ENFORCEABLE UNDERTAKING

given to the Secretary of the Australian Government Department of Health for the purposes of section 42YL of the *Therapeutic Goods Act 1989*

by

Shen Neng Herbal Medicines Group Pty Ltd (ABN 18 129 998 410)

Persons and authority

1. This undertaking is given to the Secretary of the Australian Government Department of Health by Shen Neng Herbal Medicines Group Pty Ltd (ABN 18 129 998 410) of 1 Clarke Street Guildford NSW 2161 **(Shen Neng),** for the purposes of section 42YL of the *Therapeutic Goods Act 1989* (the **Act**).

Background

TGA's role

2. The Therapeutic Goods Administration **(TGA)** is a part of the Australian Government Department of Health **(Department),** and is responsible for the national regulation of therapeutic goods including medicines, biologicals and medical devices.

3. In Australia, therapeutic goods containing ingredients such as certain herbs, vitamins and minerals, nutritional supplements, homoeopathic medicines, traditional Chinese medicines and aromatherapy products are referred to as 'complementary medicines' and regulated as medicines under the Act and entered on the Australian Register of Therapeutic Goods **(ARTG)** under that part of the Act for 'listed' goods.

Shen Neng's business

4. Shen Neng is an Australia sponsor of an extensive range of herbal and traditional Chinese medicines entered on the ARTG.

5. Shen Neng's medicines have been the subject of previous post -market compliance reviews and recall actions over the past 5 years in which issues involving non-compliance with the Act have been identified. Shen Neng has addressed a number of the issues identified by the TGA and is working with the TGA to address outstanding issues, to the extent those issues remain.

6. On 6 and 7 April 2020, inspectors within the TGA undertook a routine inspection of Shen Neng for the purpose of reviewing compliance by Shen Neng with its pharmacovigilance and other obligations under the Act.

7. At the time of inspection, there were approximately 200 products listed on the ARTG in relation to Shen Neng with about 89 products being marketed and supplied in Australia.

8. An inspection report was provided to Shen Neng on 20 May 2020 identifying a number of issues of concern.

Conduct of concern

9. The Secretary is concerned about Shen Neng's alleged non-compliance with numerous provisions of the Act as set out below including:

   (a) the failure to include mandatory warning and other statements on the labels of medicines for supply, as required by standards applicable to the goods, in contravention of subsection 14A(2) of the Act.
   (b) making an incorrect statement to the TGA, in a certification made under subsection 26A(2) in connection with an application for listing of goods, in contravention of subsection 218(1) of the Act. In particular, incorrectly certifying that medicines containing methyl salicylate contained the appropriate label warnings;
   (c) the failure to comply with record keeping and reporting requirements in paragraphs 28(5)(c), (ca) and (e) of the Act which include under regulation 15A of the *Therapeutic Goods Regulations 1990* **(Regulations)** the requirement to comply with the *Pharmacovigilance Responsibilities of Medicines Sponsors* **(PV Guidance)** including Shen Neng nominating a pharmacovigilance contact person in respect of its medicines; and
   (d) the failure to notify the TGA of certain information concerning adverse effects in contravention of section 29AA of the Act.

Acknowledgements

10. Shen Neng acknowledges that the above conduct may have constituted a contravention of the Act.

11. Shen Neng has taken action to address the possible non-compliance with the Act.

Period of undertaking

12. This undertaking commences when both of the following are satisfied:

   (a) the undertaking is executed by Shen Neng; and
   (b) the delegate of the Secretary signs the executed undertaking.

13. On commencement of this undertaking, or from the date specified in relation to the particular undertaking, Shen Neng undertakes to assume the obligations set out in paragraphs 16 to 27 below.

14. This undertaking terminates on 30 November 2023.

15. This undertaking may be terminated prior to the termination date specified in paragraph 14 on Shen Neng establishing that it has in place reasonable and adequate measures to address the concerns set out herein. A satisfactory annual review pursuant to paragraph 23 shall be deemed confirmation of reasonable and adequate measures being in place to address TGA concerns.

Undertaking

Cessation of allegedly unlawful conduct

16. Shen Neng undertakes not to, whether by itself or through its directors, employees, servants or agents or bodies corporate under its control, knowingly:

    (a) supply therapeutic goods to persons in Australia in contravention of the Act; and

    (b) aid, abet, counsel or procure, any conduct by another person of a kind which Shen Neng has undertaken not to engage in under paragraph 16(a).

Comply with the mandatory pharmacovigilance responsibilities

17. Shen Neng undertakes to use its best endeavours whether by itself and through its directors, employees, servants or agents or bodies corporate, under its control to comply with the mandatory pharmacovigilance responsibilities under the Act and the Regulations as set out in the **PV Guidance.**

Have in place and maintain an effective pharmacovigilance system

18. Shen Neng undertakes to, whether by itself or through its directors, employees, servants or agents or bodies corporate under its control to have in place by 29 October 2021, and subsequently maintain for the period of this undertaking an effective pharmacovigilance system as specified below, in accordance with external professionally qualified advice.

19. An effective pharmacovigilance system is characterised by having in place effective processes, procedures and a quality management system to monitor the safety of medicines and detect any change to the medicines' benefit-risk profile, in accordance with external professionally qualified advice.

Processes and procedures

20. Shen Neng undertakes to develop clear written Standard Operating Procedure **(SOP)** or SOPs for pharmacovigilance to ensure all roles, responsibilities, requirements and timelines are well-defined and understood by all personnel involved and documented in relevant company records:, in accordance with external professionally qualified advice.

Collection of safety information

    (a) A standard process for the collection of safety information from all available sources, including from medical information enquiries, product quality complaints, local medical literature published in Australia, global literature accessible via Pubmed,[1] and from international safety databases maintained by overseas regulators in countries manufacturing Shen Neng's products, such as China, Hong Kong, Malaysia, which are likely to include safety information related

[1] The literature search strategy shall include use of all active ingredients *considered to have safety issues by regulators such as TGA, WHO, EFSA, FDA.* The search of the regulatory data bases maintained by overseas regulators in China, Hong Kong, and Malaysia .

to traditional Chinese medicines accessed either directly by Shen Neng or via overseas PV Agreement partners.

(b) A database of Adverse Event Notification maintained by the TGA.

Management of safety information

(c) A standard process for the management of safety information in relation to each medicine entered on the ARTG in relation to Shen Neng in relation to the following matters: duplicate check; assessment of seriousness, causality, expectedness and reportabilty, follow-up and case closure;

(d) A standard process for recording information in the company safety database;

Management of product labels and reference safety information

(e) A standard process for the maintenance of product labels; and

(f) A standard process for maintenance of the reference safety information.

Ongoing safety evaluation

(g) A standard process for the ongoing safety evaluation of the products. This should include a process for the periodic review of publicly available safety databases maintained by regulatory authorities, likely to include safety information about herbal or traditional Chinese medicines,2 maintained by relevant regulators in the countries where Shen Neng's products are also manufactured and distributed (for example China, Hong Kong, Malaysia);

Quality management system

21. Shen Neng undertakes to have a quality management system in place to support the processes and procedures will be implemented as specified above, in accordance with external professionally qualified advice.

22. Shen Neng undertakes to include in its quality management system and be recorded in a SOP or SOPs, acknowledged by relevant company personnel and documented in relevant company records, the following measures:

(a) A system and procedure to manage and document pharmacovigilance records. A list of pharmacovigilance records are itemised at **AttachmentA;**

(b) Mandatory pharmacovigilance training for all staff and contractors employed by Shen Neng. This includes initial pharmacovigilance training for new staff members or contractors, and annual refresher training for all staff and contractors ;

(c) Clauses in pharmacovigilance agreements with all third parties working with Shen Neng to supply its medicines, such as manufacturers (whether based in Australia, or elsewhere) and vendors requiring that each party implement pharmacovigilance training for their staff;

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[2] The literature search strategy shall include use of all active ingredients *considered to have safety issues by regulators such as TGA, WHO, EFSA, FDA.* The search of the regulatory databases maintained by overseas regulators in China, Hong Kong, and Malaysia.

(d) Periodic review (every two years) of SOPs and pharmacovigilance processes and procedures; and

(e) The engagement of an external regulatory compliance professional to carry out pharmacovigilance audits and compliance reviews as specified below, and to give the advice required by paragraphs 18, 19, 20 and 21 above.

Pharmacovigilance quality assurance and regulatory compliance audits

23. For the period of this undertaking, Shen Neng undertakes to require an external regulatory compliance professional **(the external professional)** to provide an annual written report(s) to the TGA regarding its compliance with the Act, Regulations and this Undertaking.

24. The annual written report will, at a minimum, address and include the matters specified in **Attachment B.**

25. Shen Neng undertakes to ensure that:

(a) the first annual review is completed by the external professional and the written report relating to that review is provided by that person to the TGA prior to 30 July 2021;

(b) the second annual review is completed by the external professional and the written report relating to that review is provided by that person to the TGA prior to 30 July 2022; and

(c) the third annual review is completed by the external professional and the written report is provided by that person to the TGA prior to 30 July 2023.

26. Shen Neng will take reasonable steps to ensure that the external professional has access to the information they reasonably require for the purposes of the annual written report, subject to Shen Neng's rights to protect its confidential and commercially sensitive information.

27. Shen Neng will implement promptly, and with due diligence, any recommendations made by the external professional, that are reasonably necessary to ensure that it complies with the Act and the terms of this undertaking.

Acknowledgements

28. Shen Neng acknowledges that:

(a) this undertaking is given voluntarily; and

(b) the Secretary may make this undertaking publicly available on a public register and is obliged under the Act to publish details of the undertaking, as in force from time to time, on the internet; and

(c) the Secretary and/or the Commonwealth or officers thereof may from time to time, publicly refer to this undertaking including by means of, but not limited to, public statements, news media statements, and TGA or Department publications; and

(d) this undertaking in no way derogates from the rights and remedies available to the Secretary, the Commonwealth or any other person arising from the conduct of the Undertaking Parties; and

(e) Shen Neng will bear all its costs of compliance with this undertaking.

THIS UNDERTAKING IS GIVEN BY:

Shen Neng Herbal Medicines Group Pty Ltd (ACN 129998 410) in accordance with the requirements of section 127 of the *Corporations Act 2001* (Cth):

[REDACTED] ***[REDACTED]***
Signature *Signature*

30 June, 2021

ACCEPTED BY A DELEGATE OF THE SECRETARY OF THE DEPARTMENT OF HEALTH UNDER SECTION 42YL OF THE *THERAPEUTIC GOODS ACT 1989*

[REDACTED] signature

Dr Cheryl McRae

Delegate of the Secretary

29 July 2021

Attachment A- Pharmacovigilance Records

1. Pharmacovigilance Records is a broad term and refers to all documents which constitute a pharmacovigilance system and include, but is not limited to the following:

    a. Individual Case Safety Report **{ICSR)** source documents:

        i. Initial and follow-up communication with the reporter;

        ii. Adverse event report forms, pregnancy follow-up forms, other special situation reporting forms;

        iii. Targeted questionnaires completed on call with the reporter;

        iv. Any form of correspondence, e.g. e-mails, mail, faxes, telephone contact reports to and from the reporter, including unsuccessful attempts to contact reporter;

        v. Council for international Organizations of Medical Sciences reports received from third parties;

    b. Internal correspondence on case collection, management and reconciliation;

    c. External correspondence with third parties on case collection, management and reconciliation;

    d. Significant safety issues and related correspondence, including safety related reports;

    e. Safety related communication to internal and external stakeholders;

    f. Reference Safety Information and related correspondence;

    g. Risk Management Plans and related correspondence;

    h. Periodic Safety Update Reports and related correspondence;

    i. Safety signals and related correspondence;

    j. Safety related sections of relevant study reports, both pre- and post-marketing;

    k. Safety related correspondence with the TGA, including relevant regulatory submissions, acknowledgements, additional requests;

    l. Safety related correspondence with other regulatory agencies, in relation to products also registered in Australia;

    m. Pharmacovigilance agreements and Safety Data Exchange Agreements;

    n. Pharmacovigilance training records of all staff involved in the Pharmacovigilance system;

o. Documents confirming qualifications of the personnel involved in the PV system, such as CV, job description, training records relating to training other than in relation to Pharmacovigilance, for example:

    i. SOP-specific training; and

    ii. Product-specific training.

p. Pharmacovigilance audit records and corresponding Corrective and Preventative Actions plans.

Attachment 8- REQUIREMENTS FOR ANNUAL WRITTEN REPORT(S) (see clause 24)

1. The annual written report must address and include the following:

    a. the external professional's assessment as to whether the Undertaking Parties have implemented an appropriate pharmacovigilance system, taking into account the PV Guidance and this undertaking and the steps the Undertaking Parties can take to improve their pharmacovigilance system;

    b. copies of the policies, processes and standard operating procedures of the Undertaking Parties for the preparation and review of:

        i. the labels for the medicines; and

        ii. pharmacovigilance systems, procedures and quality management systems;

    c. records of the pharmacovigilance training undertaken by Shen Neng's employees, and executive officers during the relevant period, including any refresher training undertaken;

    d. the external professional's assessment as to whether the labels of Shen Neng's medicines comply with the Act and the Regulations and any applicable standard under the Act;

    e. copies of the labels for the medicines supplied by Shen Neng in Australia during the relevant period;

    f. an excel spreadsheet of all the medicines (identifying individual batches) that have been supplied by Shen Neng in the year prior to the provision of the report which provides the date the batch was supplied and who it was supplied to; and

    g. details of the information gathered and examined during the review.