Submission to The Department of Foreign Affairs and Trade (DFAT) on issues relevant to the negotiation of a free trade agreement (FTA) between Australia and China.

Medicines Research and Reference Reimbursement Proposals for a China-Australia Free Trade Agreement

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25 March 2005

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Executive Summary

This submission focuses on issue of encouraging research, regulatory and industry collaborations with respect to pharmaceuticals in a proposed China-Australia Free Trade Agreement (China-AusFTA).

China is one of the world's largest manufacturers of generic pharmaceuticals. In 2001, the sales income of China's (largely generic) pharmaceutical industry totaled US$21 billion. By 2020, China will have the world's largest pharmaceutical market.

The presence of a large and viable independent generic pharmaceutical industry is vitally important to the maintenance of low pharmaceutical prices in Australia. Australia has world's best practice expertise in pharmaceutical reference reimbursement processes, though the operation of its Pharmaceutical Benefits Scheme ("PBS") and in pharmaceutical safety and quality regulation through its Therapeutic Goods Administration ("TGA"). By facilitating collaboration on generic pharmaceutical manufacturing, marketing and cost-effectiveness reimbursement, a China-AusFTA could greatly benefit the Australian national interest by providing a massive incentive to enhanced development of a generic pharmaceutical industry and PBS pricing arrangements in Australia.

China has a large population base and a well organized health system. Australia possesses relevant world class expertise in conducting clinical trials suitable for developing the type of scientific data necessary to establish an Chinese innovative pharmaceutical industry with global export potential, as well as generics with levels of quality and safety suitable for the global market. Such collaboration also opens the way to partnerships and joint ventures in China and Australia concerning "innovative" pharmaceuticals, potentially worth billions of dollars in the global export market.

Collaboration on medicines research would also have great economic advantages for expanding two-way trade by reducing development costs in both countries. It would represent a powerful opportunity for ensuring that the expenditure of public monies in this area is restricted to products offering proven benefit to the community in terms of both costs and comparative effectiveness. In

order to achieve this mutually beneficial end it is important that a China-Australia FTA create the opportunity for ongoing dialogue between the drug regulatory and pricing authorities of both countries to ensure suitable regulatory harmonization, compatibility and transparency.

A core of this proposal is that a China-Australia Free Trade Agreement should include an annex establishing a "Medicines Working Committee" to evaluate such issues and other provisions creating a harmonious regulatory framework for such developments.

Economic Developments in Pharmaceuticals in China over the last decade and their implications for Australia and the East Asian region

China currently produces over 1, 350 medicines in 24 classes. Almost all these are what may be described as "generic" drugs. In recent years, China has patented only two "innovative" drugs (arteannuin and sodium dimercaptosuccinate) that have received international marketing approval. Yet China has strong ambitions in the innovative drug field, being hampered only by a present lack of access to drug design and regulatory expertise such as that possessed to a level of international excellence by Australia.

China's pharmaceutical production capacity ranks second only to the United States. In 2001, the sales income of China's pharmaceutical industry totalled US$21 billion.[1] There can be no doubt that China would view the establishment of collaborations for pharmaceutical research and development with Australia as presenting a strategic opportunity to gradually move into the developed world innovative and generic drug market.

China acceded to the World Trade Organisation ("WTO") on December 11 2001. In doing so, China agreed to restructure its domestic legal system to, amongst other things, comply with the obligations of the WTO Convention on Trade-Related Intellectual Property Rights ("TRIPs"). Early in 2005, the United States will be conducting an out-of-cycle review under the Special 301 provisions of the US *Trade Act* 1974, aimed at examining the extent to which China has succeeded in implementing its TRIPs obligations and developed domestic

enforcement mechanisms. As is characteristic with such Special 301 investigations, they are heavily slanted towards protecting and facilitating the legal rights of US companies. In its accession agreement the Chinese government listed pharmaceuticals as one of the key areas where it would continue to maintain price controls. The United States undoubtedly has been exerting pressure on the Chinese to "eliminate" such pharmaceutical price controls, as it has been in relation to many OECD countries, including Australia.[2]

China and the US had entered a *Memorandum of Understanding on the Protection of Intellectual Property* in 1992. As a result of this, on 1 January 1993 China's patent law was amended to cover pharmaceuticals. China also introduced *Regulations on the Administrative Protection of Pharmaceutical Products,* administered through the State Food and Drug Administration ("SFDA"), allowing holders of patents granted prior to 1993 to apply for patent protection. Interestingly however the system of patent protection was separated by the Chinese from local production. Under the *Measures for Examination and Approval of New Pharmaceuticals* in 1999 an independent system granted successful applicants an exclusive license and production period from 6 to 12 years.

Late in 2002, a year after its accession to the WTO and agreement to abide by TRIPS, China passed its *Measures for the Administration of Pharmaceutical Registration (for Trial Implementation*) and *Implementing Regulations for the Law of the People's republic of China for the Administration of Pharmaceuticals.* Under these laws, once a pharmaceutical has been approved for domestic production the State Food and Drug Administration ("SFDA") will not permit other companies to produce or import it for "monitoring periods" of 3-5 years. The chief purpose of these "monitoring periods" is to check for side effects, but of course it also accords a valuable period of market exclusivity. The term "pharmaceutical for which there are already State safety and efficacy standards" is used instead of "generic." A "generic" manufacturer seeking market entry makes an application to provincial drug authorities, who arrange on-site testing of samples. The SFDA will then conduct a comprehensive review, before deciding

whether to issue a Pharmaceutical Production Permit. The procedure is similar for the issuing of a Pharmaceutical Processing and Export Approval Document.

By imposing “monitoring periods” (much shorter than TRIPS patent protection) for domestically produced drugs, the Chinese have ensured the continuance of a vibrant generic pharmaceutical industry in their country, despite any increased influx of “innovative” foreign pharmaceuticals.

The interest of China in developing a strong role in the global pharmaceutical market is indicated by its increasing interest in providing the necessary type of intellectual property protection. In 2004, a record number of applications, just over 120,000, were filed in 2004 using the Patent Cooperation Treaty (PCT) of the World Intellectual Property Organization (WIPO). The biggest rates of growth came from the Asian continent, particularly from Japan, the Republic of Korea and China. The PCT is the cornerstone of the international patent system and offers a rapid, flexible and cost-effective way to obtain patent protection in its 126 signatory countries. If current rates of growth continue, China will overtake Australia in 2005 to become the twelfth largest user of the system.[3] Use of the PCT in Japan grew by 15% in 2004. The Republic of Korea (19.3% growth), and China (37.8% growth) also showed a significant increase in filings. It is to be expected that China may see global trade advantages in an international pharmaceutical patent system more conducive to generic products than that favoured by the US.

Recent trends in trade in pharmaceuticals between Australia and China

The Australia-China Trade and Economic Framework was signed during the recent visit of Chinese President Hu Jintao in October 2003. The Framework sets the direction for the trade and economic relationship in the long term and includes a commitment to conclude a Free Trade Agreement feasibility study by 31 October 2005. The purpose of the Framework is to enhance trade, investment and economic cooperation and build on Australia's commercial relations with

China in a number of key sectors. Included amongst these was pharmaceuticals. It also commits the parties to further trade liberalisation.

China has earmarked development and liberalisation of the services sector as a priority of its economic reform program. Australia has already had some success in gaining access to China's services sector, but one particularly valuable area for Australia would be medical research, particularly research into pharmaceuticals. China's pharmaceutical market currently averages 18-20% growth over the last twenty years, significantly higher than US and European growth over the same period. By 2020 it is estimated that China will be the world's largest pharmaceutical market.

Australian pharmaceutical exports were A$1.77 billion in 1999-2000 and approximately 14,ooo people are employed in the industry. The Australian generic manufacturing industry is small and characterized by much cross ownership and licensing arrangements with the large multinationals. The chief members of the Generic Medicines Industry Association (GmiA) Australia are Alphapharm Pty Ltd (NSW) (the main manufacturer of generics in Australia), Arrow Pharmaceuticals Ltd (NSW), Douglas Pharmaceuticals Australia Ltd (NSW), Hexal Australia Pty Ltd (NSW)(now part of the Novartis Group), Mayne Pharma Pty Ltd (Vic) Sandoz Pty Ltd (NSW). This industry saves the Australian taxpayer millions of dollars a year by supplying cheap products to the PBS. It is crucially dependent on the continued existence of cost-effectiveness pricing under the PBS. The PBS system of cost-effectiveness pricing could be enhanced and protected if ongoing collaboration were established via a China-AusFTA with the Chinese State Planning and Development Commission.

One of the most common models for pharmaceutical development in China involves joint ventures with local partners facilitating regulatory approval and market share. The commercial prospects for Australia pharmaceutical firms (both “generic” and “innovative” participating in such joint ventures would be significant. The infusion of venture capital in either direction could enhance the commercialization of ideas and facilitate rapid diffusion of technology.

Implementation of China's World Trade Organization accession agreement has improved market access for Australian exports and ensures that

Australian industries such as biotechnology, are able to compete on fair terms with other suppliers. Commitments by China to a continued opening of its trading system and to security of access arrangements will assist exporters to plan business with greater confidence.[4]

The Australia-China Trade and Economic Framework and possibility of pharmaceutical research and development provisions in a free trade agreement with China

The *Australia-China Trade and Economic Framework*, as mentioned, sets the direction for the trade and economic relationship in the long term and includes a commitment to conclude a Free Trade Agreement feasibility study by 31 October 2005.

There are strong indications that the Chinese would wish to collaborate with Australian enterprises in both the development of "innovative" and "generic" pharmaceuticals. The development of an "innovative" drug industry and the regulation of pharmaceutical prices are both dependent on the availability of quality research data. Further, it is likely that the Chinese Government, given its ageing population and the threat to its economy and public health from rising medicines prices, would give serious consideration to obtaining detailed information about the expertise possessed by Australian officials and academics involved with the Australian medicines comparative effectiveness and cost effectiveness pricing system known as the Pharmaceutical Benefits Scheme ("PBS").[5]

There is every indication that the Chinese would be supportive of including provisions in a Free Trade Agreement with Australia that will facilitate the collaboration in relation to generic and innovative pharmaceutical research. One particular area of interest could be the opportunity to research and develop for Western markets, the unique active ingredients of traditional Chinese medicines. The arrangement proposed could facilitate clustering, networking and partnership arrangements that allow beneficial economies of agglomeration. The

parties could develop intellectual property arrangements suitable to their particular needs.

Opportunities for strengthening and deepening commercial export and regulatory (pricing) links in pharmaceuticals with China

The presence of Australian pharmaceutical business in China is not strong currently. Yet, on 29 May 2001, the then Minister of Industry, Tourism and Resources announced a Pharmaceuticals Industry Action Agenda with an Implementation Group under the Chairmanship of Dr Graeme Blackman.[6]

Amongst the key items of the Action agenda were to "promote increased investment and exports of pharmaceuticals goods and services" (action 2); "identify opportunities and facilitate growth in the export of pharmaceuticals industry" (action 7) "promote two-way movement between industry and academia" (action 11) and "align industry activity with the National Innovation Awareness Strategy" (action 14).

The strengths of the Australian pharmaceutical industry are:

1) Excellence in basic medical research and healthcare in Australia
2) Excellent clinical and medical training programs and hospital/health infrastructure, very well integrated with basic medical R&D institutes
3) Strong continuing support by Government for medical research through the National Health and Medical Research Council ("NH&MRC")
4) World's best practise expertise in pharmaceutical regulation through the Therapeutic Goods Administration.
5) Excellent capability in critical new knowledge areas and platform technologies: genomics, bio-informatics fast screening
6) Fast growing industry sector with increasing employment, manufacturing exports and R&D activity.[7]

Over the past few years the Australian Department of Industry, Tourism and Resources has administered a $300 million Pharmaceutical Industry Investment Program that provides additional rewards for those pharmaceutical manufacturers undertaking research and development in Australia. From 1 July

2004, a Pharmaceuticals Partnerships Program will take over from the Pharmaceutical Industry Investment Program and provide an additional $150 million over the next 5 years.

The unique world class expertise Australia possesses in the pharmaceutical area relates to comparative effectiveness and cost-effectiveness evaluation and its application to regulatory and pricing decisions in a national reimbursement program. Australia posses numerous advantages with regard to the conduct of pharmaceutical trials

1) High quality researchers
2) A high level of Government funding and supervision of medical research
3) Established relationships between researchers, world class hospitals and universities
4) Ready availability of high quality statistical expertise
5) High quality IT support
6) World's best practise ethical supervision
7) Excellent training facilties
8) A relatively low cost structure.

Multinational Clinical Research Organisations with expertise in Phase III and IV trial studies have subsidiaries in Australia. Australia possesses at least three centres with expertise in conducting Phase I trials. [8]

Creation of an evidence base to inform government and industry decision making is a crucial precondition for the establishment of an innovative pharmaceutical industry. It is also vitally important for establishing and maintaining a pharmaceutical pricing system where public expenditure is allocated chiefly to those products that objectively demonstrate a therapeutic advantage at a justifiable price over competitors.

Around the world the role of generic pharmaceuticals is becoming an increasingly dominant part of pharmaceutical revenue. At the same time certain intellectual property restrictions are arising which may comprise the capacity of generic to enter markets after "blockbuster' brand name patent expiry. The accurate pricing of pharmaceuticals, both in terms of opportunity cost and community benefit has globally become a matter of uncertainty, debate and

confusion.[9] This collaboration between the China and Australia could lead to the transfer of expertise and generation of data that would best resolve many of these issues. It would also provide an essential science-based precondition for the long term profitability of generic and innovative export pharmaceutical industries in both countries.

Specific Medicines-Related Proposals for a CHINA-AUSFTA

Establishment of a Medicines Working Committee

A specific Annex in the China-Australia Free Trade Agreement could establish a Medicines Working Committee between government representatives, academics and officials (particularly in the Australian PBS and Chinese SFDA) of the two countries. Its purpose would be to facilitate co-operative research between the two countries targeted at the creation, clinical and community testing, manufacture and distribution of both innovative and generic pharmaceuticals. The Australian members of the committee would comprise experienced members of Australia's pharmaceutical pricing and monitoring agencies.

One specific area that could be mentioned for discussion by this Committee includes the establishment of an authoritative pharmaceutical patents register facilitating searches by generic manufacturers seeking to enter the respective markets. Another includes the establishment in each country of a specialised agency with both medicines approval and patenting expertise. Incentives for generic pharmaceutical development and marketing could also be discussed.

The parties could also agree to discuss how best to develop data bases of the comparative effectiveness and therapeutic significance of existing and new pharmaceuticals either manufactured or marketed in their respective jurisdictions. These data bases could consider both pre-listing and post-listing evidence of the comparative effectiveness and cost effectiveness of pharmaceuticals. In this area Australia's expertise on clinical trial design and analysis, evidence synthesis pre-listing (economic evaluation) and data collection

post-listing could be combined with China's significant population to develop a comprehensive and accurate evidence base for decision making in the area of pharmaceutical pricing and regulation.

Dialogue Concerning Principles of Best Practice Pharmaceutical Pricing

The Annex could also specify the need for ongoing dialogue between Australian pharmaceutical cost-effectiveness pricing officials and Chinese drug regulatory authorities, (particularly between the Australian PBAC and its Chinese equivalent, the State Planning and Development Commission) aimed at establishing and maintaining best practise pharmaceutical cost effectiveness pricing systems in the respective countries and signalling marginal cost of production internationally. This would perhaps be the provision most likely to benefit the PBS and medicines prices in Australia as it would signal the desire of both countries to improve and enhance the system of cost-effectiveness reimbursement for pharmaceuticals.

The Annex would also create an ongoing mechanism for dialogue between officials of the pharmaceutical pricing and monitoring in the respective parties (particularly between the Australian PBS and Chinese State Planning and Development Commission) concerning the principles that should be followed by manufacturers applying for pricing premiums because of claimed therapeutic benefit in their products and the linkage of that process with a pricing decision. Specifically, what evidence is required to demonstrate the value to patients of a claimed benefit an dhow should evidence be used to set a specific price premium for a drug? A common set of such principles would ensure that price relativities between existing and new drugs remain economically justifiable in both countries.

Such a mechanism would also provide a vehicle for dialogue between the parties' respective pharmaceutical pricing authorities concerning the power to compel from pharmaceutical manufacturers items of evidence considered essential to a proper cost-effectiveness evaluation. An example is the evidence of

the value to patients of a specific clinical benefit, not solely of that clinical benefit as derived from a clinical trial. Another item of such dialogue would be the establishment of legally enforceable price-volume agreements and the principles involved in establishing comparator class or therapeutic groupings.

Commitment to TRIPS-Only Levels of Intellectual Property Protection

Both China and Australia would greatly advantage their respective economies if the intellectual property chapter of a China-Australia Free Trade Agreement specifically directed itself to the standards established by TRIPS.

One particular area of concern for China, given the dominance of its generic pharmaceutical industry, could be need to specifically endorse the "so-called "Bolar" exceptions which allow generic manufacturers to use original brand-name data to do bioavailability and safety studies for marketing approval in order to rapidly "springboard" their products upon brand name patent expiry. This was acknowledged by the WTO Panel decision in the *Canada-Patent Protection for Pharmaceutical Products Case* in April 2002, but the parties would benefit from its direct reiteration in TRIPS terms.

The parties would also benefit, given the necessities of their geo-political location, from a statement in their Free Trade Agreement that its intellectual property articles specifically included the *Doha Declaration on TRIPS and Public Health,* including the capacity to use to full the TRIPS compulsory licensing exceptions in public health emergencies.

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