



致：嚴重急性呼吸系統綜合症 (SARS)

專家委員會秘書處

有關：意見書

查 SARS 早於 2002 年底在廣東省爆發，疫症迅速蔓延到廣州及鄰近香港的深圳地區。早期由於對疫症認識不多，各醫院給殺過措手不及。基於我們對國內醫院用藥的認識，我認為我本人有社會責任向貴專家委員會報告。

我司藥物日達仙® (Zadaxin®, 胸腺肽 $\alpha 1$, Thymosin $\alpha 1$) 是一種免疫調節劑 (Immune modulator)，在中國廣泛地用於治療慢性乙型肝炎及作為治療癌症的輔助用藥，療效得到好評。此外，日達仙在國內亦成為拯救慢性重型肝炎病人必不可少的藥物；在一些嚴重細菌/病毒感染病者，用盡一切可行之法高熱仍持續不退者，加用日達仙可望奏奇功。

深圳市東湖醫院是深圳地區的傳染病醫院，負責統一接收區內所有的 SARS 病人。疫症期間東湖醫院除使用一切有關的預防措施外，醫護人員同時注射日達仙，用來提高免疫力，對抗 SARS 感染。結果是東湖醫院醫護人員做到零感染。同時，針對 SARS 病人高燒不退及 T 輔助淋巴細胞 CD₄⁺ 低下的臨床症狀，東湖醫院及廣州市第八傳染病院和廣州中山醫科大學附屬三院傳染病科均使用日達仙來治療 SARS 病人。據醫院大夫說，療效令人滿意，病人使用日達仙後肺片吸收很快。

我在 2003 年 3 月中旬去信楊永強局長，陳馮富珍署長等 8 位高級醫療決策者，請求考慮在別無其他治療方法下，給予 SARS 患者使用日達仙。

2003 年 4 月中旬，北京開始爆發疫症，中國傳染病專家開會討論，並參照廣東省治療 SARS 經驗，由國家中央衛生部發出醫療指引，其中一項推介使用免疫增強劑。北京軍方 302 傳染病專科醫院在治療 SARS 工作小冊內更列明免疫增強劑是日達仙。北京佑安傳染病醫院某專家更在電視中說明日達仙的療效。隨後，北京全城開始出現搶購日達仙熱潮。當日達仙供貨不上時，全城退而求其次，搶購同類的胸腺肽制劑至斷市。

民間及醫院搶購日達仙，用於預防方面，據聞傳染病醫院醫護人員在進隔離病房之前，均注射日達仙。對於 SARS 病人，日達仙亦用於治療。

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時至今天，我們還沒有任何公開資料，說明日達仙在治療 SARS 病人方面的療效，但我們相信在 SARS 事件完結後，中國各大醫院及中央衛生部必會總結今次事件的經驗，為日後工作鋪路，正如貴委員會的檢討工作一樣。

日達仙被中國衛生部列入為六種主要治療 SARS 病藥物之一。當四月底日達仙供應不上時，中國政府透過外交途徑分別向我美國賽生公司總部，日達仙製造商意大利 ISF 藥廠，意大利供銷商 Sigma Tau，及比利時製造日達仙原料葯的 UCB 藥廠接觸，請求出售日達仙。

我們相信日達仙在治療 SARS 病人上，必有療效，不然中國政府不會為此著急。

北京 5 月初火速建成的小湯山醫院，由於市面缺貨，其院長通過中國國家醫藥監督局向我北京辦事處緊急取藥，也通過駐港的解放軍部隊醫院在香港緊急採購 1,000 針日達仙應急。小湯山醫院 6 月 20 日已完成任務，共收治 6 百餘名患者，死亡率是 1.2%，無一醫護人員感染。

中國外交部 ██████████ 5 月 22 日高調宣佈 ██████████ 及其訪歐隨員均接受注射五支最好的胸腺肽來提升免疫力，此事全香港報紙及有線電視、亞洲電視均有報導。

凡此種種，都可以初步說明日達仙可能在治療 SARS 上，起到一定的作用。肯定地說，胸腺肽在中國抗疫一仗上立了奇功。

我司為表揚中國前線醫護人員的工作精神，特向中央衛生部捐贈 20,000 支日達仙。此事得到衛生部頒發榮譽證書。

反觀在香港，我司葯物日達仙並沒有得到重視。由於歷史原因，日達仙在香港申請註冊的過程並不順利，由 1993 年底開始申請，到上訴成功，才在 2003 年 4 月 1 日獲准註冊，為期 9 年半。

香港醫管局轄下醫院在治療 SARS 用葯上，當病人對利巴韋林及類固醇治療無效時，寧可選用抗血癌，以及抗愛滋病那麼高毒性的葯物，也不考慮試用日達仙那麼安全的葯物，真是有點那個。

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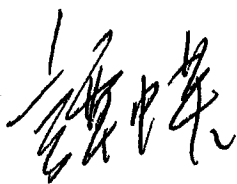
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如果因為政治原因而不試用日達仙，而事後中國政府報告証明日達仙治療 SARS 確有療效，那麼港府及醫管局怎樣面對 290 名死者及其家屬呢？

關屯門醫院謝婉雯醫生在死前一周開始使用日達仙，雖然她最終死於細菌併發症，但據聞謝醫生對日達仙治療起反應（發燒），T 淋巴細胞計數上升，以及病毒測定轉成陰性。是否早點使用日達仙，謝醫生可以不用做英雄烈士呢？

我希望貴委員會能確實檢討一下，為將來 SARS 可能捲土重來時作好準備。

為公眾利益，如有需要，本意見書將可能對外公開。



譚中英副總裁
賽生藥品股份國際有限公司
2003 年 6 月 24 日

附：

- (1) 中央衛生部頒發榮譽證書
- (2) 國家主席 ████████ 使用胸腺肽的報導
- (3) 2003 年 3 月 19 日給 ████████ 等人的信件

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June 24, 2003

To: The Hong Kong SARS working group
Advisory Committee

Re: Opinion letter

The SARS outbreak reportedly began in Guangdong province in late 2002. The epidemic spread rapidly into Guangzhou, Shenzhen and the area around Hong Kong. Because the nature and characteristic, this epidemic was not well understood, hospitals in these cities were not well prepared to respond. Based on our understanding of the SARS related experiences related to the use of our product in Mainland hospitals, I believe that I have a social responsibility to report my observations of what occurred on Mainland China to your committee.

Our product ZADAXIN[®] injection (thymosin alpha 1) is an immune system modulator that has been used very safely in tens of thousands of patients around the world. It has been widely used in China in treating chronic hepatitis B and as an adjuvant to cancer therapy with good reported efficacy. In addition, in China, ZADAXIN has become an essential drug in life-threatening situations for use in patients with chronic severe hepatitis, with severe bacterial/ viral infection with chronic fevers. Based on their understanding of our drug, Mainland doctors, not the company, have designed these treatment alternatives.

Shenzhen East Lake hospital, an infectious disease hospital in Shenzhen, was the hospital designated for all SARS patients in Shenzhen. During the SARS epidemic, the East Lake hospital exercised all necessary preventive measures, and in addition, medical staff were injected with ZADAXIN in an attempt to raise their host immunity against SARS. The result was that none of the medical staff got infected. Regarding SARS patients with symptoms such as high chronic fever and low CD4+ T lymphocytes counts, ZADAXIN was used as a drug of choice by East Lake hospital, Guangzhou No.8 Infectious Disease Hospital and the Department of Infectious Disease, Guangzhou Third Hospital, affiliated with Guangzhou's Dr. Sun Medical University. The doctors reported a satisfactory response.

I wrote to Dr. F.K. Yeoh, Dr. Margaret Chan and other six other senior medical decision makers on Mar 19, 2003 suggesting they consider the use of ZADAXIN on those SARS patients who had failed other therapies.

In mid-April 2003, when the epidemic spread into Beijing, Chinese experts in infectious diseases held a conference in Beijing to consider the situation. Understanding and appreciating the experience from the South, the China Ministry of Health issued a treatment guideline in which the use of immune system enhancers was recommended. Beijing PLA 302 Infectious Disease Hospital in its SARS treatment handbook specifically

used the name "ZADAXIN". An expert from the Beijing You An Infectious Diseases Hospital included a mention about ZADAXIN's efficacy on TV. The story of the drug's use spread and people throughout Beijing tried to purchase ZADAXIN. When supplies of ZADAXIN were exhausted people tried to purchase other generic thymic peptides and animal derived thymic preparations.

ZADAXIN was used for prevention based on the fact that medical staff took ZADAXIN before entering a SARS isolation ward. ZADAXIN was also used to treat SARS patients.

At this time, from the company point of view, we make no claim that there is clinical data or proof that ZADAXIN was effective in preventing or treating SARS. However, we believe that major hospitals in China and the Ministry of Health will summarize the SARS experience. Clearly, a report such as this should be very useful for the future in consideration of the responsibilities charged to your Committee.

ZADAXIN has been listed by the Mainland Ministry of Health as one of the six essential drugs in treating SARS. When ZADAXIN was out of stock in end April, the Chinese government used its diplomatic network to contact our US headquarters, the ZADAXIN manufacturer in Italy, the European ZADAXIN licensee, Sigma Tau and the bulk peptide supplier in Belgium.

Logic strongly suggests that as this was an urgent governmental search mission for ZADAXIN, not a commercial activity, that there may have been some demonstration of ZADAXIN's efficacy in treating SARS. Nothing else explains the Chinese government's urgent interest.

In early May, the PLA Beijing Shiu Tong Shan hospital was on the verge of having to continue operations without supplies of ZADAXIN the hospital Director using their influence had the China Drug Administration directly contact our Beijing Representative Office for the urgent supply of ZADAXIN. This hospital also purchased 1,000 vials of ZADAXIN from Hong Kong via the PLA Army Hospital in Hong Kong. Shiu Tong Shan Hospital was closed on June 20 as the last SARS patients were released. More than 600 SARS patients were treated at this hospital with a patient mortality rate of 1.2% and a zero infection rate for the medical staff.

On May 22, 2003, the China Foreign Ministry spokesman announced that [REDACTED] and the entire delegation to the G8 conference were all treated with five injections of the "best thymosin" in an attempt to raise immunity to against SARS. This news was reported by almost all newspapers in Hong Kong, cable TV and Asia TV.

In summary, ZADAXIN's role in the SARS epidemic has been empirically demonstrated as an important part role relative to treating and preventing SARS in China. We are very proud on this contribution and please that we have been able to do some good for the people of China.

At the beginning of the SARS epidemic, before we knew the size the problem would become, the company made a donation of 20,000 vials of ZADAXIN injections to the Ministry of Health. This turned out to be a very small percentage of all the vials used. We were awarded with a certificate of merit from the Ministry of Health for this action.

In Hong Kong, by way of contrast, ZADAXIN has received little attention. Perhaps because of the drug's less than smooth regulatory history in Hong Kong. The registration effort of ZADAXIN in Hong Kong took nine and half years to complete; from the time of original submission of the registration application in 1993 to the successful appeal when registration was finally granted on April 1, 2003, during which period 30 other countries approved ZADAXIN.

SARS patients were treated at hospitals under the Hong Kong Hospital Authority. As patients failed to respond to drugs like ribavirin (noted at the time by the US CDC as not effective for SARS) and corticosteroids, doctors preferred to try anti-leukemia and anti-AIDS drugs, rather than consider the use of ZADAXIN.

My concern and hope is that it was not the politics of ZADAXIN's regulatory history that kept the doctors of the Hong Kong Hospital Authority from considering the use of ZADAXIN. After the Chinese government report is issued and if it confirms the value of ZADAXIN relative to SARS it may be difficult for the Hong Kong SAR government and the Hong Kong Hospital Authority to explain to the families of the 290 victims.

We have heard that Dr. [REDACTED] of Tuen Mun Hospital started to use ZADAXIN a week before she passed away. Although Dr. [REDACTED] died from a severe bacterial infection, it appeared that she did begin to respond after the addition of ZADAXIN therapy; parameters such as fever, T- lymphocyte count increases and testing negative for the virus were observed. Should ZADAXIN have been started earlier?

I trust that your Committee can fully investigate the situation in Hong Kong and China in anticipation and preparation for the probably return of SARS in the future.

As a matter of public interest and without prejudice, this opinion letter will be open to public as needed.



Yours faithfully,

A handwritten signature in black ink, appearing to read "Vincent Tam", is written over a faint, larger version of the same signature.

Vincent Tam
Vice President
SciClone Pharmaceuticals International Ltd.

Enclosed:

1. The award certificate issued by the Ministry of Public Health, P.R. China
2. Newspaper clipping regarding President [redacted] visit to Europe
3. My letter of Mar 19, 2003 to the 8 medical decision makers.

2003年3月19日

衛生福利及食物局長
楊永強先生

尊敬的楊局長，

鑑於香港近日非典型肺炎有擴散蹟像，入院人數不斷增加，醫護人員人人自危，我想了很久，還是決定給你和其它衛生決策人員寫上這封信，希望能對治療有所幫助。

查非典型肺炎在廣州及深圳等地區流行期間，國內傳染病專家應用免疫調節藥物“日達仙”(Zadaxin, thymosin alpha 1)，來加強病者的免疫功能，據聞療效非常令人滿意。增強免疫功能更是深圳肺炎專責小組用藥的共識。

日達仙在中國的聲譽日隆，傳染學界幾已公認為搶救“慢性重症肝炎病者”的主要手段，這完全歸於它的雙向免疫調節作用，即一方面下調有害的炎症細胞因子如 TNF, IL-1, IL-6 等，另一方面上調有益的細胞因子例如 IL-2 及 IFN γ 等。日達仙治療後，內毒素水平下降。

日達仙亦在國內醫院 ICU 病房內看到其療效。很多嚴重細菌及病毒感染病者，在用盡所有現存方法，高熱仍然持續不退者，加用高劑量日達仙連續 5~7 天，高燒可望消退。

據所知，香港 [REDACTED] 在香港最少有兩個高熱不退病例，其一是小兒病毒性腦膜炎，另一是由化療引致，在無計可施下，加用日達仙即見奇效。

現正在 ICU 病房情況危殆的醫護人員，他們的免疫系統正與病原體惡鬥，生死正繫於一線間。使用日達仙來加強病者的免疫功能，可望挽救垂危病者的性命，從免疫學角度來看，這理論完全可以成立。

對這些垂危病人來說，可用的治療方法已經全用了。除了聽天由命外，還可以做些什麼呢？加用日達仙是唯一可行之法，對病人來說，如果不行也沒有什麼損失。

希望各衛生決策官員及專家，能參照國內專家用藥經驗考慮使用。

香港賽生藥品股份國際有限公司
譚中英副總裁

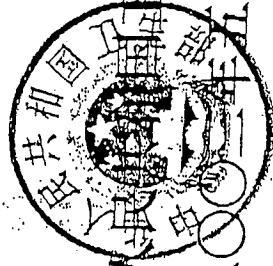
*附簡單說明資料

** 隨函夾附於 2003 年 5 月 22 日在明報刊登的剪報標題為《胡錦濤出訪團隔離防疫》。該等資料將不予披露。

荣誉证书

香港赛生药品股份国际有限公司向我国非典防治工作捐赠日达仙贰万支。

特此致谢。



中华人民共和国卫生部
二〇〇三年五月

16/16