – ranging from the large pandemic influenza vaccine manufacturers to national governments and small biotech research labs. While it is true that in order to obtain freedom to operate, a new manufacturer would not have to negotiate for a license with all these patent holders, only the patentee of the technology one wishes to make use of, this is still a difficult, time-consuming task. It may be so difficult as to be a disincentive to those manufacturers

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42 Novavax, ‘Swine-Origin Influenza A (H1N1) Virus-Like Particles And Methods Of Use Thereof’ WO/2010/148386
43 The United States Of America, As Represented By The Secretary, Department Of Health And Human Services ‘Influenza DNA Vaccination And Methods Of Use Thereof’ WO/2009/092038
44 ‘Anticommons is when the number of patents in an area of research or manufacturing becomes so dense, that it restricts innovation in the field, due a lack of freedom to operate for manufacturers’ Michael A Heller and Rebecca S Eisenberg, ‘Can patents deter innovation? The Anticommons in biomedical research’ (1998) 280(5364) Review 698 more information on anticommoms in pandemic influenza vaccine manufacturing is provided at 6.4.4
considering entering the market. In addition, while the research exemption contained within many states’ domestic patent laws may enable some degree of research on the patented virus or virus particles, should this research lead to a viable vaccine, the patent may prevent it reaching the market if a license cannot be negotiated on terms reasonable to both parties.

5.2.2 - Patents related to manufacturing process
There is a growing trend for patents on vaccine manufacturing processes, as was noted at a WHO seminar on patents and vaccines: ‘older patents were used to protect components of vaccines (organisms, antigens and conjugates), while recent patents tend to protect methods (expression system, platform technologies, purification process, formulation or even delivery devices)’. This shift has coincided with advances in the extraction, purification and production methods for PIVs.

Patents on reverse genetic engineering technologies, which are a key new technology for the production of egg-based pandemic influenza vaccines, have been identified as a barrier to production for competitors. Moreover, PIV manufacturers appear to be moving towards utilising new methods of growing viruses for vaccine production, each of which has some degree of IPR that has been identified as a potential barrier to access for competitors: firstly, cell-based influenza vaccines, the manufacturing of which is subject to ‘many intellectual property impediments. These include patents on cell lines and production systems, as well as trade secrets on safety profile of

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45 This point is addressed in more detail in the following chapter.
47 EU: Art. 10(6) EC Directives 2001/82/EC; UK: S.60(5)(i) Patents Act 1977; USA: USC. § 271(e)(1); Canada: s.55.2(1) Patents Act 1985
48 For a discussion regarding how difficult this process can be, see: Shapiro, (n16); Mark A. Lemley and Carl Shapiro, ‘A simple approach to setting reasonable royalties for standard-essential patents’ (2013) 28 Berkley Technology Law Journal 1135
cells’; live attenuated vaccines, where ‘intellectual property impediments exist on the use of strains; and patents and trade secrets cover the formulation. Seeds may need reverse genetics’; and finally ‘second generation biotech’ such as DNA vaccines where ‘impediments will depend on specific technology...it may be anticipated that these technologies will have robust IPR coverage as they are mainly being developed by biotech companies and universities seeking to sell this technology’.

Both the patents on pandemic influenza viruses, and those on the manufacturing processes outlined above, could reduce access to pandemic influenza vaccine in developing states by limiting the number of manufacturers in the market space or preventing new manufacturers from entering the market, because these manufacturers do not think they can achieve freedom to operate. From an access, and right-to-health perspective, this is concerning for two reasons. First, as a major study regarding the prices, availability, and affordability of medicines in thirty six developing and middle-income countries found, the greater the number of manufacturers of a pharmaceutical product in a market, the cheaper the cost of that product. With cheaper cost for the product clearly comes better access, particularly for developing states. Second, an increase in the number of manufacturers in the market place for pandemic influenza vaccines should lead to an increase in overall vaccine manufacturing capacity. This would increase the self-procurement options that were available to a developing state. With greater procurement options, a developing state may be able to contract with a manufacturer that did not have to satisfy an advance purchase agreement contract during a pandemic, meaning the developing state could access the vaccine more quickly.

5.3 - The Effect of Patents on Procurement of Pandemic Influenza Vaccines

5.3.1 - Patents and Prohibitive Prices

52 Ibid, 29
53 Ibid, 29
54 Cameron, (n10)
The chapters that follow examine two lines of inquiry: first, whether the intellectual property rights that are afforded to pandemic influenza vaccine manufacturers can be justified, because they incentivise the creation of pandemic influenza vaccines in the first place; second, whether the intellectual property rights in the pandemic influenza vaccine field, highlighted in this chapter, can be circumvented in order to improve access during a pandemic. However, prior to that discussion it is necessary to determine what, if any, impact the patents identified in this chapter have on procurement of pandemic influenza vaccines, and if these patents are the barrier to developing states discharging their right-to-health obligations in this regard.

A pandemic influenza vaccine costs the state approximately £3.50 per dose (excluding administration), and in order to establish full immunity against a pandemic strain a two dose strategy is typically required. Therefore, the cost of an influenza pandemic vaccination programme is likely to be very high, and in some instances may be prohibitive, particularly to developing states. This point is demonstrated by the fact that ninety-five states were deemed to have a ‘lack of ability to purchase vaccine on the commercial market’ during 2009-H1N1, and a review of the WHO Vaccine Deployment Initiative later noted that ‘the cost of deploying vaccine was a constraining factor that limited the quantity of pandemic H1N1 vaccine demanded by countries’.

It is clear that one of the reasons these ninety-five developing states were unable to meet their right-to-health obligations to ‘ensure provision of...immunization

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55 Nayer Khazeni, ‘Effectiveness and Cost-Effectiveness of Vaccination against Pandemic Influenza (H1N1) 2009’ (2009) 151(12) Annals of Internal Medicine — administration costs include cost of transportation, cold chain infrastructure, and healthcare workers to administer the vaccine to the population.


58 WHO, ‘Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative’ (2011) <http://www.who.int/influenza_vaccines_plan/resources/h1n1_vaccine_deployment_initiative_moll.pdf>
programmes against the major infectious diseases\(^{59}\) was the cost of the vaccine. As to the role patents play in prohibitive prices of pandemic influenza vaccines, some commentators have claimed that the existence of patents are the cause of high drug prices. \(^{60}\) From a right-to-health perspective, as noted above, in using their exclusionary rights to prevent generic competition in the market for a life-saving drug, patent holders may negatively impact upon an individual’s right-to-health, where that individual is prevented from accessing the life-saving drug due to the lack of cheaper generic versions. However, this linking of the existence of patents on a pharmaceutical product to the high price of a pharmaceutical product could be seen as too simplistic a standpoint.

It may be the case that patents and high prices are inextricably linked. Generic drugs are traditionally priced significantly lower than their patented counterparts,\(^{61}\) and the more generic providers that exist, the greater the reduction in price.\(^{62}\) The reasons for this are straightforward: generic manufacturers incur significantly lower costs than the innovator, as they bear none of the costs of research and development, nor the licensing of the drug. Therefore they can afford to offer the product at a reduced cost, while still being profitable. This either leads to the generic product being purchased, or the competition from the generic provider forcing the innovator to reduce their prices, in order to maintain sales.

However, it is not the existence of the patent that is the cause of high price \textit{per se}, as patent protection does not necessarily mean that the price of a product will be high.

\(^{59}\) para. 36, General Comment 14.
\(^{62}\) WTO, WIPO & WHO, (n52) 53
A patent however, does ensure the patentee can maintain their monopoly, and the monopoly in turn provides the climate for the patentee to charge the price they wish, without the fear of imitators undercutting them. It is the manufacturer having the ability to exploit a monopoly that causes the high prices of medicines, not merely the existence of the patent. The price of PIVs would not necessarily be lower if the patentee’s exclusive rights could be circumvented. ‘Natural’ monopolies are also caused by other factors, such as a manufacturer’s dominant market position, or it being financially or practically prohibitive for generic manufacturers to manufacture or license a product. The ongoing public debate about the price rises for Daraprim in the United States of America is testament to that fact. Turing Pharmaceuticals manufactures and sells Daraprim in the United States of America. Daraprim is an antiparasitic, commonly used to treat HIV patients that became headline news when the price was increased from $13.50 to $750 per pill in late 2015. Turing Pharmaceuticals was able to increase the price so substantially because it holds a monopoly over the sales and distribution of Daraprim. However, this monopoly is not provided by a patent; the patent for Daraprim expired over sixty years ago. Turing Pharmaceuticals’ exclusive rights to sell Daraprim comes from the company holding

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63 The seminal article: Guido Calabresi and A. Douglas Melamed, ‘Property rules, liability rules, and Inalienability: One view of the cathedral’ (1972) 85(6) Harvard Law Review 1089 at 1092 argues that this right to exclude in order to maintain a monopoly is indicative of patent law being akin to property law in the traditional sense.
64 Market forces play a role in determining the price of a product, as will competition or comparable products, See [n12]
65 This issue is addressed in the following chapter.
the only marketing license for Daraprim in the United States of America. In this case a monopoly is preventing cheap generic access, but it is not because of intellectual property, as some of the literature would lead one to think.

In general, patent protection may inhibit the procurement of cheap medicines by blocking the entry of generic rivals, whose presence increases availability of the product, and is likely to lead to a price reduction. Generic entry benefits the drug procurement processes of developing states by offering them an alternative, cheaper manufacturer to buy from, or by encouraging the innovator to reduce their price in order to respond to the competition in the marketplace. However, since there are no generic manufacturers for PIV, it is does not appear that it is solely the patent that maintains a monopoly for PIV manufacturers. On the contrary, it appears that PIV manufacturers have a strong monopoly, and are at little to no risk from generic competition, regardless of the patents granted on the PIVs they produce.

5.3.2 - Blocking Competitors and PIV Procurement

When discussing a patentee’s exclusive rights, one may be forgiven for thinking that these rights merely stop imitators from making ‘carbon-copy’ replicas of the patentee’s invention, and selling it for a significantly reduced price. This argument does not consider that a patent may also serve to block rival innovations.

Patent thickets and the tragedy of the anticommons metaphor will be discussed in more detail in the following chapter in relation to availability of PIVs. However it is necessary to briefly mention them in relation to their role in procurement. A patentee that holds patents related to pandemic influenza viruses may choose not to license the use of the patented virus, or virus like particles, to a rival innovator firm, just

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70 The reasons for this lack of generic competition are explored in the following chapter.

71 A patent thicket is defined as ‘a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology’ - Carl Shapiro, (n16)

72 See (n44) for an explanation of an anticommons
because they are rivals in such a small market. The main purpose of the patents in pandemic influenza vaccine technology may be to block innovation by rival firms, by creating an anticommons, rather than blocking generic manufacturers. As a result, it may be difficult for rival innovators to bring a novel PIV to market without potentially infringing another innovators patent. This inhibits the number of vaccines available for procurement by states, by creating a scenario in which growth in vaccine manufacturing capacity is reliant upon current manufacturers choosing to expand their production capacity, which there is presently no market incentive to do.\textsuperscript{73}

In order for an innovator to overcome this patent barrier, they would need to negotiate a license with the patent owner, or create a new product or process that does not infringe on any patents. As Kane noted, a manufacturer’s position is significantly strengthened in such negotiations if they hold a relevant patent that may be being infringed:

Patented compounds or methods required for vaccine production must be purchased or licensed from commercial entities who may hold patents on any of these items. The willingness to license or the licensing terms may reflect the patent-related considerations that enter the transactional evaluation. A patent could affect licensing negotiations through pricing mechanisms or limited offerings.\textsuperscript{74}

This means that capacity, and thereby procurement, will not be improved by new innovators, because the incentive to enter the market is not sufficiently strong, or they are unable to bring their innovation to market because of an inability to reasonably negotiate licenses with numerous patent holders.


\textsuperscript{74} EM Kane, 'Achieving clinical equality in an influenza pandemic: Patent realities' (2009) 39(4) Seton Hall law review 1137
Such a situation has not yet occurred in pandemic influenza vaccine reverse genetics manufacturing, and freedom to operate is possible in this field. Prior to late 2005, at least four institutions had to approve licenses in order for a PIV manufacturer to obtain freedom to operate in the reverse genetics PIV field. Reverse genetics is a key technology in stabilising pandemic influenza viruses for their inclusion in vaccines. In late 2005 MedImmune secured exclusive licensing rights to all key patents from the different rights holders, and the company has given assurances that that research and manufacturing licenses would be issued to relevant parties, ensuring freedom to operate exists in the field.

However, the situation is far from ideal; freedom to operate in PIV reserve genetics is only possible at present because MedImmune ‘has taken steps to ensure that its patent rights do not inhibit the development and commercialization of a pandemic influenza vaccine’ and has notified the WHO that that it would grant free access to its intellectual property to government organisations and companies developing pandemic influenza vaccines gratis for public health purposes. Yet the commitment MedImmune has given is not legally binding, meaning such licenses could be withdrawn or refused by the company, and there is no guarantee that they will be as forthcoming with licensing of technology in the future. Finally, reverse genetic engineering is merely one of a number of potential avenues for PIV development, and

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76 There are generally regarded to be four patent portfolios associated with the reverse genetics technology. (WO 91/03552) (WO 00/60050) (WO 01/83794) (U.S. Patent No. 6,544,785)
78 Ibid.
79 Ibid.
80 Institute of Medicine (n77), 196
no such guarantees have been given by the patent owners in the other areas of PIV research and development, meaning that freedom to operate may not be as easily achieved in DNA vaccines or cell-based PIV manufacturing.

5.4 - Conclusion
There are multiple elements of a PIV and its manufacturing processes that can be, and are, patented. To some degree, such patents have the potential to hinder procurement of PIV by creating barriers to entry for new manufacturers - barriers that look set to be reinforced with the move to utilising patented PIV manufacturing technology, such as cell-based and live attenuated influenza vaccine technology. Such barriers affect access to pandemic influenza vaccines by limiting the number of manufacturers that can utilise this technology and enter the market. This in turn limits the overall manufacturing capacity for pandemic influenza vaccines, and limits the self-procurement options for developing states; both of which reduce the ease with which developing states can discharge their right-to-health obligations during an influenza pandemic.

As patents have the potential to hinder PIV procurement, the next chapter considers the role that patents play in the development of pandemic influenza vaccines, and determines whether the existence of patent protection on the vaccines, the components of the vaccines, and vaccine related technology, provides a net benefit to PIV procurement by incentivising the creation of PIVs in the first place. I will argue that it does not.
CHAPTER VI
DO PATENTS INCENTIVISE THE CREATION OF PANDEMIC INFLUENZA VACCINES?

In the previous chapter I argued that patents have the potential to negatively impact upon pandemic influenza vaccine procurement by developing states by granting a temporary monopoly to the patent holder which creates barriers to entry for rival manufacturers - which can keep prices high, and limit procurement options. In this chapter I consider the relationship between patents and pandemic influenza vaccines in more detail. I consider the role which patents play in the development of pandemic influenza vaccines, determining if the existence of patent protection being granted on the vaccines, vaccine related technology provides a net benefit to pandemic influenza vaccine procurement, by incentivising the creation of pandemic influenza vaccines in the first place. From this I argue that intellectual property is not required to incentivise the creation of pandemic influenza vaccines; the unique market conditions of pandemic influenza vaccine achieves this.

6.1 - Patents and Access to Knowledge

Patents provide property rights in knowledge generated by way of an invention. In pure economic terms, knowledge is a public good; an intangible asset of which anyone can consume as much of as desired, without diminishing the amount available for others.\(^1\) For example, the knowledge required to manufacture aspirin could be transferred from Person A, to Persons B, C, D and E, without diminishing Person A’s knowledge.

Once a public good is created it is difficult, or impossible, for the creator to stop people from using it who have not paid for it; this is commonly known as the free rider problem. The free rider problem is considered undesirable within economic markets as businesses cannot charge for each unit of a public good that is consumed, meaning that there is little incentive to generate, produce or enhance public goods. If a public good is just as useful to society as a comparable private good, then it can typically be said that the public good is under-produced and that this is inefficient for the society as a whole.

Patents move knowledge from being a public good, where there is no legal control over dissemination, to being an intangible asset which a person or organisation may have property rights in. A patent grants the patentee the right to exclude others from utilising the knowledge, for the life of the patent. Patents in the field of pharmaceuticals are controversial because of the importance of the knowledge which they exclude others from utilising, as Outterson notes: ‘the goal of [intellectual property] laws should be to maximize nonrival access to pharmaceutical knowledge, with just enough legal support for the appropriation of rents to protect socially optimal [research and development]. Since pharmaceutical knowledge is nonrivalrous, it should be disseminated in the widest possible fashion at the lowest possible cost for the greatest possible benefit to global public health.’

6.2 - The Economic Theory of Patent Protection

The economic theory of patent protection is the most cited theory of intellectual

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2 Paul A. Samuelson (1954), ibid.
3 Suzanne Scotchmer, Innovation and Incentives (The MIT Press 2005)
6 Although there are some limited circumstances in which a patented product can be exploited without the consent of the patentee. These circumstances are outlined in the next chapter.
7 Kevin Outterson, ‘Pharmaceutical arbitrage: Balancing access and innovation in international prescription drug markets’ (2005) 5(1) Yale Journal of Health Policy, Law, and Ethics 2
property in the literature,\textsuperscript{8} government reports,\textsuperscript{9} and by the courts.\textsuperscript{10} It is also specifically argued in relation to pharmaceutical research and development by the pharmaceutical industry itself: The BioIndustry Association has claimed that the pharmaceutical industry is ‘totally dependent on the availability of patent protection to ensure continued research findings into newly discovered biological material with possible therapeutic use’.\textsuperscript{11} More specifically in the field of pandemic medicine, the Chief Executive Officer of Roche claimed that ‘without patent protection, there is no research.’\textsuperscript{12}

The economic theory of patent protection originates from the work of Jeremy Bentham, who at the end of the eighteenth century wrote on intellectual property:

The protection against imitators [is necessary because] he who has no hope that he shall reap will not take the trouble to sow...the inventor would almost always be driven out of the market by his rival, who finding himself, without any expense, in possession of a discovery which has cost the inventor much


time and expense, would be able to deprive him of all his deserved advantages by selling at a lower price.\textsuperscript{13} Supporters of this theory claim that if imitators have the same costs of production as an innovator, but none of the initial development costs for the product, then imitators would be able to sell the imitation product at significantly less than the innovative product. Therefore, potential investors would not fund the development of innovator products as they know they will not recoup their initial investment, leading to a stagnation in research and development, which would be catastrophic in modern medicine.

Drahos claims that the economic theory of patent protection adequately justifies the existence of the patent system on the basis that people respond positively to incentives and reward.\textsuperscript{14} He further claims that, if profit is to be made from abstract objects which are ‘non–rivalrous’\textsuperscript{15} in their consumption, then in order to maintain a system of incentivisation the rights to these public good ‘have to be locked up in some way, at least temporarily’.\textsuperscript{16} In theory, the claims made by Drahos and Nordhaus that patents adversely affect the efficient use of knowledge by restricting, or ‘locking up’ knowledge have some merit, after all the fundamental purpose of a patent is to control the use of the knowledge generated for the life of the patent. Supporters of this theory appear to assume that the patent is the only factor preventing the patented knowledge from being used by others, and but for the patent, knowledge required in order to manufacture and work the invention would revert to being a public good that could be freely used by anyone, in turn disincentivising the creation of new inventions. In practice this is not the case, and there are many barriers to working an invention regardless of whether patent protection has been granted.

\textsuperscript{15} Drahos uses this term to refer to public goods, see: Samuelson, (n1).
\textsuperscript{16} Drahos, (n14) at 6.
First, the technology needed to make use of the knowledge may be inaccessible due to price barriers, or the technological know-how required to work the invention is not included in the patent, and not in the public domain; second, elements of the technology required to work the invention may be ‘locked up’ by trade secrets, non-disclosure, or an inability to be reverse engineered; and third, the knowledge may be generated in jargon or impenetrable language. Each of the above factors impact upon the extent to which knowledge may be used, regardless of the patent protection which has, or has not, been granted over the knowledge. As I go on to argue in this chapter, other barriers to utilising knowledge related to pandemic influenza vaccine manufacturing exist that have nothing to do with the patents that exist on the innovation.

6.3 - The Economic Theory of Patent Protection and Pandemic Influenza Vaccines

Proponents of the economic theory advance that but for the patent protection on the product, numerous other manufacturers will replicate the product for a significantly cheaper price, undercutting the original producer, thereby stifling development. This is a legitimate concern for products which are easily and cheaply replicable by numerous generic companies, such as oral solid drugs. However, there are a number of factors which distinguish the research, development and marketability of pandemic influenza vaccine from oral solid drugs, thereby challenging the applicability of this theory.

6.3.1 - A Viable Market

18 As is the case with a number of technological innovations within Formula 1 motorsport: Maria Solitander and Nikodemus Solitander, ‘The sharing, protection and thievery of intellectual assets’ (2010) 48(1) Management Decision 37
20 It has been noted that ‘it seems a reasonable hypothesis that the issue of patents on vaccines as end-products and their possible impact on access is different from that in pharmaceuticals.’ in Christopher Garrison, ‘Background paper for WHO workshop intellectual property rights and vaccines in developing countries background paper for WHO workshop on IP and vaccines’ (WHO 2004) <http://www.who.int/intellectualproperty/events/en/Background_paper.pdf>
While it is important to note that ‘undermining patent protection could discourage innovative activity on the part of industry’,\textsuperscript{21} it is equally important to take into account that patent rights can only stimulate innovation and investment in products that are likely to achieve adequate return on investment. Patents, regardless of how stringently they are enforced, cannot incentivise the development of products in a weak market — where financial rewards are likely to be lower than the investment made.\textsuperscript{22} The sole incentive for corporations to invest in any product is the prospect of future sales through which they can appropriate a return on their investment. The lack of a viable market therefore, is a crucial factor affecting product development, irrespective of patentees’ rights. Garrison, in drafting a background paper for the World Health Organization noted this point regarding vaccines: ‘It is not possible to divorce effectiveness of the [intellectual property] system in stimulating research and development from the viability of the underlying market in which it provides monopoly rights.’\textsuperscript{23}

Given that influenza pandemics occur on a sporadic basis, there may be little incentive for vaccine manufacturers to invest in, and develop, products that may not see a return on the investment made until the next pandemic occurs, by which time a patent may have expired. To this end, a WHO meeting on the role of intellectual property in vaccine access and development concluded that it is unlikely that implementation of the TRIPS Agreement patent standards will have an effect on the rate of innovation in products for which there is no strong financial incentive from the market.\textsuperscript{24}

However, despite the \textit{ad hoc} nature of pandemics, pandemic influenza vaccines are developed and manufactured, therefore some degree of market stimulus exists for

\begin{footnotes}
\item[23] Garrison, (n20)
\item[24] Kaddar, (n22)
\end{footnotes}
manufacturers. This may be related to the fact the vaccines are prophylactic products with population level sales; during an influenza pandemic, pandemic influenza vaccines are in very high demand amongst the governments of developed states, who are in a strong financial position to purchase them. The fact that the vaccines are also in demand by developing states, who may not be able to afford the product, may be of little consequence to the viability of the market. It has been noted that: ‘the fact that governments (and international agencies) are major purchasers, limits the scope for producers to secure higher prices through exercising their exclusionary rights’, due to the limited target market for producers. However, it appears that when considering pandemic influenza vaccines the opposite is actually true; first, demand for the vaccine will outstrip supply during an influenza pandemic; second, as compulsory licenses or government-use authorisations, are not viable tools to procure pandemic influenza vaccine, means that there are very few options available to a national government seeking to procure pandemic influenza vaccine, aside from purchase directly from the manufacturer, or await donations. These factors mean that contrary to the statement above, governments and NGOs make particularly desirable customers for pandemic influenza vaccine manufacturers; as each government is hoping to secure as much of the finite vaccine as they can to protect their population, and most have few viable alternatives aside from direct purchasing from innovators.

6.3.2 - Entering the Market

25 For some vaccine markets, this market stimulation is provided by push and/or pull mechanisms being provided for by organizations such as GAVI and BARDA: Michael Kremer, 'Creating Markets for New Vaccines - Part I: Rationale' in Adam B. Jaffe, Josh A. Lerner, and Scott Stern (eds), Innovation policy and the economy: V. 1 (National Bureau of Economic Research 2001) This is not the case for pandemic influenza vaccines.
26 Garrison, (n20) 5.
27 Governments may be able to nationalise domestic production as discussed at: Lance C Jennings and others, 'Stockpiling prepandemic influenza vaccines: a new cornerstone of pandemic preparedness plans' (2008) 8(10) The Lancet Infectious Diseases 650; Benjamin Capps and Tamra Lysag, 'Challenging the Production of Vaccines for a Future Influenza Pandemic' (2013) 5(2) Asian Bioethics Review 110; however, the political implications of such a decision, and the fact that a state must have domestic manufacturing facilities in their territory to nationalise means that this is also not a viable alternative for the majority of developing states.
Pandemic influenza vaccines are manufactured in the same facilities, by the same companies that manufacture seasonal influenza vaccines,\(^{28}\) of which there are currently twenty-five manufacturers, running thirty-four production facilities worldwide.\(^{29}\) Such facilities require both the use of specialised biocontainment facilities, and the introduction of genetic manipulation techniques in order to make the virus safe to include in a vaccine preparation.\(^{30}\) The amount of investment required to enter the influenza vaccine market may discourage investment, regardless of patent protection. Between 1999 and 2004 the United States lost two of the four domestic influenza manufacturers due to the cost of upgrading manufacturing plants to meet safety standards.\(^{31}\) Since this time, however, the U.S. Department of Health and Human Services has invested heavily in the industry, to ensure the US has domestic vaccine manufacturing capacity in the event of a pandemic.\(^{32}\)

Therefore, setting up a vaccine manufacturing plant requires a highly skilled workforce and technical experience and knowledge that may be specific to only one particular vaccine. For example, one of the identified reasons for the limited number of manufacturers of pandemic influenza vaccine is the lack of the necessary technical knowledge for emerging manufacturers,\(^{33}\) as ‘the technical know-how – even of conventional egg-derived influenza vaccines – is not readily found outside existing influenza vaccine production plants. Thus, even for procedures for which there are no patents, securing working partnerships with technology holders may be necessary’.\(^{34}\)

\(^{28}\) Catherine Gerdil, 'The annual production cycle for influenza vaccine' (2003) 21(16) Vaccine 1776
\(^{29}\) Jeffrey Partridge and Marie Paule Kieny, 'Global production capacity of seasonal influenza vaccine in 2011' (2013) 31(5) Vaccine 728
\(^{30}\) Rudi Daems, Giuseppe Del Giudice, and Rino Rappuoli, 'Anticipating crisis: Towards a pandemic flu vaccination strategy through alignment of public health and industrial policy' (2005) 23(50) Vaccine 5732
\(^{32}\) John Iskander and others, 'Pandemic Influenza Planning, United States, 1978–2008' (2013) 19 Emerging Infectious Diseases 879
\(^{33}\) World Health Organisation, ‘Mapping of Intellectual Property Related to the Production of Pandemic Influenza Vaccines’ (2007) <http://www.who.int/vaccine_research/diseases/influenza/Mapping_Intellectual_Property_Pandemic_Influenza_Vaccines.pdf> concluded that technical know-how and access to regulatory dossiers are more significant barriers than patents.
In order to address this, the WHO have lead efforts to transfer pandemic influenza vaccine manufacturing technical know-how to manufacturers in developing states, through the influenza vaccine technology ‘hub’. 35 Manufacturing capacity has increased since this policy was implemented in 200636 however, 75% of this growth has been to meet the needs of developed states.37

Further reasons for the limited appeal of the pandemic influenza vaccine market can be identified as: the limited market for seasonal influenza vaccines disincentivising new manufacturers from entering the market;38 large up-front costs and small profit margins;39 an uncertain rate and timeframe for return; a lack of production knowledge;40 and, the possibility of national takeovers of all important aspects of pandemic vaccine production and distribution during a pandemic.41 These factors combined make initial investment in such facilities, or the expansion of existing facilities, less appealing

[t]hus manufacturer prices for [influenza] vaccines reflect competition rather than regulation. Given the high fixed costs and low marginal costs and total absence of storability of [influenza] vaccine, it is not surprising that competition leads to low prices. Faced with low prices and volatile demand, manufacturers have chosen to exit rather than incur the significant costs of bringing manufacturing capacity up to the high standards required.

35 For information on how the hub facilitates transfer of technology see: Martin Friede and others, ‘Technology transfer hub for pandemic influenza vaccine’ (2009) 27(5) Vaccine 631
36 Jeffrey Partridge and Marie Paule Kieny, ‘Global production of seasonal and pandemic (H1N1) influenza vaccines in 2009–2010 and comparison with previous estimates and global action plan targets’ (2010) 28(30) Vaccine 4709; Jeffrey Partridge & Marie Paule Kieny, (n29)
37 Jeffrey Partridge & Marie Paule Kieny, (n29) at Table 2.
38 World Health Organisation, ‘open-ended working group of member states on pandemic influenza preparedness: sharing of influenza viruses and access to other benefits: technical studies under Resolution WHA63.1’ (2011)
39 WTO, WIPO & WHO, Promoting access to medical technologies and innovation: Intersections between public health, intellectual property and trade (WTO Publishing 2013)
40 ibid.
Unpredictability resulting from the production technology and the very short demand window are also critical.\textsuperscript{42} Given the significant risks involved in investing within the influenza market, and the low return on investment that innovators can expect, it is unsurprising that many manufacturers have left the market, rather than incur the costs to remain competitive. Moreover, if the economic theory holds true, and the product can be quickly, easily, and cheaply replicated by imitators (without adequate patent protection in place), then manufacturers will be even less likely to invest in the market.

6.3.3 - The Risk from Imitators

It is important to note that a patent does not allow a patentee to \textit{do} anything with the knowledge contained within the patent; it merely allows them to exclude others from utilising the knowledge without permission. It is argued using the economic theory that this ability to exclude others from utilising patented knowledge protects and stimulates investment and innovation, and, but for the patent, investment and innovation would be significantly hampered.

The economic theory supporter assumes that a product can be easily and cheaply replicated by generic imitators, who will offer the product significantly cheaper than the innovators. However, due to the regulations concerning the licensing of vaccines this is not the case for pandemic influenza vaccines. When attempting to license a pandemic influenza vaccine, even a ‘generic copy’ of an already licensed product, the manufacturer must generate a comprehensive novel regulatory dossier, rather than being able to rely upon the safety and efficacy data generated by the innovator, as generic manufacturers can for small molecule drugs.\textsuperscript{43} This involves generating extensive data from pre-clinical and clinical trials that adequately demonstrate the safety and efficacy of the product in humans. Such requirements significantly increase costs and time for generic companies. Furthermore, there are additional regulatory

\textsuperscript{42} Patricia M. Danzon and Nuno Sousa Pereira, 'Vaccine Supply: Effects of Regulation and Competition' (2011) 18(2) International Journal of the Economics of Business 239

\textsuperscript{43} See Article 10 of Directive 2001/83/EC for the European Medicine Agencies abridged application process for generic drugs.
requirements associated with vaccine manufacturing, including increased pharmacovigilance monitoring to ensure ongoing safety and efficacy of the product.\textsuperscript{44} Such requirements make the manufacturing of a ‘generic’ vaccine much more costly and time consuming than developing generic versions of traditional solid drugs, meaning that the benefits of generic competition cannot be fully realised for pandemic influenza vaccines. Moreover, this significantly limits the extent to which developing states can make use of the TRIPS flexibilities in order to increase access to pandemic influenza vaccines, as the next chapter discusses in more detail.

Such complex (but entirely necessary) and expensive licensing requirements therefore affect the price of pandemic influenza vaccines, and significantly reduces the incentive for, and ability of, generic companies to enter the market. This in turn, reduces the risk from imitators, irrespective of the patent protection that exists on the product.

6.3.4 - The Role of Patent Thickets

According to the economic theory, patents incentivise future research into products by providing protection for investments made into research and development. However, given that patent protection on vaccines exist not only on the vaccine, and the components contained within it, but also on the extraction and manufacturing processes, it may be more difficult to justify these patents using the economic theory because of the impact such patents have on future research and development. As part of ongoing research and development into future pandemic influenza vaccines it may be necessary for a third-party to exploit a process of extracting components from a virus,\textsuperscript{45} or an element of the manufacturing process that is patented, which, if a license is not granted authorising such an exploitation, may prevent further research and development of new vaccines by a third-party innovator.

\textsuperscript{44} S. D. Roger and D. Goldsmith, ‘Biosimilars: it’s not as simple as cost alone’ (2008) 33(5) Journal of Clinical Pharmacy and Therapeutics 459

\textsuperscript{45} it is worth noting that access to, and use of, viral samples from developing countries to manufacture said vaccines is highly controversial, see: Laurie Garrett and David Fidler, Sharing H5N1 Viruses to Stop a Global Influenza Pandemic, 4 PLoS Medicine e330 (2007). for details of what has become known as ‘the Indonesian virus-sharing incident’
It is reported via the Commission on Intellectual Property Rights, Innovation and Public Health that

[m]any of the institutions working on vaccine development have encountered difficulties of various kinds in accessing or licensing technologies (‘research tools’) needed for research and development that are protected by IPR. Since they often work on specific diseases with a limited number of different approaches to reaching their research goals, these obstacles may be more difficult to overcome than in ‘mainstream’ research, where companies may more easily circumvent obstacles by changing their approach to a research problem, or indeed switching to another problem altogether if they cannot easily achieve ‘freedom to operate.’

When discussing a patentee’s exclusive rights, one may be forgiven for assuming that these rights merely stop imitators from making a carbon-copy replica of the patentee’s invention, and selling it for a significantly reduced price. This argument does not take into account that a patent may also serve to block innovation by rival innovators in the marketplace. The role of patents in research and development is not limited to preventing imitators from replicating products and undercutting the innovators. Some commentators have argued that patents may actually deter innovators from entering a market, thereby stifling innovation because of ‘patent thickets’. A patent thicket has been described as: ‘a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology.’

Heller and Eisenberg have argued that the pharmaceutical industry has become particularly susceptible to what they refer to as ‘the tragedy of the anticommmons’, which emerges when the number of patents in an area of research or manufacturing

6 This information was obtained by CIPRIPH via ‘data collection and proposals from different actors involved in the sector’ – WHO, ‘Resolution WHA60.27, Sixtieth World Health Assembly’ (2007)
47 Predominantly Shapiro, and Heller & Eisenberg. Further details are provided below.
becomes so dense, that it restricts innovation in the field, due a lack of freedom to operate for manufacturers.\(^{49}\) Therefore, in order to assemble the required ‘technology package’, i.e. to gather all of the technologies necessary for development of the product, a researcher must identify the patented technologies, locate their owners, and negotiate a voluntary license in order to use and/or make the patented product.\(^{50}\) Heller and Eisenberg argue that when patent rights are held in this way by multiple institutions, the negotiations required in order to be able to license the use of the technology may fail, quashing the pursuit of research and development in the field,\(^{51}\) leading to a situation whereby a limited number of patentees control innovation in the field.\(^{52}\)

While subsequent empirical work has questioned the validity of the claims put forward by Heller and Eisenberg,\(^{53}\) there are reasons to believe that the pandemic influenza vaccine manufacturing industry may be susceptible to an anticommons scenario. The WHO has already noted specific examples of patent thickets in vaccine manufacturing and development whereby the use of patented ‘expression systems, fusion partners, immunostimulators, adjuvant systems, excipients and delivery devices may be required [in order to manufacture a new vaccine], and [to negotiate and license] access to each patented component may limit the feasibility of making a vaccine’.\(^{54}\) These patent thickets have the potential to restrict the development and manufacturing of future vaccines, due to a lack of freedom to operate in the market.\(^{55}\) While in principle market forces are thought to be able to help resolve the problems

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\(^{49}\) Michael A Heller and Rebecca S Eisenberg, ‘Can patents deter innovation? The Anticommons in biomedical research’ (1998) 280(5364) Review 698


\(^{51}\) Dan L Burk and Mark A Lemley, ‘Biotechnology’s Uncertainty Principle’ (2003) 54 Case W. Res. L. Rev. 691 305 (outlines the role these patent thickets have on disincentivizing potential investment, and development, in the biotechnology industry.)

\(^{52}\) Ibid.


\(^{54}\) WHO, (n46) at 12.

\(^{55}\) WHO, (n46) at 12.
associated with patent thickets, through initiatives such as the cross licensing of patented technology, in practice, transaction costs, uncertainty over the scope and validity of patent claims, complex patent landscapes and diverging business interests can result in stalemate between companies.\textsuperscript{56} Moreover, the complex patent landscapes and patentees’ interest in maintaining a monopoly often leads to voluntary license negotiations failing between established and new innovators,\textsuperscript{57} further restricting the research and development agenda, and the attractiveness of the market to new, or expanding manufacturers. Patent thickets causing anticommons such as this leads to a scenario whereby sub-optimal innovation in a sector occurs.

Patent thickets have the potential to negatively impact upon the development of pandemic influenza vaccines by reducing the incentive for new manufacturers to enter the market, limiting the number of manufacturers, resulting in the manufacturing capacity for pandemic influenza vaccine being reliant upon a set number of established manufacturers. As highlighted elsewhere, these established pandemic influenza vaccine manufacturers have Advance Purchase Agreements with developed states in place for the supply of pandemic influenza vaccine, which they are obliged to fulfil before taking or shipping order to other states without such Agreements.\textsuperscript{58} Therefore procurement of pandemic influenza vaccine is also impaired by patent thickets because the thickets limit the number of purchasing options available to states, by disincentivising from entering the market.

Worryingly, the research and development of influenza vaccine may be particularly susceptible to the negative effects of patent thickets\textsuperscript{59} in influenza vaccine technology. On this point, the WHO in response to a request by member states found that

\begin{itemize}
  \item \textsuperscript{56} WHO, (n46) at 12.
  \item \textsuperscript{57} Yochai Benkler, 'Intellectual Property: Commons-Based Strategies and the Problems of Patents' (2004) 305(5687) Science 1110; Burk & Lemley, (n51)
  \item \textsuperscript{58} Mark Turner, 'Vaccine procurement during an influenza pandemic and the role of advance purchase agreements: Lessons from 2009-H1N1' (2015) 11(3) Global Public Health 1
  \item \textsuperscript{59} ‘patent thicket’ is a term coined by Shapiro, and is defined as being ‘a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology,’ per Shapiro, (n48)
\end{itemize}
[t]here are no significant patent barriers to the manufacturer of any of the marketed types of influenza vaccines. Some patents protect specific products or processes, but for each of the types of market vaccines, there is sufficient freedom to operate to permit manufacturers in developing and emerging economies to make the vaccine of their choice. For future vaccines, based on new technologies, there are potential intellectual property barriers; however, it is not known which, if any, of those technologies could make a marketable vaccine that could be sustainably produced.60

Patent thickets are particularly relevant to pandemic influenza vaccines because of the patents that have applicability during numerous pandemic, but seasonal and future pandemics, as outlined above. Of particular concern in this area are the patents that cover elements of the virus, or the Virus like Particles (VLPs), as any vaccine formulation must make use of the virus or VLP in order to be effective. The patentee may choose not to license the use of the VLP covered by their patent to an innovator firm, particularly as they are rivals in such a small market. Indeed, the main purpose of the patent in pandemic influenza vaccine manufacturing may be to block innovation by rival firms, rather than generic manufacturers. As a result, it may be difficult for rival innovators to bring a pandemic influenza vaccine to market, without potentially infringing another innovator’s patent. This harms innovation, by creating an anticommons, and may also inhibit availability in the procurement process, by creating a scenario where growth in manufacturing capacity is reliant upon current manufacturers choosing to expand their production capacity.

6.4 - Licensing Pandemic Influenza Vaccine Manufacturing Technology

In order for an innovator to overcome this patent barrier, they would need successfully to negotiate a license with the patent owner, or create a new product or process that does not infringe on any patents. As Kane noted, a manufacturer’s position is significantly strengthened in these negotiations if they hold a relevant patent, which may be being infringed: ‘Patented compounds or methods required for

60WHO, 'Technical Studies under Resolution WHA63.1' (WHO 2011) <http://www.who.int/influenza/resources/technical_studies_under_resolution_wha63_1_en.pdf> 24;
vaccine production must be purchased or licensed from commercial entities who may hold patents on any of these items. The willingness to license or the licensing terms may reflect the patent-related considerations that enter the transactional evaluation. A patent could affect licensing negotiations through pricing mechanisms or limited offerings. This means that capacity, and thereby procurement, will not be improved by new innovators, because the incentive to enter the market is not sufficiently strong enough, or the new innovator is unable to bring their innovation to market because they cannot reasonably negotiate licenses with numerous patent holders.

Fortunately, such a situation has not yet occurred in pandemic influenza vaccine reverse genetics manufacturing, and freedom to operate is possible. Indeed, prior to late 2005, at least four institutions had to approve licenses in order for a pandemic influenza vaccine manufacturer to obtain freedom to operate in the reverse genetics pandemic influenza vaccine field. Reverse genetics manufacturing is a key technology in stabilising pandemic influenza viruses for their inclusion in pandemic influenza vaccines, and is therefore integral to the manufacturing process. This is a crucial barrier to establishing freedom to operate in the pandemic influenza vaccine manufacturing industry which prevents new manufacturers, generic or otherwise, from entering the market and increasing competition in the field. In late 2005 MedImmune secured exclusive licensing rights to all key patents from the different

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62 There are generally regarded to be four patent portfolios associated with the reverse genetics technology, see Mt. Sinai School of Medicine, Recombinant Negative Strand RNA Virus Expression Systems and Vaccines (WO 91/03552) (2002); Wisconsin Alumni Research Foundation, Recombinant Influenza Viruses for Vaccines and Gene Therapy (WO 00/60050) (2014); St. Jude Children's Research Hospital, Production of Infectious Influenza Viruses (WO01/83794) (2006); Mount Sinai School of Medicine Of New York University, Helper-Free Rescue of Recombinant Negative Strand RNA Viruses (US 6544785 B1) (2008).
rights holders, and the company has given assurances that that research and manufacturing licenses would be issued to relevant parties, ensuring freedom to operate exists in the field.

However, the situation is far from ideal; freedom to operate in pandemic influenza vaccine reverse genetics is only possible at present because MedImmune has taken steps to ensure that its patent rights do not inhibit the development and commercialisation of a pandemic influenza vaccine and has notified the WHO that that it would grant free access to its intellectual property to government organisations and companies developing pandemic influenza vaccines gratis for public health purposes. Yet, the commitment MedImmune has given is not legally binding, meaning such licenses could be withdrawn or refused by the company, and there is no guarantee that they will be as forthcoming with licensing of technology in the future. Finally, reverse genetic engineering is merely one of a number of potential avenues for pandemic influenza vaccine development, and no such guarantees have been given by the patent owners in the other areas of pandemic influenza vaccine research and development, meaning that freedom to operate may not be as easily achieved in DNA Vaccines or cell-based pandemic influenza vaccine.

There are multiple elements of a pandemic influenza vaccine and its manufacturing processes which can be, and are, patented. To some degree, such patents have the potential to negatively impact upon procurement of pandemic influenza vaccine by creating barriers to entry, barriers which look set to be reinforced with the move to utilising patented pandemic influenza vaccine manufacturing technology such as cell-based and live attenuated influenza vaccine technology. Such barriers impact upon pandemic influenza vaccine procurement by limiting the number of manufacturers.

65 Ibid.
66 Ibid.
67 Ibid.
that can use technology and enter the market, unless a MedImmune style scenario exists, in which granting licenses is commonplace, purchasers are reliant upon the already established manufacturers for procurement of pandemic influenza vaccine. If this happens, and manufacturers do not believe it to be commercially viable for them to expand their own capacity, due to the high costs of expansion or because of the sporadic timing of when their product is in demand (as is the case with pandemic influenza vaccine), then capacity will remain the same. Moreover, market forces, regardless of the incentive to create that stringent enforcement of patent rights is meant to provide, will be unable to address the challenges in procurement for developing states.

The fact that new vaccines are developed and manufactured in good time during an influenza pandemic, and the primary delay in bringing these vaccines to market lies in the complicated manufacturing and licensing, not a lack of will on behalf of the innovators, would suggest that there is no such tragedy of the anticommons in pandemic influenza vaccines. However, as increased innovation is not occurring by new innovators entering the market, or by new innovators in developing states, suggests that the tragedy of the anticommons metaphor to pandemic influenza vaccine is applicable to pandemic influenza vaccines. This is concerning, as it creates a scenario whereby innovation is dependent upon a small number of established manufacturing companies, that that essentially control the pandemic influenza vaccine market, through their large, far-reaching patent portfolios. It must be noted however, that there are also a number of small biotech firms that feed into this innovation, but do not manufacture vaccine; instead they license their technical developments to the established manufacturers. While this industry may have the hallmarks of one that has an anticommons, this may be justifiable if granting patents on this technology is the reason for the technology existing in the first place, as proponents of the economic theory of patents would argue.

68 Klaus Stöhr, ‘Textbook of Influenza’ in Robert Webster and others (eds), Textbook of Influenza (2nd edn, Wiley-Blackwell 2013) 352
69 Farah Huzair, The Influenza Vaccine Innovation System and Lessons for PDPs, 8 Human Vaccines & Immunotherapeutics 407 (2012).
6.5 - Conclusion

Applying the economic theory of patent protection to pandemic influenza vaccine development and innovation inevitably leads us to the question ‘but for the patent, would such innovation occur?’ It appears that in the case of pandemic influenza vaccines the answer to this is ‘yes’. The economic theory advances that a patent serves only to incentivise innovation by providing a manufacturer with a monopoly, and protecting them from the threat posed by imitators who wish to make a cheap replica, undercutting the innovator. However, even without a patent, pandemic influenza vaccine manufacturers are in this position; because of the complicated regulatory and licensing frameworks to bring a pandemic influenza vaccine to market, manufacturers have a monopoly position, and are at little to no risk from generic imitators. Moreover, the fact pandemic influenza vaccine manufacturers are selling a product for which demand outstrips supply, to a captive market of states and organisations each hoping to secure as much vaccine as possible provides a very strong incentive to innovate in this field.

The unique conditions associated with pandemic influenza vaccine may prove to be more of an incentive to innovate and research in this field, than the fact that the innovations can be patented. It appears as if the patent protection on pandemic influenza vaccine actually provides very little benefit to manufacturers, it does not protect from imitators (the regulatory and licensing conditions already do that), and it does not incentivise innovation in the field (the unique market conditions do that).

To this point I have argued that intellectual property rights may negatively impact upon procurement of pandemic influenza vaccines by developing states, by creating an anticommons in the pandemic influenza vaccine manufacturing field, which acts as a barrier to entry for other manufacturers, who may be able to expand the manufacturing capacity for pandemic influenza vaccines or meet the procurement needs of developing states. I have also argued that these same intellectual property

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70 This is discussed in further detail, in the next chapter.
rights cannot be justified on the basis that such rights incentivise the creation of pandemic influenza vaccines in the first place. The next chapter addresses the one unanswered question in relation to the relationship between intellectual property and pandemic influenza vaccines: can these patent barriers be overcome by developing states, by making use of the TRIPS flexibilities, in order to introduce generic competition in the pandemic influenza vaccine manufacturing field?
CHAPTER VII
THE TRIPS FLEXIBILITIES AND PANDEMIC INFLUENZA VACCINE PROCUREMENT

In this chapter I argue that, while the flexibilities contained within the TRIPS Agreement may be suitable to ensure developing states can improve their access to medicines, when applied to oral solid drugs, the flexibilities lack utility when applied to pandemic influenza vaccines. I further argue that if a developing state attempted to use the full range of patent flexibilities available to them in order to improve their procurement of pandemic influenza vaccines, no benefit would be seen. I contend that the flexibilities lack utility when applied to pandemic influenza vaccines because the predominant barrier to generic entry in the field is not intellectual property, as is often argued in the literature, but rather, proprietary, non-patented knowledge.

7.1 - TRIPS and the Right to Health

Since its creation, concern has been expressed that implementation of the intellectual property standards prescribed in the TRIPS Agreement have had a detrimental effect on access to medicines in developing states, and the extent to which developing states are able to realise their right-to-health obligations in this respect. Much of this concern has focused on the fact that more stringent patent rights prevent, or limit, developing states from producing and/or importing generic medicines at lower prices,

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by requiring them to grant and enforce patents on pharmaceutical products. This protects the patentee’s monopoly, and hinders procurement by limiting the number of generic producers.

The domestic patent legislation of WTO member states must be compliant with the standards provided in the TRIPS Agreement. TRIPS requirements fall broadly into three categories. First, all state parties must ratify several pre-existing international agreements on intellectual property. Second, it imposes fairness requirements, ensuring equal treatment to citizens of all members. Finally, TRIPS requires members to provide minimum standards of intellectual property rights in their domestic legal systems. TRIPS provides that states must allow for granting patents on inventions in any field of technology providing the invention is novel, involves an inventive step and has industrial applicability, and patent protection must be granted for at least twenty years from the date of filing. There is some flexibility regarding timescales for implementing TRIPS standards for developing states.

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3 States are free to offer as much, or as little patent protection as they wish. However, as over 80% of states are members of the WTO, the majority of states are either TRIPS compliant, or going through TRIPS transitional periods, which prescribes standards for member’s domestic patent law.

4 TRIPS Articles 2 & 3 requires states to comply with Articles 1 through 12, and Article 19, of the Paris Convention (1967) which are concerned with the priority rights of applicants, national treatment of applicants, and provisions relating to the granting and circumventing of patents, trademarks, and industrial designs.

5 Articles 1(3) & 4 requires states to ensure that when an applicant files an application for intellectual property rights in another TRIPS compliant jurisdiction that the application receives the same treatment as if it came from a citizen of that jurisdiction. Moreover, states must ensure the owner benefits from the same protection and the same legal remedy against any infringement as if the owner was a national owner of this right: expect when any advantage, favour, privilege or immunity accorded by a Member is compliant with the provision of Art4(1)(a)-(d).

6 TRIPS, Article 1(1)
7 TRIPS, Article 27(1)
8 TRIPS, Article 33
9 TRIPS, Article 66.1 provides that LDCs are granted a period of 10 years in which to become fully TRIPS compliant. Through a serious of extensions granted by the TRIPS council, LDCs currently have until 1st July 2021 to become TRIPS compliant – Council for Trade-Related Aspects of Intellectual Property Rights, ‘Extension of the Transition Period Under Article 66.1 for Least Developed Country Members, Draft Decision of the Council for TRIPS of 11th June’ (2013) Document IP/C/64
The intense criticism which TRIPS standards came under, coupled with some confusion as to when the flexibilities contained within the Agreement could be used by developing states, led to the Doha Declaration being issued by the Ministerial Council of the WTO in 2001. In which the member states of the WTO confirmed that:

The TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members’ right to protect public health and, in particular, to promote access to medicines for all.

In this connection, we reaffirm the right of WTO members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose.

7.2 - The TRIPS Flexibilities

To this end, TRIPS provides for a number of flexibilities which allow states to balance their obligation to provide adequate patent protection on pharmaceutical products, with their desire to meet the pressing public health needs of their population by ensuring access to medicines. The relevant flexibilities are: The Principles, Exclusions to Patentability, and Use without Authorisation of the Right Holder provisions. Adequate incorporation and application of these flexibilities may provide developing states with the ability to enhance the procurement of pandemic influenza vaccines, to the point where they are able to discharge their right-to-health obligations, by: ensuring a developing state’s domestic intellectual property legislation is able to meet

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10 For example see the discussion in Kevin Outterson, ‘Should access to medicines and TRIPS Flexibilities be limited to specific diseases?’ (2008) 38(1) American journal of Law & Medicine
11 World Trade Organisation, Doha Ministerial Declaration on the TRIPS Agreement and Public Health of 20 Nov. 2001, WT/MIN(01)/DEC/2
12 Paragraph. 4, ibid
13 TRIPS, Articles 7 & 8
14 TRIPS, Article 27.3(b)
15 TRIPS, Article 31
the public health needs of its population; that the state is able to manufacture or import patented products without the patentee’s permission; or the state can take measures to ensure that certain inventions are not patentable or commercially exploited, while remaining TRIPS compliant. These flexibilities have been noted as one of the most important tools that developing states may make use of, when attempting to improve access to medicine, most notably by Anand Grover in his role as UN Special Rapporteur on the Right to Health. Grover noted ‘The full use of TRIPS flexibilities can help countries meet their obligations to protect, promote and fulfil the right-to-health by improving access to affordable medicines.’ To this end, as noted at 1.4.3 it is pursuant upon states themselves to regulate the pharmaceutical industry in their territory in such a way so as to ensure that industry respects and upholds the Right to Health. Making full use of the flexibilities, by imposing restrictions on the extent to which the pharmaceutical industry can fully exercise the exclusionary rights granted by the patents they hold, or what the industry can actually obtain patent rights on, is one such way in which states could regulate a domestic pharmaceutical industry in order to advance the Right to Health.

To this end, in the context of pandemic influenza vaccine, Resolution 58.5 of the World Health Assembly urges Member States ‘to take all necessary measures during a global pandemic, to provide timely and adequate supplies of vaccines and antiviral drugs, using to the full the flexibilities contained in the Agreement on Trade-Related Aspects of Intellectual Property Rights.’ This clearly implies that making use of the flexibilities provided within TRIPS would be of benefit to states when attempting to procure sufficient levels of vaccines in a timely manner during a pandemic.

16 Adnan Grover, ‘Promotion and protection of all human rights, civil, political, economic, social and cultural rights including the right to development: Report of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health’ (United Nations General Assembly 2009) <http://www2.ohchr.org/english/bodies/hrcouncil/docs/11session/A.HRC.11.12_en.pdf>
17 WHA, ‘Resolution 58.5, Fifty-Eighth World Health Assembly’ (2005) 1(10)
The extent to which this is true, and the flexibilities can be used by developing states in order to discharge their right-to-health obligations in respect of access to vaccine during an influenza pandemic, is the focal point of this chapter.

7.2.1 - Principles

The Principles of the TRIPS Agreement are found at Article 8, this mandates that in creating domestic laws, member states

[m]ay, in formulating and amending their national laws and regulations, adopt measures necessary to protect public health and nutrition...provided that such measures are consistent with the provisions of this Agreement.\(^1\)

Article 8 is to be read in conjunction with the Objectives of the Agreement, at Article 7, which states that

[t]he protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations.\(^2\)

Article 8 provides a guiding principle upon which all other provisions of TRIPS should be read, and appears to afford considerable scope and flexibility to members to ensure their domestic intellectual property legislation meets their population needs, explicitly mentioning public health.

The influence of the Principles of the Agreement appear to have been bolstered by the Doha Ministerial Round, as both the Doha Ministerial Declaration (Ministerial Declaration)\(^3\) and the Declaration on the TRIPS Agreement and Public Health (Doha Declaration)\(^4\) documents strongly reinforced the objectives and principles set forth in Articles 7 and 8 of the TRIPS Agreement, and their applicability to public health related issues. Paragraph 19 of the Ministerial Declaration stated that ‘in undertaking

\(^{18}\) TRIPS, Article 8
\(^{19}\) TRIPS, Article 7
\(^{20}\) WTO, ‘Ministerial Declaration on the Doha Declaration’, (2001) WT/MIN(01)/DEC/1
\(^{21}\) WTO, (n11)
[the work outlined in this paragraph], the TRIPS Council shall be guided by the objectives and principles set out in Articles 7 and 8 of the TRIPS Agreement and shall take fully into account the development dimension.\(^{22}\) In the Doha Declaration, the Ministers agreed that

...the TRIPS Agreement does not and should not prevent members from taking measures to protect public health.....we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all.\(^{23}\)

Despite the direct language of these two paragraphs, the extent to which member states may rely upon the Doha statements to justify taking measures to protect public health in line with the Principles and Objectives of the Agreement is unclear. As Correa noted after the Doha Round:

There are different possible interpretations for this paragraph. On the one hand, it may be viewed as a statement of fact rather than a rebalancing of the Agreement. On the other, it may be regarded as an indication that in cases where there is conflict, IPRs should not be an obstacle to the realisation of public health.\(^{24}\)

Regardless of how the Doha Declaration is interpreted, the scope of Article 8 is significantly limited, through the use of the word ‘necessary’, which indicates that the national government does not have absolute discretion to use measures to meet these goals. Further, it is not the case that it is upon what the member thinks is necessary, but that this power is subject to oversight and review by the WTO, through the Appellate Body.\(^{25}\) The extent to which members may be able to rely upon Article 8 as justification for incorporating public health measures into domestic patent legislation is further limited by the inclusion of ‘consistent with the provisions of this

\(^{22}\) Paragraph 19 (n20)
\(^{23}\) Paragraph 4, (n20)
\(^{25}\) TRIPS, Article 64
Agreement’, which as Gervais noted ‘means that it would be difficult to justify an exception not foreseen under the Agreement, unless it is an exception to a right not protected under other provisions of the TRIPS Agreement or those of other international instruments incorporated in TRIPS’. 26

Regarding the utility of Article 8 in assisting developing states that lack access to PIV, it seems unlikely that it will have significant impact on procurement of PIV, and the extent to which developing states are able to discharge their right-to-health obligations in respect of pandemic influenza vaccines. The Doha and Ministerial Declarations have afforded the principles contained in Article 8 concerning public health an elevated status, meaning that developing states can rely upon it in interpreting other Articles of TRIPS, or in dispute resolution at the WTO. 27 However, as the principles include the terms ‘necessary’ and of ‘consistent with the provisions of this Agreement’ significantly curtails this flexibility for developing states, by ensuring that any public health related IP reform must comply with the other Articles of TRIPS, is subject to oversight from the WTO, and can be challenged by other member states.

7.2.2 - Exclusions

Further to the provisions regarding when a patent is to be granted, 28 TRIPS provides that members may exclude certain subject matters from patentability in their territory, with Article 27(2) stating:

Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such

27 Correa, (n24)
28 TRIPS, Article 27(1)
exclusion is not made merely because the exploitation is prohibited by their law.\textsuperscript{29}

While this Article is concerned with states’ abilities to prohibit the patenting of certain inventions, the actual factors on which such a prohibition can occur are vague: \textit{ordre public} and morality. The European Patent Office (EPO) has attempted to define these terms, stating that \textit{ordre public} is concerned with security, such as riots and public order, thereby banning the patenting and commercialisation of inventions that may lead to criminal or other generally offensive behaviour;\textsuperscript{30} and defining morality as the totality of accepted norms which are deeply rooted in a particular culture, and the prohibition of granting a patent on any invention that would be so abhorrent for the public that its patenting would be inconceivable.\textsuperscript{31} However, this is merely the European interpretation of these terms, and the terms have been interpreted and incorporated into domestic legal systems in a fairly broad manner amongst members.\textsuperscript{32} As Gervais noted both morality and \textit{ordre public} seem to depend, for the purposes of this Article, on the particular culture of a country or region.\textsuperscript{33} However, despite the point raised by Gervais it is necessary to note the integral role that Europe (along with the United States of America) played in negotiating and drafting the TRIPS Agreement, therefore an inference can be drawn that the scope of the exclusions are likely to be close to European norms in this area.\textsuperscript{34}

Article 27(2) provides states with considerable flexibility over patentability within their domestic legal system. The fact that Article 27(2) allows members to ‘exclude from patentability inventions...necessary to protect \textit{ordre public} or morality, including to protect human, animal or plant life or health’, means that developing states could argue that pandemic influenza, and their population not having access to PIV, is a

\textsuperscript{29} TRIPS, Article 27(2)
\textsuperscript{32} For an overview of how \textit{ordre public} and morality has been defined and incorporated in differing jurisdictions see: UNCTAD-ICTSD, Patents: Ordre Public and Morality, (CUP, 2005)
\textsuperscript{33} Gervais, (n26) 149
\textsuperscript{34} See ‘Part A’ of Gervais, (n26)
moral or public order issue, thereby allowing developing states to incorporate social, ethical, and moral considerations into the domestic patent regime, and potentially allow the state to refuse to grant a patent on the manufacturing processes involved in PIV development, or patentable components of the vaccine.

The utility of Article 27(2) in the attempt to increase access to medicines has been discussed by Cann, in the context of the Article being used to deny the patentability of HIV/AIDS drugs, and thereby enhance procurement though the introduction of generic medicines:

[If a nation takes the position that the prevention and treatment of the HIV/AIDS epidemic is necessary to protect the ordre public,...[TRIPS] would apparently allow that nation to deny patent protection to relevant pharmaceuticals and then distribute those products, assuming they are attainable, on a non-profit, non-commercial basis. Since there could be no discrimination between the rights of foreign and domestic producers, as neither would be allowed to engage in commercial exploitation, such a strategy would appear consistent with the terms of...[TRIPS].]

In theory, the solution Cann put forward is also applicable to PIV. Developing states have the right to deny patent protection on elements of the manufacturing process, or components of the PIV and virus, on the ground that commercial exploitation of such inventions is immoral during a pandemic when access to PIV is so crucial to public health. However, in practice, it does not appear as if this solution would provide a scenario in which developing states would be better able to procure PIV during a pandemic.

Such a solution does not appear workable in the context of PIV, as it is wholly dependent on a developing state being able to or produce pandemic influenza vaccine, in order to then distribute them on a non-profit, non-commercial basis. Such

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a solution is not possible in the field of pandemic influenza vaccines, because, even if
the patents on pandemic influenza vaccines did not exist, manufacturers in developing
states would not have the knowledge required in order to manufacture pandemic
influenza vaccines. While it is entirely correct that patents are an effective way in
order for innovators to ‘lock up’ knowledge, it is important to acknowledge that a
patent is not the only way in which the dissemination and use of knowledge can be
‘locked up’ by an innovator. In the case of pandemic influenza vaccines, knowledge is
locked up by key information required in order to manufacture pandemic influenza
vaccines not being placed in the public domain, and not being made available outside
of the small number of established pandemic influenza vaccine manufacturers:

the technical know-how – even of conventional egg-derived influenza vaccines
- is not readily found outside existing influenza vaccine production plants.

Thus, even for procedures for which there are no patents, securing working
partnerships with technology holders may be necessary.

Access to, and an ability to make use of proprietary, non-patented knowledge, that is
not available outside of the established pandemic influenza manufacturers is clearly a
barrier to developing states establishing a nationalised influenza manufacturing
facility in order procure from. In addition to this, an inability to make use of this of
proprietary, non-patented knowledge also limits the extent to which developing
states can make use of use without authorisations of the right holder provisions. This
is particularly concerning from a right-to-health perspective, as it is these provisions
which developing states typically make use of in order to increase access to patented
medicines.

7.3 - Use without Authorisation of the Right Holder

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36 Drahos P, A Philosophy of Intellectual Property (Dartmouth Publishing Co 1996) 6; M. P.
Ryan, Knowledge diplomacy: Global competition and the politics of intellectual property (Brookings
Institution 1998); David Downes, ‘How intellectual property could be a tool to protect traditional
knowledge’ (2000) 25 Columbia Journal of Environmental Law 253; Peter Drahos and John
2008’ (WHO/IVB/09.05 2009)

<http://apps.who.int/iris/bitstream/10665/70018/1/WHO_IVB_09.05_eng.pdf> 33
Typically, if a state offers patent protection for pharmaceutical products, generic drugs can only be introduced to a market when the patent protection on the original drug has expired, or is otherwise unenforceable. In order to make a generic copy of a patented product generic manufacturers require authorisation in order to lawfully circumvent the exclusive rights over the product provided by the patent. Authorisation is granted by the patentee, who has the right to refuse to grant a license. However, since the nineteenth century there has been a tradition that, if it can be justified in the public interest, governments may allow the exploitation of the patent by a third-party without the patentee’s authorisation. In such cases, the public interest of ensuring broader access to the patented product is deemed to be more important than the interest of the patentee in retaining their exclusive rights.

The use without authorisation of the right holder provisions within TRIPS outline a limited number of circumstances and scenarios in which the exclusive rights of a patentee may be set aside without the permission of the patentee, which are outlined below.

7.3.1 - Compulsory Licenses

As noted in the literature review above, a compulsory license is a legal instrument that allows a government to grant itself, or a third party, the right to produce a patented product without authorisation from the patentee, subject to certain conditions, which are outlined in the below paragraph. In the context of the drug procurement,
compulsory licensing is seen as an effective tool to lower drug prices, in order to increase access to expensive patented medicines.\textsuperscript{41}

Under the TRIPS Agreement, states are only limited with regard to the procedure and conditions to be followed in granting compulsory licenses. Article 31 sets out the conditions to be met in granting such licenses. It provides that a compulsory license can only be granted after the state has attempted to negotiate a voluntary license with the patentee on reasonable commercial terms, and this has failed (except in an emergency where the negotiation requirement may be waived); the authorisation is predominantly for the supply of the domestic market; the authorisation is limited to the purpose for which it was authorised, and adequate remuneration must be paid to the rights holder by the licensing state.\textsuperscript{42}

One of the most controversial elements of the TRIPS compulsory license provisions was Article 31(f), which stated that that ‘any such use [of compulsory licenses] shall be authorised predominantly for the supply of the domestic market of the Member authorising such use’;\textsuperscript{43} Article 31(f) was controversial as it only allowed for the compulsory licensing of products for use in the domestic market; meaning that unless a state could issue a license to a manufacturer within their territory, they could not make use of the flexibility.\textsuperscript{44} This requirement had the effect of excluding those states without domestic manufacturing capacity in their territory from being able to make


\textsuperscript{42} TRIPS, Article 31

\textsuperscript{43} TRIPS, Article 31(f)

use of the provisions, which a study by the United Kingdom Commission on Intellectual Property Rights concluded was ‘likely to have a significant effect on the world supply of low price medicines and vaccines.’

7.3.2 - Article 31(f) Waiver
At the 2001 Doha Ministerial Conference a Declaration was adopted to reaffirm that the TRIPS Agreement patent protection standards do not, and should not, prevent states from taking measures to address public health issues in their territory. Further to this, in 2003, a waiver to Article 31(f) of the TRIPS Agreement was adopted by the WTO General Council to allow states to produce pharmaceuticals under compulsory licenses for export purposes, under certain circumstances and conditions, in order to enable states that lacked manufacturing capacity to benefit from the compulsory licensing provisions. Subsequently, at the 2005 meeting of the WTO members, the Article 31(f) waiver was proposed as a permanent amendment to the TRIPS Agreement. Two-thirds of WTO members are required to ratify the amendment before it can be made permanent; at the time of writing this has not yet been achieved, and members have until 31 December 2017 to ratify the amendment, until then, the waiver remains in force.

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45 Frederick Abbott, ‘Commission on intellectual property rights study paper 2a WTO TRIPS agreement and its implications for access to medicines in developing countries’ <http://www.iprcommission.org/papers/pdfs/study_papers/sp2a_abbott_study.pdf>;
46 WTO, (n12) Paragraph 4
47 WTO General Council, (n40)
50 Ibid.
The Article 31(f) waiver was hailed as a major breakthrough for developing states,\textsuperscript{51} yet, the fact remains that the system has only been used once since 2003.\textsuperscript{52} Despite its limited use some commentators have shown support for the waiver on the basis that its existence has encouraged and led to voluntary licenses being agreed between governments and patentees, such as those agreements that occurred in Brazil and Thailand regarding antiretroviral treatments for HIV/AIDS.\textsuperscript{53} This is because by threatening to invoke a compulsory license, a developing state gains far greater power in negotiations, ultimately leading to licenses being granted on a voluntary basis by the patent holder. However, a recent evaluation of the trends in compulsory licensing found only twenty-four instances of a government official proposing a compulsory license since 1994, with the number falling dramatically since 2008.\textsuperscript{54} This may be due to Governments no longer needing to ‘propose’ a compulsory license as a threat to patentees in order to for them to issue a voluntary license, although it is difficult to determine if this is the case.\textsuperscript{55}

7.3.3 - Crown Use


\textsuperscript{54} Kuhn and Beall, ibid.

\textsuperscript{55} Historically similar arguments have been made regarding compulsory licenses generally e.g. ‘The practical value of the existence of compulsory license provisions in the Patent Law is that the threat of it usually induces the grant of contractual licenses on reasonable terms, and thus the objective of actually working the invention is accomplished.’ – Stephen P Ladas, Patents, trademarks, and related rights: national and international protection (Harvard University Press 1975) 427; Friedrich–Karl Beier, ‘Exclusive Rights, Statutory Licenses and Compulsory Licenses in Patent and Utility Model Law’ (1999) 30(1) International Review of Intellectual Property 251
Crown use is a non-voluntary license that authorises a government, or government agency, to use a patented product without authorisation from the patentee. Crown use provisions have been successfully used in order to improve access to medicines in developing states. The World Bank’s technical guide on procuring antiretroviral drugs in developing states refers to crown use licenses as ‘the principal means enabling procurement authorities to overcome patent barriers’. While the specific provisions of crown use legislation vary from state to state, TRIPS prescribes that it is to be used during a ‘national emergency’ and ‘circumstances of extreme urgency’, although no further guidance is given within the Agreement as to what scenarios satisfy these terms.

While no guidance is provided as to what constitutes a ‘national emergency’ in this context, a South Centre review of developing states’ crown use provisions concluded that:

Where domestic laws provide for government use or public, non-commercial use of patents, the provisions are generally sufficiently broad to provide governments with the flexibility to take necessary measures to meet public health needs. However, there may be a need to establish procedures to give rapid effect to such provisions...the requirements for prior efforts to have to be made to obtain a voluntary license from the patent holder is waived in the case of public, non-commercial use of patents. This should be properly reflected in the provisions, in order to maximise the flexibility afforded by the TRIPS Agreement.

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56 TRIPS, Article 31(b)
60 TRIPS, Article 31(b)
61 Susie Musungu and Cecilia Oh, ‘The Use of Flexibilities in Trips by Developing Countries: Can They Promote Access to Medicines?’ (WHO 2005)
The majority of the conditions outlined at Article 31 of the TRIPS Agreement apply equally to crown use and compulsory licenses, but there are important differences between the two. Most notable is that the requirement for the government to seek a voluntary license from the patentee in the first instance applies to compulsory licenses but not crown use.62 Under TRIPS, governments utilising crown use provisions are merely obliged to inform the patentee of the use of the patented invention as soon as is practicable,63 thereby skipping the negotiation stage. This fast-tracking of authorisations is highly beneficial to a licensing government during a public health emergency, especially a pandemic, when early introduction of a treatment into a health system can greatly improve community resilience to the outbreak.64

Crown use of patents allows the government to import generic versions of a patented drug from states where the product does not have patent protection, either because it has expired, or because the states do not recognise the patentability of the product, or where the manufacturer has a license to manufacture the product (either compulsory or voluntary).

7.4 - Use without Authorisation of the Right Holder during an Influenza Pandemic

7.4.1 - Solid oral drugs
The use without authorisation provisions in the TRIPS Agreement are widely promoted in the literature as a route that could be used by developing states to enhance their procurement of patented drugs,65 and such provisions have been successfully used by a number of developing states to regulate the pharmaceutical industry within their

62 TRIPS Article 31(b)
63 Ibid.
territory in such a way that advances the Right to Health, enabling the state to procure cheaper generic versions of patented drugs. Use without authorisation provisions have been used during an influenza pandemic to increase access to oseltamivir (Tamiflu), a patented solid oral drug for the treatment of influenza. Further, the threat of a state utilising compulsory licensing or crown use provisions appears to have encouraged the patentee to issue a voluntary license to allow the generic manufacturing of the patented product.

It is clear that use without authorisation provisions are suitable in order to increase access to patented oral solid drugs, including during an influenza pandemic. The fact that the provisions have been used to great success by developing states in the fight against HIV/AIDS is testament to this. Use without authorisation provisions by developing states have also featured prominently in the right-to-health literature as one of the methods developing states can employ in order to improve access to patented oral solid drugs in order to meet their right-to-health obligations.

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67 NICE, ‘Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza’ (1 September 2008) <https://www.nice.org.uk/guidance/ta158>
69 Voluntary licenses were granted to India, Vietnam, and South Korea by Roche for Tamiflu during 2005-H5N1 influenza outbreak, it has been argued that such voluntary licenses were granted to prevent the compulsory licenses being issued for further doses; Esther van Zimmeren and Gilles Requena, 'Ex-officio Licensing in the Medical Sector: The French Model' in Geertrui van Overwalle (ed), Gene patents and public health (Bruylant 2007)
As was noted in the literature review above, much of the literature has assumed that there is a ‘degree of commonality’ between oral solid drugs and vaccines, the impact of intellectual property rights have on access, and the appropriateness of methods to improve access. However, as has been stressed throughout this research, this assumption is misplaced. To reiterate:

Strategies to improve access to medicines have thus coalesced around the goal of enabling generic production. This has led many of these efforts to focus on patent protection as a key barrier to the availability of affordable generic medicines. A crucial assumption that underlies this strategy is that it is fairly straightforward to reverse engineer a given drug; in concept, the problem is not that generic drug manufacturers would be unable to exactly replicate a drug, it is that they are prohibited from doing so by patent law. Although this is generally the case for small molecule drugs, this basic assumption does not hold true for biologics, including vaccines.

Therefore, the extent to which use without authorisation of the right holder provisions can be used as an effective strategy in order to improve access to pandemic influenza vaccines needs to be examined in light of, on the one hand, the suitability of these provisions when seeking to improve access to oral solid drugs, and the lack of commonality between oral solid drugs and vaccines, on the other.

7.4.2 - Pandemic Influenza Vaccines

As noted above, during 2009-H1N1 the cost of a PIV was approximately £3.40 per dose. Given the fact in order to establish full immunity against a pandemic strain may require a two dose strategy, even vaccinating ‘at risk’ members of the population

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72 Stephen Marks and Adriana Benedict, ‘Access to Medical Products, Vaccines and Medical Technologies’ in Jose M. Zuniga, Stephen P. Marks, and Lawrence O. Gostin (eds), Advancing the human right-to-health (Oxford University Press 2013) 305
74 Nayer Khazeni, 'Effectiveness and Cost-Effectiveness of Vaccination against Pandemic Influenza (H1N1) 2009' (2009) 151(12) Annals of Internal Medicine – administration costs include cost of transportation, cold chain infrastructure, and healthcare workers to administer the vaccine to the population.
is likely to be an expensive undertaking. If developing states were able to procure a cheaper version of the necessary PIV, they would be able to vaccinate more of their population, which would slow down the spread of the infection, and protect individuals.

The ability of a state to introduce cheap generic versions of patented drugs is dependent on three factors: the ability to circumvent the patent holder’s exclusive rights; the existence of generic manufacturers willing and able to manufacture a generic version of the patented product at a lower price; and the ability to rely upon licensing test data generated by innovators, in order to keep costs low. The first of these factors is straightforward to meet, even in the field of pandemic influenza vaccines; the majority of developing states have in place legislation that would allow them to use compulsory licensing or crown use to increase access to medicines, and those that do not, are able to make suitable reforms to their domestic patent regime, while remaining TRIPS compliant. Therefore, in theory, any patent-related barrier to introducing generic PIVs could be overcome by states making use of the flexibilities available to them. This is certainly the case for the introduction of solid-dose drugs: numerous developing states have overcome patent barriers, by making use of ‘use without authorisation’ provisions, allowing them to introduce cheaper generic version of patented drugs.

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75 WHO define at risk groups for influenza vaccines as being ‘pregnant women, health-care workers, the elderly, those with risk conditions and children aged 6-59 months’ - WHO, ‘Meeting of the Strategic Advisory Group Of Experts On Immunization, April 2012 – Conclusions and Recommendations’, Weekly Epidemiological Record, 87 (2012) – data from developing states is not available, but within the EU it is estimated that 49.1% of the population fall into one or more of the WHO’s risk groups for the purposes of influenza vaccination - James Ryan and others, ‘Establishing the health and economic impact of influenza vaccination within the European Union 25 countries’ (2006) 24(47-48) Vaccine 6812
76 Pedro Plans-Rubió, ‘The vaccination coverage required to establish herd immunity against influenza viruses’ (2012) 55(1) Preventive Medicine 72
78 Musungu and Ho (n61)
However, in order to regulate the pharmaceutical industry in a territory in such a way that limits the negative impact the industry has on the Right to Health, there must actually be a pharmaceutical industry within a territory to regulate. The benefits of limiting the ability of a pharmaceutical manufacturer to exercise their patent rights are only realised if the right to manufacturer the product can be transferred to another manufacturer, that is willing and able to produce the pharmaceutical product, within that territory. 80 This is not the case with pandemic influenza vaccine manufacturing. As noted previously, manufacturing capacity for PIV is concentrated in a small number of developed states, and no such capacity can be readily found in developing states. This inherently limits the extent to which developing states can utilise use without authorisation provisions in order to regulate the pharmaceutical industry in order to advance the Right to Health.

The final criteria, in relying upon the test data generated by the innovator, is not as straightforward in the field of pandemic influenza vaccines, for reasons explored below.

7.4.3 - Licensing of Generic PIVs

In order to bring a pharmaceutical product to market, a manufacturer must prove that the product is safe and effective in humans; this involves three phases of clinical trials in humans,81 with costs averaging £260 million per trial.82 It is on the basis of the results of these trials, made by the manufacturer and submitted to national or international regulatory authorities, that a market authorisation may be granted on the pharmaceutical product.83 Generic drugs are priced that much lower than their

80 in some very limited circumstances, a developing state can contract with a manufacturer based in a developed state to manufacture the drug using the Paragraph Six system - however, as noted at 7.3.2 this system has only been utilised by a developing state once, and is fraught with difficulty.
81 Lawrence M Friedman, Curt D Furberg, and David L DeMets, Fundamentals of Clinical Trials (4th edn, Springer 2010) provides a thorough breakdown of these phases at 2-8
82 E. L Eisenstein and others, 'Sensible approaches for reducing clinical trial costs' (2008) 5(1) Clinical Trials 75
innovator counterparts as they are able to use a shortened (in both time and expense) regulatory pathway for their drug.\textsuperscript{84} When a national government utilises ‘use without authorisation’ provisions and introduces a generic drug, this does not just have the effect of allowing them to temporarily set aside the patentee’s exclusive rights to use the patented invention; it usually\textsuperscript{85} also allows the generic manufacturer to make use of a curtailed regulatory pathway for the generic drug,\textsuperscript{86} because they are able to rely upon the safety and efficacy data generated for the innovator drug.\textsuperscript{87}

This ability to rely upon the safety and efficacy data generated by others is due to the bioequivelency of the generic and innovator products. Bioequivelency is based upon the Fundamental Bioequivalence Assumption that if two drug products are shown to be bioequivalent in average bioavailability, it is assumed that they will reach the same therapeutic effect and can be used interchangeably.\textsuperscript{88} Once a generic manufacturer can prove Fundamental Bioequivalence Assumption a generic manufacturer may rely on the test data of the innovator product, in order to demonstrate the safety and efficacy of the generic one.\textsuperscript{89}

With regards to PIVs, the Fundamental Bioequivalence Assumption cannot be relied upon as ‘there is general consensus that the standard methodology for the assessment of bioequivalence is not appropriate for the assessment of biosimilarity of follow-on biologics, which highlights the need of more complex and specified

\textsuperscript{84} Correa, (n77)
\textsuperscript{86} Timothy W. Ames and Aaron Sigler, ‘ANDA Regulatory Approval Process’ in Leon Shargel and Isadore Kanfer (eds) (CRC Press 2013)
\textsuperscript{88} Shein-Chung Chow and Jen-pei Liu (eds), Design and Analysis of Bioavailability and Bioequivalence Studies (3rd edn, CRC Press 2008) 451
\textsuperscript{89} WHO, Marketing authorization of pharmaceutical products with special reference to multisource (generic) products: a manual for National Medicines Regulatory Authorities (NMRAs) (2nd edn, WHO 2011)
regulation and approval tracks’.\textsuperscript{90} As it is not possible for a manufacturer to prove that their version is a bioequivalent of the original biologic,\textsuperscript{91} they are unable to rely upon the test data generator by the innovator in order to make use of a curtailed regulatory pathway.

The World Health Organisation provided ‘Guidelines on Evaluation of Similar Biotherapeutic Products’\textsuperscript{92} in 2009. These aimed to ‘provide globally acceptable principles for licensing biotherapeutic products that are claimed to be similar to the reference products that have been licensed based on a full licensing dossier to aid with the regulation of biosimilar products, such as vaccines’\textsuperscript{93} Regional and national regulatory frameworks for the licensing of Biosimilars have also been provided in the European Union (EU),\textsuperscript{94} the US,\textsuperscript{95} and Canada.\textsuperscript{96} While each of these regulatory systems have subtle differences in the definition of Biosimilars or in the efficacy requirements,\textsuperscript{97} each of them requires the biosimilar manufacturer to develop an extensive regulatory dossier,\textsuperscript{98} including clinical trials in humans,\textsuperscript{99} prior to a market authorisation being granted for a bioequivalent product. Such requirements must also be met even if a biologic is manufactured under a compulsory licence or crown use. Each of these regulatory frameworks creates some form of curtailed regulatory framework, whereby some data generated by the innovator can be relied upon,\textsuperscript{90,91,92,93,94,95,96,97,98,99}

\begin{thebibliography}{99}
\bibitem{92} WHO, (n86)
\bibitem{93} Ibid, 4
\bibitem{95} Biologics Price Competition and Innovation Act (2009)(U.S.A.)
\bibitem{96} Health Canada, ‘Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics (SEBs)’ (2010)
\bibitem{97} For more information on the differences between these systems see: Wang & Chow (n89)
\bibitem{98} See: S.2 BPCIA (2009); Health Canada (n95) at 2.3; EMEA/CHMP/437/04. at 5.2
\bibitem{99} See: S.2(a)(cc) BPCIA (2009); Health Canada (n95) at 2.3.2.1; EMEA/CHMP/437/04. at 5.2
\end{thebibliography}
although how much data, and the extent to which it can be relied upon, varies between the jurisdictions.\textsuperscript{100} Moreover, data exclusivity provisions exist within the regulations in the US,\textsuperscript{101} Canada\textsuperscript{102} and the EU\textsuperscript{103}, which further limits the opportunity to rely upon data generated by others when licensing a biosimilar in these jurisdictions.

Such requirements, while being entirely necessary to ensure the safety and efficacy of the product, have a significant impact on the utility of introducing generic PIV competition via use without authorisation provisions. The biosimilar manufacturer must generate an extensive regulatory dossier in order to prove biosimilarity, safety, and efficacy, therefore the sunk costs of the biosimilar manufacturer increases. As the sunk costs increase, so the likelihood of price reduction decreases. Indeed, it is estimated that biosimilar biologics will cost 65-80\% the price of the innovator product,\textsuperscript{104} whereas generic oral solid drugs are often under 33\% the cost of the innovator product.\textsuperscript{105}

In addition to the significant cost of compiling a regulatory dossier for PIV, such a requirement is also time consuming. As the table below outlines, the timeframe from the vaccine manufacturer optimising conditions for viral growth, clinical trials and the PIV receiving marketing approval is approximately three months, with the entire process from virus identification taking five months. Even if a generic manufacturer were capable of manufacturing a ‘generic’ PIV under a crown use or compulsory license, it would take at least three months for them to meet the necessary

\begin{table}
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\begin{tabular}{|c|c|}
\hline
Requirements & Timeframe (months) \\
\hline
Vaccine manufacturer optimising conditions & 3 \\
Clinical trials & 3 \\
PIV receiving marketing approval & 3 \\
Virus identification & 5 \\
\hline
\end{tabular}
\end{table}

\textsuperscript{100} See: Health Canada, ‘Guidance Document: Data Protection under C.08.004.1 of the Food and Drug Regulations’ (2011) 2.3.1.1; s.4-7 BPCIA (2009); EMEA/CHMP/437/04. 5.1.1
\textsuperscript{101} S.7(A) BIPCA;
\textsuperscript{102} Health Canada, (n95) 2.6
\textsuperscript{104} Bruno Calo-Fernández and Juan Martínez-Hurtado, ‘Biosimilars: Company strategies to capture value from the Biologics market’ (2012) 5(12) Pharmaceuticals 1393
\textsuperscript{105} A Cameron and others, ‘Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis’ (2009) 373(9659) The Lancet 240
manufacturing and licensing requirements, after which time the PIVs may no longer be as useful, or the pandemic may even be over.

Table 3. World Health Organisation, Pandemic Influenza Vaccine Manufacturing Process and Timeline

<table>
<thead>
<tr>
<th>Activity</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
<th>Month 4</th>
<th>Month 5</th>
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<tbody>
<tr>
<td><strong>At WHO Collaborating Centres</strong></td>
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<tr>
<td>Identification of new virus</td>
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<tr>
<td>Preparation of the vaccine strain</td>
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<tr>
<td>Verification of vaccine strain</td>
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<tr>
<td>Preparation of reagents to test vaccine</td>
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<tr>
<td><strong>At Manufacturer</strong></td>
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<td></td>
</tr>
<tr>
<td>Optimization of virus growth conditions</td>
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<tr>
<td>Manufacture of bulk vaccine</td>
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<tr>
<td>Quality control</td>
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<tr>
<td>Vaccine filling and release</td>
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<tr>
<td>Clinical trial (in certain countries)</td>
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<tr>
<td><strong>At Regulatory agency</strong></td>
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<tr>
<td>Review and release</td>
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</table>

Although the regulatory pathway for PIVs can be curtailed slightly, it is clear that the licensing requirements are likely to be a barrier to the production of generics, and therefore, to any price reductions that may subsequently occur when generics are introduced. The implication for PIV procurement is that, although use without authorisation provisions have been used to good effect to procure cheaper oral solid drugs, they are unable to provide the same benefits when addressing procurement of PIVs.

Returning once more to the ‘appropriate access’ criteria by which we are determining if a procurement method is capable of ensuring a developing state can discharge their right-to-health obligations in respect of pandemic influenza vaccines, it is clear that the TRIPS flexibilities cannot ensure this. Regarding the first criteria of the two-part test (vaccination levels), merely granting compulsory licenses to a manufacturer in a developing state will not, in and of itself, improve procurement of pandemic influenza vaccines at all. This is because manufacturers would not be able to manufacture any

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PIV, without access to the technical, proprietary non-patented knowledge of how to manufacture an influenza vaccine, even if a compulsory license has been granted. On the second part of the two-part ‘appropriate access’ test even if manufacturing could be commenced merely on the basis that a compulsory license has been granted (which it cannot), there would be a delay in said manufacturing commencing in a developing state, due to the delay caused by the negotiating and granting of, what is likely to be multiple licenses, with multiple patent holders. This of course means that developing states that procured their pandemic influenza vaccines via this method, will not receive their vaccine in the same timeframe as developed states, and therefore the second part of the appropriate access test is not fulfilled either.

7.5 - Conclusion
TRIPS provides a number of flexibilities which may be used by developing states in order to enhance the procurement of medicines. Such flexibilities have been used successfully by developing states to procure medicines to meet their health needs, and discharge their right-to-health obligations in respect of oral solid drugs, however, it does not appear as if such benefits are transferable to PIV procurement.

The utility of the TRIPS flexibilities as a method for achieving sufficient access for pandemic influenza vaccines is curtailed largely by three factors. First, as the technology package which is required in order to establish pandemic influenza vaccine manufacturing capacity is covered by multiple patents, owned by multiple patentees, makes the negotiating licenses for all of this technology a difficult process. Second, even if the licenses for all of the technology in this package could be negotiated, manufacturing capacity cannot be established purely on this basis, because much of the knowledge that is required to manufacture a pandemic influenza vaccine is not patented, or known outside of the established pandemic influenza manufacturers in developed states. Finally, the benefits of generic entry, which is realised by using TRIPS, are not as available when attempting to increase access to pandemic influenza vaccines, due to the timescale, and significant costs associated with generating regulatory dossiers for ‘generic PIVs’, which is required in order to ensure the vaccine is safe and efficacious. Such regulatory hurdles appear insurmountable at this stage.
because of the complex structure and manufacturing processes of PIVs, meaning that even if a state were to issue a compulsory license in order to make use of the patented technology associated with manufacturing PIVs, as they would be required to go through such a technically demanding, time consuming and expensive process in order to license the PIV, makes it appear as if the benefits of issuing a compulsory license will be negligible, particularly to developing states that lack the infrastructure to manage such an undertaking in the first place.
CHAPTER VIII – RECOMMENDATIONS

This chapter outlines the recommendation flowing from this thesis. It focuses on a practical solution to the problem of procurement of pandemic influenza vaccines, and what I have identified as the predominant causes of the problems in procurement. The model outlined in these recommendations seeks to ensure that developing states are able to obtain ‘appropriate access’ to influenza vaccines during an influenza pandemic, while ensuring that an appropriate balance can be struck between access to medicines as a manifestation of the right-to-health, and the right of everyone to benefit from the protection of the moral and material interests resulting from any scientific production of which he or she is the creator.

8.1 – Reforming the Procurement of Pandemic Influenza Vaccines

I started with an ambition to make a number of empirical and normative observations regarding the procurement of pandemic influenza vaccines. Empirically, I set out to determine how developing states procure vaccine during an influenza pandemic; what role the international agreements and policies of the WTO and WHO play in improving or inhibiting procurement by developing states; and if, when making use of the full gamut of relevant mechanisms found within these international agreements developing states could ensure they had sufficient access to pandemic influenza vaccines, in order to discharge their right-to-health obligations in respect of access to PIV. Normatively, I set out to determine if developing states could not use full gamut of mechanisms in order to ensure they had sufficient access to PIV, how this situation might be improved for developing states. To this point this thesis has determined that the relevant mechanisms are not appropriate to ensure developing states have

* as quoted in: René J. Dubos, Louis Pasteur, free lance of science (2nd edn, Da Capo Press 1986) 85
sufficient access during an influenza pandemic, and therefore an alternative solution is required for developing states.

The aim in this regard is for developing states to become self-sufficient in their procurement of pandemic influenza vaccines. That is, to manufacture sufficient levels of pandemic influenza vaccines in order to achieve herd immunity, without being reliant upon procurement from established pandemic influenza vaccine manufacturers in developed states, or receiving donations from the WHO. This may seem somewhat contrary to the current literature on the benefits and cons of local production of medicines and vaccines. Kaplan et al have claimed that ‘In many parts of the world, there is no reason to produce medicines domestically since it makes little economic sense; and if local production is adopted by many countries, it may lead to less access to medicines, since there are no economies of scale in having a production facility in each country.’¹ Moreover, Garrison noted on this point ‘As regards the field of vaccines rather than pharmaceuticals, the scale issues may be even more important.’²

Despite the concerns expressed by Kaplan and Garrison, I propose that developing states becoming self-sufficient in their procurement of pandemic influenza vaccines is the most appropriate way to address the problems of access in developing states. This would allow developing states that were self-sufficient to manufacture their own pandemic influenza vaccines in the same timeframe as established pandemic influenza vaccine manufacturers, enabling them to better meet the health needs of their population.³ The importance of developing states becoming self-sufficient in

³ As noted at 1.5.1 – ‘speed is of the essence to deliver a pandemic vaccine’ ...and [being able to administer a PIV] as quickly as possible, reduces disease transmission, and uses the efficacy of the vaccine to fight the disease.
pandemic influenza vaccine manufacturing, and the importance of developing states acquiring knowledge from established pandemic influenza vaccine manufacturers has also been noted by the World Health Assembly\textsuperscript{4} and the Developing Countries’ Vaccine manufacturing Network.\textsuperscript{5} Establishing manufacturing capacity in developing states may be best achieved through regional groups of developing states pooling resources together into one pandemic influenza vaccine manufacturing facility, in order to maintain economies of scale and minimise the disruptions that could be potentially be caused by changes in political will caused by changes of government at the domestic level.

The establishment of domestic influenza vaccine capacity in developing states is necessary, as merely encouraging the established influenza vaccine manufacturers to expand their production capacity would actually have very little impact on developing states obtaining sufficient access to the vaccine, because, as noted at 3.3, the Advance Purchase Agreements of developed states would need to be fulfilled prior to developing states order being met. In addition to addressing the timing problem of ‘sufficient access’ it is possible that developing states established pandemic influenza vaccine manufacturing capacity in their own state through a state-owned pharmaceutical manufacturer, may result in that state securing a price reduction on the end product, as compared with purchasing directly from an establish pandemic influenza vaccine manufacturer. Though it is important to note that the timing of access and/or an inability to access pandemic influenza vaccines appears to be the predominant problem in vaccine procurement during a pandemic, rather than price. Finally, establishing a self-sufficient vaccine manufacturing plant would also enable developing states to produce seasonal influenza vaccines, which could feed into a seasonal influenza vaccination campaign: this is a particular benefit of self-sufficient influenza vaccine manufacturing, as access to seasonal influenza vaccines is also


\textsuperscript{5} Suresh Jadhav and others, ‘The developing countries vaccine Manufacturers’ network (DCVMN) is a critical constituency to ensure access to vaccines in developing countries’ (2008) 26(13) Vaccine 1611
significantly lower in developing states when compared with their developed neighbours.\textsuperscript{6}

It is worth mentioning that success of the self-sufficient model is not dependent on direct state ownership of the pandemic influenza vaccine manufacturing capacity. While there may be benefits arising from having a state owned pharmaceutical manufacturer establish pandemic influenza vaccine manufacturing capacity, such as by ensuring direct state control of the research and manufacturing priorities of the manufacturer, or through ensuring the resulting vaccines can be purchased at cost price, this is not a necessary precondition for success of the self-sufficiency model. Establishing domestic manufacturing capacity in a developing state, even if it were private industry, would be beneficial to developing states, as this would allow the government some degree of control over what products private industry researches or manufactures. Mechanisms and incentives such as tax breaks, subsidies, and the scales of government buying powers would all allow for some degree of government control over market conditions, and provide suitable incentives for research or expanding capacity in this field for private enterprise. Moreover, having domestic capacity present in a state, even if privately owned, allows for the possibility of nationalised production or the restriction of product exports to ensure domestic demand is met during a pandemic. Such reasoning has led to BARDA investing heavily in domestic influenza manufacturing in the US, to ensure domestic demand can be met in the event of a pandemic.\textsuperscript{7}

In order to achieve this, clearly developing state manufacturers require the knowledge that is not readily found outside of the established pandemic influenza vaccine manufacturers in order to manufacture vaccines. As Piketty notes in Capital in the Twenty-First Century

\textsuperscript{6} Jeffrey Partridge and Marie Paule Kieny, ‘Global production capacity of seasonal influenza vaccine in 2011’ (2013) 31(5) Vaccine 728
historical experience suggests that the principal mechanism for convergence at the international as well as the domestic level is the diffusion of knowledge. In other words, the poor catch up with the rich to the extent that they achieve the same level of technological know-how, skill, and education, not by becoming the property of the wealthy. The diffusion of knowledge is not like manna from heaven: it is often hastened by international openness and trade (autarky does not encourage technological transfer).  

Meaning that a situation whereby knowledge can be diffused from developed states, to developing states, is clearly a desirable one. To this end, the quotation from Pasteur at the head of this chapter that ‘Science knows no country, because knowledge belongs to humanity’ is certainly admirable in its sentiment. However, it is not reflective of how the knowledge generated in modern science is managed and distributed, particularly in the field of pharmaceutical research and development. In light of this quotation, a person interested in access to pharmaceutical products may be compelled to direct their mind to the question ‘How do we arrive at a scenario whereby knowledge of how to manufacture pharmaceutical products does belong to humanity?’ This question would likely lead them to the answer of abolishing a system that allows for the knowledge of how to manufacture pharmaceutical products to be owned by individuals: the intellectual property system.

However, during this research the argument has been advanced that knowledge not locked up by the intellectual property system is actually the significant barrier to new manufacturers entering the market, particularly in developing states, and therefore this is the major barrier to self-sufficiency in developing states. Those of us interested in access to pharmaceutical products appear to be directing our minds to the wrong question. The question ought not to be ‘How do we arrive at a scenario whereby knowledge belongs to humanity?’ but rather ‘How to we ensure that knowledge, regardless of who it belongs to, is usable by humanity?’ It is this distinction between ownership of knowledge, and ability to use knowledge, regardless of ownership, that I argue is the crux of this matter. It is noteworthy that the key information that

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manufacturers in developing states would need access to in order to establish manufacturing capacity is not ‘owned’ in any formal sense, in that, no property rights have been granted over this knowledge by way of intellectual property. A lack of property rights over this knowledge would typically lead us to the assumption that this knowledge is therefore utilisable by humanity, because there are no property rights preventing utilisation occurring, however, as this thesis has demonstrated, this is not the case.

Despite the fact that the lack of accessible knowledge that is not locked up by the intellectual property system is the major barrier to developing states establishing pandemic influenza manufacturing capacity in order to become self-sufficient, there is a significant success story in this area. The Butantan Institute in Brazil began producing pandemic influenza vaccines in 2011, a case study of this is provided below, which outlines how Brazil successfully established the necessary level of technological infrastructure in order to commence self-sufficient manufacturing of pandemic influenza vaccines. This case study can be used in order to determine how Brazil has achieved such significant success in this field through the Butantan Institute, and what factors will determine if such success is replicable in other developing states. As this case study highlights, it is particularly noteworthy that it was not necessary to license any intellectual property rights to the Butantan institute by established pandemic influenza vaccine manufacturers, but significant transfer of know-how and infrastructure was transferred by established manufacturers, in order for Butantan to establish manufacturing capacity in Brazil.

8.1.1 - Butantan influenza vaccine production case study

In early 2003, in the midst of the highly pathogenic avian influenza outbreak that was spreading through many states in Southeast Asia, the Ministry of Health of Brazil identified self-sufficiency in producing pandemic influenza vaccines as a major public

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9 Institute of Medicine, The Threat of Pandemic Influenza: Are We Ready?: Workshop Summary (S Knobler and others eds, 1st edn, National Academies Press 2005) 10
health priority. During this outbreak, it was anticipated that states that lacked self-sufficiency in pandemic influenza vaccine manufacturing, or did not have an Advance Purchase Agreement in place to procure vaccines, would have to wait approximately a year for delivery of vaccine supplies. In order to address this public health priority, the Ministry of Health instructed the Butantan Institute, a state-owned pharmaceutical research and production facility, to develop and produce sufficient quantities of influenza vaccine, in line with the self-sufficiency policy.

The Butantan Institute was able to overcome the knowledge and intellectual property barriers outlined above by way of a transfer of technology agreement with Sanofi Pasteur, a private institution that is one of the largest influenza vaccine manufacturers in the world. The technology transfer agreement between Sanofi and Butantan comprised of Sanofi having oversight of the production plant design and selection of equipment (partly produced in Brazil), supervision of the construction of the plant and its validation, assistance in the selection of an adequate source of eggs, staff training, and transfer of vaccine formulation for pandemic vaccines. A license for patent rights held by Sanofi Pasteur to The Butantan Institute was not included in the transfer of technology agreement, presumably because there were no patent rights held by Sanofi in Brazil that could have acted as a barrier to developing and producing the seasonal and pandemic influenza vaccines Butantan sought to produce. The fact that there was no need to license intellectual property rights, only technical knowledge and understanding, to Butantan in order for them to develop manufacturing capacity demonstrates the point that it is not intellectual property

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10 C Miyaki, 'Influenza vaccine production for Brazil: A classic example of successful North–South bilateral technology transfer' (2011) 29S Vaccine
11 Ibid.
12 For a history of the Institute and its role in addressing public health priorities in Brazil see: Marcelo De Franco and Jorge Kalil, 'The Butantan Institute: History and Future Perspectives' (2014) 8(7) PLoS Neglected Tropical Diseases e2862
13 Miyaki, (n10)
14 De Franco & Kalil, (n12)
15 Miyaki, (n10); Michael Watson (Sanofi Pasteur), 'Technology Transfer from the Perspective of IFPMA vaccine members' (WHO – Workshop on Technology Transfer for Local Manufacturing Capacity of Vaccines) <http://www.who.int/phi/news/Presentation11.pdf>
16 Julie B. Milstien, Patrick Gaulé, and Miloud Kaddar, 'Access to vaccine technologies in developing countries: Brazil and India' (2007) 25(44) Vaccine 7610
rights that are the barrier to self-sufficient manufacturing being developed in developing states.

In 2011 The Butantan Institute delivered the first lot of vaccines against influenza entirely produced in Brazil. Currently, the Butantan Institute is able to manufacture both seasonal and pandemic influenza vaccines, and has manufacturing capacity for approximately 20 million doses. While it is important to note that this is not sufficient manufacturing capacity to meet the target to immunise 33% of the Brazilian population, it is sufficient for approximately 10% coverage, which is significantly higher than the 1.4% vaccination coverage which is the best case scenario that could be achieved by developing states procuring from the Pandemic Influenza Preparedness Framework.

8.1.2 – Scaling up the Butantan Model

The success of the Butantan model demonstrates that it is possible for developing states to overcome the technology and knowledge related barriers which currently prevent them from being self-sufficient in producing their own pandemic influenza vaccines. In addition, given that Sanofi is a private institution, it would appear that this transfer of technology is merely a straight forward commercial agreement, and that therefore the chief barrier to scaling up such a model to other developing states is simply the spending capacity, or political will, of developing states’ governments. However, the transfer of technology from Sanofi to Butantan was not instigated through the WHO Influenza Vaccine Technology Transfer Initiative and hub, but rather through a private agreement between the two parties, outside of the WHO mechanism for transferring influenza vaccine technology. This further undermines the

17 Ibid.
20 Put simply, in a best-case scenario, developing states could achieve vaccination coverage of approximately 1.4% if procuring from the PIP Framework. For more details See 4.5 – ‘SMTA2 Commitments by Industry’
utility of the Vaccine Technology Transfer Initiative, as the major success story in transfer of technology transfer in pandemic influenza vaccines occurred without the input of the Initiative. However, this is not an appeal for the WHO to take a laissez-faire approach to transfer of technology to developing states from pandemic influenza vaccine manufacturers. On the contrary, as the rest of this chapter outlines, the WHO has a crucial role in scaling up the Butantan Model to other developing states, but significant reform is required.

The WHO has a crucial role to play in this scale up for a number of reasons. Firstly, as Butantan staff wrote in a paper on the transfer of technology from Sanofi to Butantan:

[technology transfer is complex. It entails a great deal of responsibilities on the part of the technology provider and technical and managerial capability on the part of the recipient. Above all, technology transfer is a joint venture based on mutual trust and commitment. A major objective must also be for the project to be sustainable, which implies incorporation of new developments into the process and, ultimately, technology independence for the recipient.]

Given the complexities of transfer of technology, the negotiations, and the need for standardisation of recipient technical capabilities as well as standardisation of technology to be transferred to recipient states, in order to ensure all states are capable of producing the same high-quality vaccine, there is a need for the WHO to manage and coordinate such a programme of transfer of technology. The Sanofi to Butantan model of transfer of technology for pandemic influenza vaccines is something of an anomaly in many ways, and we cannot expect transfer to happen from established PIV manufacturers to developing states in a similar fashion in the future. Butantan is a state-owned and prestigious scientific institution, which has engaged in scientific research and pharmaceutical research, development and manufacturing since 1900. It has been in receipt of extensive funding from the State, which has enabled it to develop numerous, high-quality research and production

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21 Miyaki, (n10)
22 Miyaki, (n10)
facilities. Butantan has also had significant experience since the 1970s of producing biologic products, including vaccines. The advanced knowledge and infrastructure that were already in place in the Butantan Institute are not readily found in developing states, and even less common is for such infrastructure to be state-controlled and financed, which therefore means the drugs and vaccines developed by the Butantan Institute are determined by the Brazilian state. Such an advanced infrastructure and knowledge base would have clearly made the decision to transfer technology regarding pandemic influenza vaccines easier. Indeed, there is a significant amount of literature which argues that there exists an implied or specific requirement of a capacity to implement the technology successfully before the transfer can occur.

The decision to transfer technology to Butantan appears to have been influenced by the fact that, as Wayne Pisano, President and Chief Executive Officer of Sanofi Pasteur said: ‘Sanofi Pasteur and Butantan Institute are historical and successful partners who will bring a tailored response to public health needs in the context of pandemic influenza in Brazil.’ Sanofi has been building and managing facilities in Brazil on behalf of the Brazilian state since 1975. This historic relationship between Sanofi and Butantan would have heavily influenced the decision of the Brazilian state to select Sanofi as a technology partner, and the decision for Sanofi to agree to the transfer. This prior relationship, and the trust this would have developed between the parties

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23 De Franco & Kalil, (n12)
26 De Franco & Kalil, (n12)
cannot be understated as an impetus to engage in technology transfer. As Zuscovitch said of the role of trust in transfer of technology agreements:

Trust is a tacit agreement in which rather than systematically seeking out the best opportunity at every instant, each agent takes a longer perspective to the transactions, as long as his traditional partner does not go beyond some mutually accepted norm.\(^{27}\)

Similar sentiments about the importance of trusts between parties in transfer of technology agreements have been expressed elsewhere.\(^{28}\)

Unfortunately, the majority of developing states, or regional groups of developing states, that could benefit from transfer of technology do not have a historic relationship with one of the major pandemic influenza vaccine manufacturers, nor do they have a state-owned pharmaceutical research and development company with extensive experience of developing vaccines for public health emergencies, all of which make the prospect of bilateral transfer from a manufacturer to a developing states less likely. Therefore, in absence of these factors in almost all developing states, the role of the WHO in ensuring transfer of technology for pandemic influenza vaccines is crucial to ensure that recipient states are sufficiently prepared to receive and manage technology transfer. The WHO would also need to have a key role to play in encouraging pandemic influenza vaccine manufacturers to transfer technology, and ensuring that transfer is standardised across all states in order to ensure all recipient states are capable of producing the same, high-quality vaccine.

The first of these roles for the WHO would require it to provide seed funds to developing states to improve manufacturing infrastructure, and ensure a specific level of infrastructure was in place prior to transfer occurring. This would require direct

\(^{27}\) Ehud Zuscovitch, ‘Networks, Specialisation and Trust’ in Patrick Cohendet, Patrick Llerena, and Hubert Stan (eds), The Economics of Networks (Springer 1998) 243

intervention, leadership and significant funding from the WHO; merely setting a level of technical infrastructure for developing states to meet is unlikely to lead to such states meeting the level required for transfer to occur. This is demonstrated by the consistent failure of developing states to meet the core capacity infrastructure requirements included within the International Health Regulations.\(^{29}\)

The second goal is arguably more difficult to achieve, given that the WHO has attempted to facilitate transfer of technology from established PIV manufacturers to developing states previously, through the WHO Influenza Vaccine Technology Transfer Initiative and hub, which was largely unsuccessful\(^ {30}\). Therefore, in order to make the second role of the WHO more likely to succeed, the WHO needs to be empowered to compel technology holders to actively engage in facilitating transfer of technology to developing states via the WHO. There are two options which could be pursued by the WHO in order to achieve this: the creation of binding international law regarding the transfer of technology from PIV manufacturers to the WHO, or reform to the Pandemic Influenza Pandemic Framework. The second option is preferable in order to make a more innovative access and benefit system sharing system which directly links PIV manufacturers’ access to viral samples via the PIP Framework with compulsory transfer of technology provisions.

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\(^{29}\) To meet the IHR requirements, states were required to develop, strengthen, and maintain core response capacities for public health risks and Public Health Emergencies of International Concern (core capacities were required to be met regarding: Legislation and policy; Coordination of public health emergencies; Surveillance, Laboratory standards and Disease Reporting; Response and Preparedness; Risk communication; Points of entry and Quarantine standards) before June 15, 2012 (five years after the IHR were passed). Despite this, the most recent review of states progress in meeting the core capacity targets set out in the IHR in 2013, found that the majority of developing states had failed to meet the core requirements. World Health Organisation, ‘International Health Regulations (2005): Summary of States Parties 2013 Report on IHR Core Capacity Implementation (Regional Profiles) (WHO/HSE/GCR/2014.10)’ (WHO 2013) <http://apps.who.int/iris/bitstream/10665/145084/1/WHO_HSE_GCR_2014.10_eng.pdf?ua=1> it must be noted however, that it is not immediately apparent whether these states have failed to meet the Core Capacity requirements due to a lack of political will, or a lack of resources. Regardless of the cause, it is clear that developing states would require significant assistance in order to meet any requirements set by the WHO.

\(^{30}\) See 4.6.1 - Transfer of Technology for PIV Manufacturing and the WHO for more information.
Prior to suggesting how the PIP Framework ought to be reformed, it is first necessary to outline why the creation of binding international law is not considered suitable in this scenario.

8.2 – The WHO, Transfer of Technology and International Law

The World Health Organisation has only exercised its powers to make binding international law on three occasions in its history,\(^{31}\) despite the Constitution of the WHO empowering the Organisation to make hard law obligations on any matter deemed to be within the competence of the Organisation.\(^{32}\) As Gostin notes ‘The WHO could do more to assert its authority and its mandate by serving as a platform for the negotiation of major treaties. Greater use of hard law would boost the legitimacy of the regulatory system, raising the moral, legal and political stakes for compliance by national governments.’\(^{33}\) Despite this, As mentioned at Chapter 4, ‘Soft law’ obligations are much more typical for law made via the WHO, which has been criticised on the basis that states tend to be more compliant with treaty obligations than soft law norms.\(^{34}\) Fidler identifies three potential reasons for the WHO neglecting using binding international law in order to meet its objectives:

First, the neglect may reflect WHO’s institutional culture, which is dominated by public health experts, physicians and medical researchers. In such an environment, the use of international or national law received low or no priority. Second, the WHO’s activities have been focused on delivery of biomedical tools…and international legal initiatives were not necessarily needed in order to achieve this. Third, the WHO’s


\(^{32}\) Article 19, Constitution of the World Health Organisation (1946)


limited experience with trying to create regulatory regimes are fraught with controversy and conflict.\textsuperscript{35}

Regardless of the WHO’s largely unsuccessful past with creating binding international law, the benefits of the WHO codifying obligations by way of binding international law are clear, even in the area of transfer of technology. When considering how weak the company obligations that Sanofi, GSK and the Serum Institute of India have signed up to via their SMTA2s with the WHO, we see pandemic influenza vaccine manufacturers are not taking their obligations to supply the WHO with vaccine, or transfer technology to member states, as seriously as we would hope. Ensuring any commitments are binding in international law would appear to be a sensible way to eliminate this problem.

8.2.1 – States as the Subjects of International Law

However, empowering the WHO to compel technology holders to actively engage in facilitating transfer of technology to developing states via binding international law has a fundamental limitation: the dominant actors and subjects of international law are states, not private corporations. This is a significant barrier to the WHO being able to use international law in order to achieve its aim in this regard, as it is the behaviour of private corporations that the WHO is seeking to change regarding transfer of technology.

Of course, the WHO could create an international legal instrument that compels states to compel pandemic influenza vaccine manufacturers to engage in transfer of technology to the WHO. Indeed, as noted at 1.4.3 it is pursuant upon states themselves to regulate the pharmaceutical industry in such a way so as to ensure that industry respects and upholds the Right to Health - the WHO as the global coordinator on global health matters could play a strong role in setting standards and expectations regarding the pharmaceutical industry. These standards could then trickle down to become binding upon the pharmaceutical industry via the member states of the WHO.

\textsuperscript{35} David Fidler, ‘International Law’ in R Smith and others (eds), \textit{Global Public Goods for Health: Health economic and public health perspectives} (Oxford 2003)
However, this is problematic for two reasons. Firstly, it is unlikely that international law which places strong obligations upon states with PIV manufacturers in their territory to force said manufacturers to engage with transfer of technology to the WHO would ever actually be enshrined in law, due to the significant power imbalances in the international law making process. Therefore, it is much more likely that any resulting law would be more likely to encourage developed states to encourage pandemic influenza vaccine manufacturers to engage with transfer of technology, rather than compel them to do so. Secondly, but intrinsically linked with the prior point, is that those provisions within the TRIPS Agreement which seek to encourage developed states to encourage industry within their territory to transfer technology to developing states are weakly worded, and have been criticised for actually achieving very little.

8.2.2 – Power, Politics, and International Law.

It would be remiss to suggest radical reform of the international legal landscape through the creation of binding international law regarding the transfer of technology from PIV manufacturers to the WHO, without paying any regard to the question of whether such reform would actually be enshrined in law. While it is beyond the limitations of this thesis to delve into the multitude of theories of international relations scholarship that attempt to understand and explain state behaviour, it is important to note that it does not require a great leap to see international law, and the international law making process, as merely a reflection of the interest of powerful states. On this point in the context of international health law making, as Fidler

36 TRIPS, Article 68.2
38 Within international relations scholarship this is most likely to be considered a form of ‘international realism theory’ for more information see: Richard Steinberg and Jonathan Zasloff, ‘Power and International Law’ 100 The American Journal of International Law 64; O. Hathaway, ‘Between Power and Principle: An Integrated Theory of International Law’ (2005) The University of Chicago Law Review 72 469
notes, ‘if the great powers of public health, such as the United States of America and the European Union are not engaged in the production of specific global public goods for global health, then the chances for producing such goods are diminished’.\(^{39}\)

In this context it is important to note that Fidler does not refer to ‘production’ to mean to make or manufacture, but ‘to have a direct interest in bringing about’. Therefore, it is safe to assume that if reform of international law does not benefit these great powers of public health (which is where pandemic influenza vaccine manufacturing capacity is largely housed), it is unlikely the reform will make it through the international law making process. It has also been argued that developed states with established pharmaceutical industry within their territory consistently seek to protect that industry during international health law negotiations, to the detriment of global health and development.\(^{40}\)

For the above reasons it is more likely that reform to the Pandemic Influenza Preparedness Framework is more likely to lead to technology holders being compelled to actively engage in facilitating transfer of technology to developing states, via the WHO.

8.3 – Reforming the Pandemic Influenza Preparedness Framework

As noted at 4.11, the Pandemic Influenza Preparedness Framework already contains provisions intended to improve transfer of technology from technology holders to developing states wishing to be in receipt of said technology, via SMTA2 Agreements. However, as also noted at 4.11, no manufacturer that is a party to an SMTA2 has agreed to any transfer of technology provisions as part of their Company Obligations. Had any technology holder agreed to engage in transfer of technology via the PIP Framework, they would have agreed to

\(^{39}\) Fidler (n35)
grant to manufacturers in developing countries licenses on mutually agreed terms that should be fair and reasonable including in respect of affordable royalties, taking into account development levels in the country of end use of the products, on technology, know-how, products and processes for which it holds IPR for the production of (i) influenza vaccines, (ii) adjuvants, (iii) antivirals and/or (iv) diagnostics\textsuperscript{41}

and/or:

grant royalty-free licenses to manufacturers in developing countries or grant to WHO royalty-free, non-exclusive licenses on IPR, which can be sublicensed, for the production of pandemic influenza vaccines, adjuvants, antivirals products and diagnostics needed in a pandemic. WHO may sublicense these licenses to manufacturers in developing countries on appropriate terms and conditions and in accordance with sound public health principles.\textsuperscript{42}

The problems with the current transfer of technology provisions including in the PIP Framework are that there is little incentive for technology holders to engage with SMTA2 generally, and even less incentive to engage with the specific transfer of technology provisions within the SMTAs; transfer of technology occurs bilaterally between states leading to inconsistencies in technology implementation; and it does not expressly link together the work of the WHO Influenza Vaccine Hub, and the PIP Framework. The recommendations I make below are intended to address each of these problems. These recommendations take the form of an amendment to the PIP Framework that will maintain the link between providing established pandemic influenza vaccine manufacturers with access to viral samples, and compelling these manufacturers to share the resulting benefits, which the Framework has rightly connected. In order to ensure the problems identified above are minimised, a much more robust legal framework is required, with compulsory provisions in relation to transfer of technology and intellectual property rights in return for access to viral

\textsuperscript{41} PIP Framework, Annex 2, SMTA2, Article 4.4.1.A5 WHO
\textsuperscript{42} PIP Framework, Annex 2, SMTA2, Article 4.4.1.A6,
samples from the WHO. Secondly, transfer of technology and intellectual property rights should be transferred to a technology HUB as opposed to individual states.

8.3.1- An Intellectual Property and Information Clearing House
The proposal is to fuse the PIP Framework’s mechanism for sharing viral samples with influenza vaccine manufacturers with the WHO Technology Hub, thereby creating a PIP/Hub Clearing House, managed by the World Health Organisation. While the term Clearing House originates in the banking sector, it has more recently been used to describe a mechanism whereby generators of goods, services and/or information are matched with potential users. Clearing houses are rare in practice, there have been some attempts to bring Clearing Houses online, particularly in the life sciences sector, with varying degrees of success.

The proposition here is for a royalty collection Clearing House. A royalty collection Clearing House has been defined as comprising of, and serving, several functions: identifying patents and patent claims, matching licensees with licensors, developing and supplying standardised licenses, collecting royalties, monitoring whether users respect licensing conditions, and providing dispute resolution services such as mediation and arbitration. In addition to these characteristics identified by Van Zimmeren, the PIP/Hub Clearing House proposed here would also identify and match licensees and licensors in relation to proprietary information which is not protected by intellectual property rights.

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45 Van Zimmeren, (n43)
What we are concerned with at this stage is the transfer of proprietary, non-patented, information from a pandemic influenza vaccine manufacturer that controls said information and has not placed it in the public domain, to another institution, be it private or public, in a developing state. The question we must now turn our attention to is how best to achieve this. One significant issue to bear in mind in terms of attempting to facilitate the transfer of this proprietary information is that numerous attempts, both through the TRIPS Agreement and the PIP Framework, which have attempted to encourage manufacturers to engage in transfer of technology and information to developing states have been unsuccessful. In contrast, the holders of proprietary information that have actively chosen not to place certain information in the public domain have been compelled to make this information available to rival corporations in developed states. Presumably these corporations wanting to remain in business within these markets is a major incentive for compliance with such orders, however, such an incentive is not readily apparent if we are discussing the transfer of proprietary, non-patented, information to developing states, which are not attractive markets for the corporations. This is particularly true of the pandemic influenza vaccine market, as 3.4.1 demonstrated on average developing states only procured approximately 10% of their vaccine directly from the manufacturer during 2009-H1N1.

The creation of this Clearing House would mean that viral samples would be provided from the WHO to established pandemic influenza vaccine manufacturers, in return for them engaging with transfer of technology with the Clearing House. This could include the transfer of patented and non-patented information required for pandemic influenza vaccine manufacturing capacity to be established. This information would be transferred from the manufacturer to the Clearing House, and licensed in such a way that would provide full rights for the Clearing House to sub-license, and pass the

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46 Encourage, in the context of the TRIPS Agreement means that Article 68.2 states: ‘Developed country Members shall provide incentives to enterprises and institutions in their territories for the purpose of promoting and encouraging technology transfer to least-developed country Members in order to enable them to create a sound and viable technological base.’ Whereas in the context of the PIP Framework encouraging refers to the fact that agreeing to technology transfer is an optional term of agreeing to an SMTA2, with ill-defined parameters and expectations.

information on to developing states in order for them to establish PIV manufacturing capacity.

Figure 1. Proposed Clearing House for Pandemic Influenza Vaccine Technology

The proposed Clearing House model does not allow for bilateral transfer of technology from a PIV manufacturer to a developing state, as the current company obligations under Article 4.4.1.A5 of the current SMTA2 obligations state. Instead, all transfer from PIV manufacturers must be made to the Clearing House, then from the Clearing House onwards to developing states. While this may appear to be an unnecessary, bureaucratic burden, it is integral to the success of the Clearing House. Having the WHO act as Clearing House administrator allows the WHO to use its expertise in this area to identify the relevant technology that the hub would need to acquire from relevant technology holders, bundle it together into a technology package and oversee the implementation of this technology package in developing states, in order for such states to establish vaccine manufacturing capacity. Moreover, not allowing for bilateral transfer from technology holders to developing states will ensure parity in technology uptake by developing states, as the WHO will be free to sublicense the
technology to as many developing states as have the capacity to benefit from it, whereas currently manufacturers need only to transfer technology to one developing state in order to have met the criteria outlined at Article 4.4.1.A5.

8.3.2 - Incentivising Technology Holders to Engage With Transfer of Technology

The success of the Clearing House is dependent upon PIV manufacturing engaging with it, and committing to provide it with transfer of technology and proprietary information. One potential method of ensuring pandemic influenza vaccine manufacturers engage with the clearing house model is sanctions. The WHO could create a system whereby they impose fines on pandemic influenza vaccine manufacturers that fail to engage with the new model, but this is undesirable for a number of reasons. First, unlike a number of other international organisations, such as the WTO, the WHO does not have a formal disciplinary body, or experience of imposing sanctions — either upon member states that are not compliant with WHO rules, or external entities, such as pharmaceutical manufacturers. As noted above, ‘Soft law’ recommendations are fairly typical for law made via the WHO: obligations are rarely provided by way of binding conventions with sanctions. Second, as noted at 8.2.1 states are the subject of international law, not corporations. Creating a scenario whereby the WHO is able to impose sanctions on private corporations would meet the same difficulties as discussed at 8.2.1 in respect of using ‘hard law’ to compel manufacturers to transfer technology. Namely that the WHO is unlikely to be able to use international law in order to sanction private corporations without those corporations agreeing to sanctions in the first place, or the states in which said corporation are resident in agreeing to impose sanctions on behalf of the WHO, and then actually doing so.

Instead, this Clearing House model proposal relies upon an inbuilt mechanism in order to incentivise pandemic influenza vaccine manufacturers to engage with the Clearing House model and transfer knowledge and technological understanding to the WHO. As the influenza vaccine manufacturers’ ability to manufacture pandemic influenza vaccines is dependent on them having access to the viral samples, provided to the Clearing House by developing states, they have a clear incentive to engage with the Clearing House, as viral samples will only be provided to manufacturers if they have met their obligations to transfer technology to the Clearing House. Moreover, the impact upon established PIV manufacturers from engaging with transfer of technology to the Clearing House and having manufacturing capacity being established in developing states will be minimal. The developing states which could establish PIV manufacturing capacity through the Clearing House are not a strong, viable market for pandemic influenza vaccine manufacturers; therefore capacity being establishing in developing states is unlikely to affect sales of pandemic influenza vaccines by the established manufacturers. Moreover, a term of the onward transfer of technology and capacity from the Clearing House to developing states would be that the manufacturing in developing states agrees to use the vaccine for domestic uses, and commits to not parallel export the product out of their domestic territory, therefore, there will be no impact in the markets relevant to pandemic influenza vaccine manufacturers.

8.3.2 – Limitations to the Proposed Clearing House Model
There are three potential limitations to the proposal outlined above. The first potential limitation is that scientific advance in this field seems to suggest that in the future it will be possible to manufacture pandemic influenza vaccines without access to the specific viral samples of the target candidate virus which the vaccine is to provide immunity against. Instead, researchers and manufacturers will merely need access to any influenza virus sample and be able to genetically engineer these samples
to match the target candidate virus.\textsuperscript{50} Though this technology is in its infancy, the ability to manufacture pandemic influenza vaccines without viral samples could seriously limit the incentive for pandemic influenza vaccine manufacturers to engage with the Clearing House in the future. If this were to occur the technology that the Clearing House managed would quickly stagnate and a gulf in technological capacity would grow again between manufacturers in developed states that had access to the new genetic modification technology, and the manufacturers in developing states, still reliant on the conventional egg-based manufacturing process which they would have acquired from the Clearing House.

However, it is worth noting that creating vaccine candidate viruses by reverse genetics is a field of technology that is very much in its infancy, and its uptake by the manufacturing community (even if it is possible) will not happen for some considerable time. In the interim, manufacturers will still require access to viral samples from the WHO. During this time, the Clearing House still has the potential to acquire considerable technological knowhow from manufacturers, and use this technology to establish manufacturing capacity in developing states. If in the future established PIV manufacturers no longer need viral samples from the Clearing House, as they are able to create their own candidate viral samples by way of reverse genetics, a significant benefit of the Clearing House model will already have been realised in developing states, by establishing PIV manufacturing capacity there in the first place.

The second limitation to the model is that its success is dependent on all states that have samples of the target candidate virus during a pandemic being willing to transfer them to the Clearing House for transfer to PIV manufacturers. If a developing state, unhappy with the benefit they have received from the Clearing House, were to

attempt to enter into a bilateral agreement with a PIV manufacturer directly, in the way Indonesia did during 2005-H5N1, the utility of the Clearing House would clearly be jeopardised. A developing state entering bilateral negotiations with a manufacturer in this way would considerably undermine the work of the Clearing House, as it would provide a separate source of viral samples for PIV manufacturers, without burdening them with having to make contributions to the Clearing House.

There are two reasons why this potential limitation should not inhibit the Clearing House model being pursued. Firstly, the widespread international condemnation directed towards Indonesia when it refused to comply with international virus sharing norms during 2005-H5N1 is testament to the fact that the international community takes such a breach of viral sharing norms seriously, and as Indonesia eventually reversed its position and began open sharing again demonstrates that this international condemnation is an effective tool to ensure states comply with such norms. Secondly, even if a developing state did directly transfer viral samples to an influenza vaccine manufacturer and not to the Clearing House, other manufacturers would still require access to viral samples to make their vaccines, as it is unlikely that a manufacturer that received viral samples from a developing state would transfer these samples on to their rival manufacturers, as this would remove the manufacturers exclusive ability to manufacture that vaccine. Therefore, the Clearing House model would still be able to impart significant benefits for its members (both vaccine manufacturers and developing states), even if some access and benefit sharing transactions occurred outside of the Clearing House.

Finally, while this model may appear to focus on developing states and pandemic influenza vaccine manufacturers, developed states and the WHO both have crucial roles to play in the success of the Clearing House. The Clearing House model outlined above would require significant financial and technical support from the WHO and developing states, as well as reforms to the PIP Framework in order to succeed. Regarding financing, the Medicines Patent Pool (MPP) is a United Nations-backed

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51 See 4.1 Indonesia H5N1
organisation offering patent pooling for drugs for HIV, TB, and Hepatitis C - which operates in a similar manner to the Clearing House model described above, albeit with a focus on patents, as opposed to proprietary knowledge. The MPP is provided with yearly funding of over US$5million from the UN, excluding benefits in kind such as office space and IT support. Given that the MPP does not provide any technical or financial support to establish manufacturing capacity in a developing state, whereas the Clearing House would, it is likely the Clearing House would require significantly more funding than the MPP. Given that the majority of the WHO’s programme budget is provided for by way of voluntary contributions from a small number of developed states, financial and technical support from these states is crucial to the success of the Clearing House.

8.4 Justifying the Clearing House Model

It may appear that the Clearing House model relies on a desert based system of distributive justice, whereby both the developing state and the pandemic influenza vaccine manufacturers are only entitled to the benefits arising from the Clearing House if they too contribute, but this is not actually the case. A desert based model of distributive justice uses what has become known as the three-place relation, in order to justify benefits being distributed. This can be expressed as ‘A is deserving of benefit B, because of characteristic or action C’. Applying this justification to the Clearing House model, a desert based justification would hold that developing state A, is deserving of transfer technology from the Clearing House, leading to influenza manufacturing capacity in their territory, because they transferred viral samples to

53 In the first five years of the The WHO influenza vaccine technology transfer initiative it had a budget of US$367 million to create regionally based, independent and sustainable pandemic influenza vaccine production capacity in developing countries. As outlined at 4.6.1, this initiative has been largely unsuccessful.
the Clearing House for onward transfer to the manufacturers that engaged in transfer
of technology to the Clearing House. But what of developing states B that had no
sample of this virus to pass on? What of Developing state C, that only acquired sample
after initial samples had been passed to the Clearing House and onward to
manufacturers? A desert based system of reciprocity for contributing to the Clearing
House would not lead to reciprocity for these developing states that do not have any
viral samples to pass to the Clearing House, only those that did. However, while this
proposal may appear to be desert based at first glance, it is actually a proposition
based on what appears to be the most effective manner by which the right-to-health
can be realised in developing states during an influenza pandemic, while not
interfering with the economic and social rights of the relevant intellectual property
rights holders.

The overall aim of this thesis was to ensure a system whereby the right-to-health could
best be realised in relation to an influenza pandemic, by ensuring all developing states
are able to immunise at least one third of their population during an influenza
pandemic. Clearly, to meet this end, a desert based system of reciprocity would not
realise the right-to-health for all developing states, just those ones that had viral
samples to pass on to the Clearing House. Therefore, only a system that disregarded
desert based claims is able to realise the right-to-health, and the aims set out at the
introduction of this thesis.

It is argued, as a conclusion to this thesis, that the Clearing House system outlined
above is the best model by which the four elements of access to medicines in the
right-to-health ‘availability, accessibility, acceptability and quality’ can be realised in
relation to pandemic influenza vaccines in developing states. It is important to note
that the Clearing House model has been designed so as to enable the realisation of
the right-to-health in developing states, through access to essential medicines, while
not unjustly interfering with the notion of intellectual property. This is important to
note for two reasons. Firstly, while it is not the case in pandemic influenza vaccines,
intellectual property rights are an important means of incentivising the creation of
new knowledge for the betterment of society, including in the field of
pharmaceuticals,\textsuperscript{56} and it is important that such a system of incentivisation is maintained where possible. Secondly, while the argument for better procurement of pandemic influenza vaccines by developing states has been framed around the notion of the right-to-health, it is important to note that there are other internationally accepted rights and norms which can appear to conflict with the right-to-health in the sphere of access to medicines, one of which is the right to intellectual property rights. In General Comment No. 17, the UN Committee on Economic, Social and Cultural Rights set out ‘the right of everyone to benefit from the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he or she is the author is a human right, which derives from the inherent dignity and worth of all persons’.\textsuperscript{57} The Committee recognised in the text of General Comment No. 17 ‘that The right to the protection of the moral and material interests resulting from one’s scientific, literary and artistic productions is subject to limitations and must be balanced with the other rights recognized in the Covenant’\textsuperscript{58}, and that ‘limitations on the rights protected under article 15….must be determined by law in a manner compatible with the nature of these rights, must pursue a legitimate aim, and must be strictly necessary for the promotion of the general welfare in a democratic society.’\textsuperscript{59}

This, I would argue, is a balance that has suitably been achieved in the Clearing House model above. Firstly, under the Clearing House model, there is very little interference with the intellectual property rights of contributors to the Clearing House, as the majority of the knowledge that is required to be transferred is not formally defined as intellectual property. Even if we take a particularly broad definition of ‘scientific authorship’, and include knowledge and information which does not have formal authorship through intellectual property, a suitable balance has been stuck between

\textsuperscript{56} As I demonstrated at 6.2
\textsuperscript{57} Para 1, UN Committee on Economic, Social and Cultural Rights (CESCR), General Comment No. 17: The Right of Everyone to Benefit from the Protection of the Moral and Material Interests Resulting from any Scientific, Literary or Artistic Production of Which He or She is the Author (Art. 15, Para. 1 (c) of the Covenant), 12 January 2006, E/C.12/GC/17,
\textsuperscript{58} Para 22, ibid.
\textsuperscript{59} ibid.
these two competing rights because engagement with the Clearing House is to be on a mutually beneficial, consent basis.

8.4.1 - Ethics and the Clearing House model

I would argue that this Clearing House model is well placed to ensure the community benefits of pandemic influenza vaccine programmes, as described at 1.5.1 can be fully realised. Indeed, as I went on to argue at 1.5.1 when discussing access to pandemic influenza vaccines as a right-to-health obligation, we are not just discussing access to pandemic influenza vaccines on an individual basis, but also the right to benefit from the herd immunity which is established within a community when sufficient vaccine is administered. Whilst I have argued that this is a key component of my vision of the right-to-health, Gostin has argued that is what the right-to-health will look like if justice is added to it. He has argued that

This picture of what justice in global health looks like entails a fundamental shift in our understanding of the right to health. The right to health must be conceived of primarily as a collective right, imposing obligations on governments, and in turn implicating all of society. There remains an important role for safeguarding individual rights and the rights of vulnerable groups, but the implementation of broader public health measures is a precondition for securing these more targeted rights. This is the population-based approach, which brings the benefits of improved health for all with an embedded form of social justice.60

A number of commentators have highlighted the problem with this community based approach to the right-to-health, namely that rights based approaches, by their very nature, are individual not collective.61 As Widdows and West-Oram argue ‘many social goods do not easily fit the model of individual rights—particularly shared and

60 Lawrence O. Gostin, Global health law (Harvard University Press 2014) 426
communal goods. Goods such as health goods which require collective action and the delivery of basic group goods (such as clean water, sanitation and a clean environment) are not best conceived of as individual."^62 Widdows and West-Oram use this argument as a basis for moving away from ‘rights based approaches’ towards a more public good rationale for positive action in respect of infectious diseases. This argument applies to pandemic influenza vaccines - the benefit of ‘sufficient access’ to PIV being realised in a state, are felt well beyond those individuals to whom the vaccine is administered. The community as a whole benefits from the herd immunity established by the vaccination campaign. Whilst I appreciate the relevance of the argument presented by Widdows and West-Oram it is important to note that the right-to-health is a tool - a conduit through which goods, be they individual or collective can be realised - rather than the end goal.

In the context of the right to health, the ‘end goal’ is set out at Article 12(1) of the ICESCR as “the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.”^63 - a Sisyphean target, due to the fact that the level set for the highest attainable standard is constantly being set higher, as health conditions, expectations, and medical technology improves. On the contrary, the tools which states can use to work towards this ‘end goal’ is set out in the ICESCR at 12(2) as being:

The steps to be taken by the States Parties to the present Covenant to achieve the full realization of this right shall include those necessary for:

(a) The provision for the reduction of the still birth rate and of infant mortality and for the healthy development of the child;

(b) The improvement of all aspects of environmental and industrial hygiene;

(c) The prevention, treatment and control of epidemic, endemic, occupational and other diseases;

(d) The creation of conditions which would assure to all medical service and medical attention in the event of sickness.^64

^62 Heather Widdows and Peter G. N. West-Oram, ‘Revising global theories of justice to include public goods’ (2013) 9(2) Journal of Global Ethics 227

^63 Article 12(1), ICSECIR.

^64 Article 12(2), ICSECIR.
Continuing this analogy to pandemic influenza: the end goal is for 33% of the population to be immunised in good time, thereby triggering the community benefits of herd immunity. The right-to-health is the legal or political tool by which a state could seek to secure sufficient access to pandemic influenza vaccines in order to achieve this goal.

8.5 Conclusion
The one unanswered question in this thesis is why would the international community wish to develop any of the recommendations proposed, when the current system appears so agreeable to the key relevant actors? Pogge has convincingly argued elsewhere that the international community has a clear moral obligation to mitigate the causes of poor health outcomes in developing states. However, as I have attempted to evaluate the relevant legal and political doctrines by taking into consideration the practical, real-world implications of them, this is a key, and difficult, question that must be addressed, unfortunately without the idealism of Pogge. This is a particularly difficult question because the current system ensures that pandemic influenza vaccines are actually researched and developed by creating a clear pathway between those states that have access to viral samples, and those manufacturers based in developed states that have the technological ability to create pandemic influenza vaccines from said samples. Moreover, the current system ensures that the pandemic influenza vaccine industry based in politically influential developing states is able to flourish with very little threat from developing state manufacturers. Finally, and perhaps most importantly, if we are to consider international law, even international health law, as merely a reflection of the interest of powerful states, the current system ensures these states are able to procure pandemic influenza vaccine in sufficient quantities and in a timely manner, due to their Advance Purchase Agreements. Reform of this area does not appear to be a pressing concern for the key international actors.

However, the recent outbreaks of Ebola and Zika virus in developing states has reignited the debate surrounding global responses to novel pandemics, and access to treatments and vaccines for these viruses, both at the academic and international policy level, meaning that a reconsideration of how vaccine for global health emergencies are developed and accessed is likely forthcoming. On the point of the Clearing House model outlined above, I would argue that it is not as controversial to the key international actors as it may first appear. Firstly, the model outlined above is unlikely to impact upon the markets for pharmaceutical manufacturers, as developing states purchase so few vaccines directly from the manufacturers during a pandemic. Secondly, nor will the model interfere with intellectual property rights of the established pandemic influenza vaccine manufacturers. Key international actors such as the United States, the EU and Japan tend to adopt protectionist policies regarding the pharmaceutical industry, and are wary of any policy development which may undermine the markets or intellectual property rights which the industry enjoys.

Given that the Clearing House does neither of these things it should (in theory) be agreeable to the key international actors.

In addition, improving the timing and availability of vaccines in developing states during an influenza pandemic will improve the global response to a novel strain of pandemic influenza by minimizing the spread of the virus through communities. While this may only appear to be of direct benefit to the community that is immunised,

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68 John Abraham, 'The pharmaceutical industry as a political player' (2002) 360 The Lancet 9344
because of the rapid spread of novel influenza strains in the post-globalisation era, the direct benefits of a rapid, effective immunisation campaign in a developing state will also be reaped in developed states many thousands of miles away.

The major step forward in procurement of pandemic influenza vaccines that the PIP Framework represents demonstrates that reform is possible in this area, even if it does not improve the situation for the key relevant actors outlined above. Indeed, up until the passing of the Framework, the World Health Organisation had little leverage it could employ against pandemic influenza vaccine manufacturers to encourage them to donate vaccines to developing states beyond the usual rhetoric about solidarity and justice. The Pandemic Influenza Preparedness Framework was the first step beyond this rhetoric, which represented an attempt to provide proper incentives to manufacturers to donate vaccines to those states that could not access them during a pandemic. The Framework also rightly linked together the notion of access to viral samples for manufacturers with the supplying of benefits to developing states. However, as argued in the previous chapter, the Framework is not fit for purpose. The amendments proposed in this chapter represent the next step for the international community to take regarding the procurement by developing states of pandemic influenza vaccines in a timely manner, to build upon the work which has been achieved by the current incarnation of the Pandemic Influenza Preparedness Framework. The PIP Framework set out with the objective of ‘improv[ing] pandemic influenza preparedness and response....with the objective of a fair, transparent, equitable, efficient, effective system for, on an equal footing: (i) the sharing of....influenza viruses with human pandemic potential; and (ii) access to vaccines and sharing of other benefits’, the proposed amendments outlined above represent the next logical step the WHO could take in order to achieve this objective.

\[\text{PIP Framework, Article 2}\]
CHAPTER IX – CONCLUSION

This thesis has advanced four main claims. First: During the 2009-H1N1 influenza pandemic a small number of developed states dominated procurement of the vaccine; and as a result many developing states were unable to procure vaccine, or only procured it at a later stage of the pandemic, when it was no longer as useful. Second: Circumventing patent holders’ rights, or denying the patentability of pandemic influenza vaccines and related technology, will not benefit developing states in improving their procurement of vaccine during an influenza pandemic, because, in the case of pandemic influenza vaccines, intellectual property rights are not a barrier to procurement by developing states. It is the knowledge which innovators in this field do not patent which is the barrier to self-sufficient vaccine development in developing states. Third: The stockpile created by the Pandemic Influenza Preparedness Framework will have little impact upon procurement of vaccine by developing states during the next pandemic, because the capacity of the stockpile is far too small to meet the needs of developing states. Fourth: As a result, during the next influenza pandemic, developing states will again be reliant upon attempting to procure pandemic influenza vaccines from the traditional, unsuccessful methods. In addition to these claims, I have proposed a suitable alternative model that would enable developing states to become self-sufficient in their procurement of vaccine during an influenza pandemic.

The status quo is undesirable for a number of reasons. Firstly, procuring from established manufacturers will not enable developing states to have sufficient access to vaccine because the limited pandemic influenza vaccine capacity is reserved for developed states via Advance Purchase Agreements, and manufacturers lack the market incentive to expand their capacity to meet the needs of developing states. Secondly, receiving donations from the PIP stockpile and/or the Vaccine Deployment Initiative (if one is set up again1), will not enable developing states to have sufficient access to pandemic influenza vaccines, because neither stockpile has the necessary

1 Of which there is no guarantee.
capacity to enable developing states to procure enough vaccine to meet the 33% vaccination coverage threshold required in order to establish herd immunity. Therefore, it would be fair to say that little has changed from the manner in which developing states procured vaccine during 2009-H1N1.

Given the manifest failings of the status quo, the contributions this thesis makes to the academic discourse on this topic are three fold; the first contribution urges a reconsideration of how patents are discussed in relation to access to pharmaceutical products, and how the relationship between patents on pandemic influenza vaccines and procurement of the vaccine by developing states is formulated. The second contribution from this thesis also urges a change in discourse, this time in relation to differentiating between types of drugs when discussing ‘access to medicines’. The final, and much loftier ambition, seeks to suggest a potential practical solution to the problems identified within this thesis.

A significant amount of the academic literature regarding access to medicines presents patent protection on pharmaceutical products as the cause of developing states having poor or limited access to life-saving pharmaceutical products. This literature also advances the viewpoint that making use of provisions within domestic

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patent legislation such as compulsory licensing or limiting the patentability of pharmaceutical products is the most effective tool a developing state can use in order to improve their procurement of these products. I do not seek to challenge this viewpoint per se. Indeed, this viewpoint is justifiable in certain circumstances; there is compelling evidence that demonstrates the impact which patent protection has on access to oral solid drugs, and additional evidence that demonstrates how the procurement of oral solid drugs has been improved in developing states when patent flexibilities have been used by governments.

However, I would challenge the viewpoint that the patent is the only or primary barrier to access to medicines in developing states, in all circumstances. It may be the case that because the patent system is a genuine barrier to access to medicines in some circumstances has led to the mistaken assumption that patents are a barrier in all circumstances where there is a problem with access to medicine in a developing state. To this end, the consistent focus on the role of patents in access to medicines can be a distraction from other (arguably more important) barriers. This is certainly the case in access to, and procurement of, pandemic influenza vaccines, as I argued at 4.6, 5.3.2, 6.4.4 and 7.4.2.

As I argued at these points it is not the patent protection that innovators hold over pandemic influenza vaccines and associated manufacturing technology that is the

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5 Note the literature highlighted at (n2), particularly those that discuss Thailand and Brazil improving procurement of ARV through the use of compulsory licenses and Sean Flynn, Thai Law on Government Use Licences (American University Press 2006); Kristina M. Lybecke and Elisabeth Fowler, 'Compulsory Licensing in Canada and Thailand: Comparing Regimes to Ensure Legitimate Use of the WTO Rules' (2009) 37(2) The Journal of Law, Medicine & Ethics 222; Suwit Wibulpolprasert and others, 'Government use licenses in Thailand: The power of evidence, civil movement and political leadership' (2011) 7(1) Globalization and Health; Inthira Yamabhai and others, 'Government use licenses in Thailand: an assessment of the health and economic impacts' (2011) 7(1) Globalization and Health
barrier to ensuring sufficient access to pandemic influenza vaccines. If the entire patent landscape associated with pandemic influenza vaccines\textsuperscript{6} were abolished, it would have no discernible impact on access to, and procurement of, the vaccines by developing states. This is because it is the inaccessibility of knowledge related to the manufacturing process for pandemic influenza vaccines, which is not patented or in the public domain, which is the barrier. As Chapter 3 outlined, even if the patents related to pandemic influenza vaccines did not exist, or were lawfully circumvented in developing states, it would be impossible for imitators to produce their own pandemic influenza vaccines without technological know-how regarding manufacturing the vaccine being provided by established manufacturers. It is somewhat ironic that, while academics and policy makers with an interest in access to medicine decry the intellectual property system as the fundamental barrier to access to medicines, that the patenting of all relevant knowledge generated in pandemic influenza vaccine development and manufacturing could actually overcome this problem. To this end, patents are actually intended to prevent the problem identified in this thesis, by incentivising innovators to place the knowledge of their innovation in the public domain, by way of patenting it, in return for no longer holding such information as a trade secret, they gain exclusive rights over using the knowledge for a limited time.\textsuperscript{7}

Given the proliferation of use without authorisation provisions in developing states patent legislation, which provides such states with an effective tool in order to circumvent patent barriers where they exist, it could be argued that in some cases, such as pandemic influenza vaccines, that inaccessible knowledge is now the primary barrier to introducing generic pharmaceutical products, not, as the literature tends to

\textsuperscript{6} See 5.2 for more details, but in short, the following elements of the vaccine and manufacturing processes are patentable: expression systems, fusion partners, immunostimulators, adjuvant systems, excipients and delivery devices, processes which manufacture the vaccine, and in some instances, the inactive virus, or genetic structures within the virus contained within the vaccine.

suggest, patent rights. An acknowledgement of, and engagement with, the additional barriers will enhance the discourse concerning developing states’ procurement of products such as vaccines, and potentially lead to more appropriate solutions to the problem of procurement in developing states being proposed by the academic community.

Further to the above, the majority of the academic literature concerning patent rights and pharmaceutical products discusses ‘access to medicines’, or ‘pharmaceutical patents’, and these all-encompassing terms are used in a manner that implies that the argument advanced within these papers applies equally to all pharmaceutical products, or all medicines. However, as this thesis has argued, this is simply not the case and the impact intellectual property rights have on incentivising the creation of, or access to, pharmaceutical products can vary greatly between different classifications of pharmaceutical products.

In order to advance the academic debate in this field, and ensure that that the discussions in the literature accurately reflect the nuanced reality of the relationship between intellectual property rights and access to pharmaceutical products, it would be beneficial to move forward from discussions of ‘pharmaceutical patents’ and ‘access to medicines’, and instead talk of ‘access to biologics’ or ‘access to oral solid drugs’. Such a change in discourse is necessary in order to better reflect what appear to be the primary barriers to access or procurement in each of these classifications of pharmaceutical products. When discussing access to oral solid drugs it does appear that intellectual property rights are the primary barrier to access to these products in developing states. Determining a sustainable intellectual property system capable of

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8 For example see: Drahos & Mayne, (n2); Carlos Correa, 'Bilateralism in intellectual property: Defeating the WTO system for access to medicines' (2015) 36(1) Case Western Reserve Journal of International Law; Abbott and Reichman, (n2)

incentivising the creation of oral solid drugs while ensuring all those that require access to the drug are not unduly denied it due to those intellectual property rights, should rightly be the focus of academic and policy attention in this area. As a result, the academic discourse on access to pharmaceutical products has heavily focused on the intellectual property rights that act as barriers to access pharmaceutical products, and a myriad of potential solutions to overcome these barriers has been suggested by the academic community. These suggestions have ranged from widespread compulsory licenses being issued by developing states,\textsuperscript{10} patent pooling for essential medicines\textsuperscript{11}, abolishing the patenting of pharmaceutical products,\textsuperscript{12} and even creating an entirely new system of incentive and reward for manufacturing pharmaceutical products outside of the patent system.\textsuperscript{13} These solutions may prove adequate to address the barriers to access for oral solid dose drugs, however, because they talk of access to medicines in a general sense, they are presented in a manner that either directly or implicitly suggests that they apply to all pharmaceutical products.

However, merely addressing intellectual property rights in relation to some biologics, such as pandemic influenza vaccines, would have no impact on improving access to the products in developing states.


\textsuperscript{12} Jayati Ghosh, 'Medical Knowledge' in Richard Smith and others (eds), \textit{Global Public Goods for Health: Health Economics and Public Health Perspectives} (OUP 2003); Michele Boldrin and David K Levine, 'The case against patents' (2013) 27(1) Journal of Economic Perspectives 22

The change of discourse advocated in this section would lead to a more nuanced discussion regarding access to oral solid dose drugs or biologics, which is required in order to reflect the considerable differences between these products, and the barriers to access to each of them. In addition, it would be beneficial if further data on the intellectual property and knowledge landscape could be mapped for other pharmaceutical products,\(^{14}\) and the hypothesis advanced in this thesis was tested against that data.

This research would be useful to determine what sort of monopoly is currently preventing developing states from accessing or manufacturing specific pharmaceutical products e.g. a traditional patent based monopoly; a monopoly provided by knowledge not covered by intellectual property; or a test-data exclusivity monopoly; or a combination of the above. The gathering and clarification of this information is necessary in order to determine if it is intellectual property or other knowledge based barriers which prevents wide scale uptake and access in developing states. This information is required in order to fully inform academic and policy discussions regarding access to these products in developing states, and ensure appropriate reforms can be made to domestic and international legal rules, to enable more effective access to these products.

\(^{14}\) For instance biopharmaceutical products and treatments such as: stem cells; monoclonal antibodies; therapeutic enzymes; thrombolytic agents; and hormones or other pharmaceutical products such as medical devices.
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