ISURA Standard:

Certification for natural health product authentication, purity, potency, and processing & handling

INTRODUCTION

The safety of natural health products (NHP) is paramount to all stakeholders—growers, raw material suppliers, manufacturers, regulators, retailers, healthcare providers, and ultimately consumers. Everyone in the global NHP supply chain recognizes how crucial it is to ensure that only products of the highest quality and integrity reach consumers. Increasingly, consumers want to know what is in the NHPs they are buying and they want that information right on the product label. The natural health product industry's integrity and future will be determined by the effectiveness of its response to these challenges.

ISURA is an independent, non-profit analytical testing and certification organization. Its mandate is to provide certification services for stakeholders and serve as an analytical competence centre for the analysis of NHPs at all stages of processing and manufacturing with the following goals:

- Augmenting the safety of NHPs
- Ensuring label accuracy
- Increasing consumers' confidence in NHPs
- Providing education on NHPs
- Supporting research and development for improved test methodologies and analytical equipment.

The standards for ISURA's certification services for NHPs are among the world's highest. They meet or exceed standards or recommendations for NHPs set by organizations such as:

- AOAC (Association of Official Analytical Chemists)
- CFIA (Canadian Food Inspection Agency)
- CRN (Council for Responsible Nutrition)
- EU (European Union)
- FDA (United States Food and Drug Administration)
- HC (Health Canada: Natural & Non-prescription Health Product Directorate)
- TGA (Therapeutic Goods of Administration of Australia)
- USP (United States Pharmacopeia)
- WHO (World Health Organization)

Furthermore, ISURA's laboratories meet ISO 17025 laboratory standards for specific methods and ISURA is an ISO 9001 certified organization adhering to rigorous Quality Management System standards.

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1.0 ISURA CERTIFICATION STRATEGY AND SEAL OF APPROVAL OVERVIEW

The ISURA Seal of Approval is a scientific certification. To earn the ISURA Seal of Approval, NHPs must undergo a full-range of laboratory tests that confirm that the product is:

- Authenticated,
- Contaminant-free/Safe from contamination/Adulterant-free,
- Non-GMO compliant,
- Accurately and inclusively labeled/Has label integrity/Meets potency claims.

ISURA Laboratories lie at the core of the ISURA certification strategy. ISURA's in-house test centre takes a comprehensive approach to product analyses, and utilizes a combination of state-of-the-art equipment/methods, such as:

- Mass spectrometry (MS):
    - Headspace Gas Chromatography
    - Gas Chromatography Triple-Quadrupole
    - Ultra-high Performance Liquid Chromatography Triple-Quadrupole
    - Inductively-coupled Plasma (ICP)
- Real Time Quantitative Polymerase Chain Reaction System (qPCR)
- DNA Sequencer
- High Performance Liquid Chromatography (HPLC)
- High Performance Thin-Layer Liquid Chromatography (HPTLC)
- Ultraviolet-visible Spectrophotometer (UV-Vis)
- Infrared Spectrometer (IR)
- Microplate Spectrophotometer
- Microplate Fluorometer and Luminometer

These instruments enable the use of proven testing methods to identify and quantify potential contaminants as well as confirm the presence of specific active ingredients and excipients in product samples.

ISURA employs both targeted and un-targeted approaches to NHP analysis and profiling.

- Un-targeted profiling is a more general, less-sensitive analysis designed to identify a wide-range of unknown compounds or contaminants in a test sample. This approach looks for fraudulent adulterants, substitutions or contaminants not known to be present.
- In contrast, targeted analysis is more sensitive, and can verify and quantify specific active ingredients or contaminants in a test sample.

ISURA offers verification and certification to NHP distributors – for finished products, and to manufacturers – for raw materials, finished products, and responsible processing and handling practices.

2.0 ISURA STANDARD: AUTHENTICATION, PURITY, POTENCY, PROCESSING & HANDLING

2.1 AUTHENTICATION:

ISURA provides product identification and authentication based on chemical testing methods that produce profiles of test samples that can then be compared to applicable reference profiles or the source botanical material. Currently, ISURA confirms identification of test samples using High Performance Liquid Chromatography (HPLC), High Performance Thin-Layer Liquid Chromatography (HPTLC), Mass Spectrometry profiles, Fourier Transform Infrared Spectroscopy (FT-IR) and Nuclear Magnetic Resonance Spectroscopy (NMR).

INNOVATION: As a leading edge analytical testing centre, ISURA is committed to research and innovation, and determining how best to incorporate such knowledge into routine use within the NHP industry. As such ISURA seeks to include appropriate advanced analytical tests into its laboratory testing methods as they become available, validated, and prove to be reliable and feasible.

At this time, ISURA is developing standardized techniques for testing raw materials and NHPs using DNA barcoding analysis and Quantitative-Polymerase Chain Reaction (qPCR) in order to authenticate the active ingredients in a NHP. This work is important as some NHPs, such as herbal extracts or other highly processed ingredients, may not contain intact DNA material, therefore a valid, reliable, replicable protocol also needs to be developed to enable the testing of the biological material from which such extracts or ingredients were obtained.

ISURA is also establishing a larger library of chemical fingerprinting profile for NHPs and investigating the best ways to utilize techniques such as: nuclear magnetic resonance (NMR), mass spectroscopy profiles, chiral profiles, compound specific isotope ratio profiling (GC-Combustion-IRMS), and other emerging test methods.

2.2 PURITY:

ISURA tests for a wide-range of potential contaminants, including GMO (genetically modified organisms). Through its advanced testing, ISURA can certify a NHP is below standardized safe thresholds for about 600 contaminants and that it is non-GMO compliant.

2.2.1 Non-GMO verification:

The ISURA threshold limit for detectable GMO is 0.1% in tested samples, compared to the higher threshold limits for the European Union at 0.9%, and the Non-GMO Verified Project at 0.25% (for seeds and propagation materials) and 0.9% (for human food ingredients, supplements).

ISURA utilizes Quantitative-Polymerase Chain Reaction (qPCR), also known as Real-Time PCR, to verify non-GMO compliance of a NHP: qPCR is used to detect genetically modified organisms (GMO) DNA sequences in the product or the raw material. At this time, it is the most sensitive and most reliable test method available for GMO screening as it looks at the DNA found in a NHP, detects specific GMO sequences and quantifies the amount of genetically modified DNA. The qPCR testing method can detect and quantify extremely low GMO concentrations of 0.01% in a wide range of materials, often even after they have been processed.

2.2.2 Other Contaminants:

Contaminants may be present in a NHP due to environmental contaminations, cultivation practices or production processes. ISURA verifies if potential contaminants are present in a NHP, and if they are present that they are within established safe threshold limits for human consumption as part of its certification process.

ISURA employs advanced testing methods and equipment, including highly sensitive mass spectrometry, that are capable of identifying and quantifying about 600 contaminants – many more than the number of detectable contaminants identified in the United States Pharmacopeia (USP) standard.

The following is a summary of the types of contaminants ISURA tests for:

- Pesticides,
  - insecticides,
  - herbicides,
  - fungicides,
- Mycotoxins,
- Persistent organic pollutants: dioxins, PCBs, PAHs,
- Solvent residues,
- Plasticizers,
- Toxic heavy metals,
- Microbiological contaminants,
- Radiation contamination at ultra-trace concentration levels (very low levels)

Threshold limits for specific contaminants vary with the type of contaminant, the product being tested, and its intended use. See the Appendices for listings of ISURA threshold levels for exemplar contaminants.

2.3 POTENCY: LABEL INTEGRITY

ISURA requires that all certified products and materials be tested at the finished product stage to ensure label integrity – that is, to demonstrate that the potency of the active ingredient(s) in the finished product meets or exceeds that stated on the product label, and that all active ingredients noted on the finished product label are, in fact, present.

ISURA utilizes its advanced equipment and technology to confirm that the potency of a NHP is due to the stated active ingredient(s) and not due an adulterant(s). In this context, an adulterant is a substance that may be added to a product to give a false result with respect to its potency. For example, melamine may be added to a whey protein product in order to inflate the apparent amount of protein in it; however melamine is not a whey protein and may even be harmful in high doses. If one was simply testing for the presence of protein vs. whey protein, then the melamine would “read” as protein in a test sample.

To verify potency, and whether or not adulterants are present, ISURA uses instruments such as HPLC, UV-Vis and microplate spectroscopy, and standardized test methods published as regional, national or international standards by reputable scientific/technical organizations (i.e. USO, FCC) or in relevant scientific journals or texts. This enables ISURA to certify that a finished NHP, or even a raw material, contains the stated active ingredient(s), is adulterant-free, and has label integrity.

2.4 PROCESSING & HANDLING

In addition to product tests, ISURA offers verification and certification to manufacturers with respect to the manufacturing (processing and handling) of NHPs according to industry best practices. Good Manufacturing Practices (GMP) must be in place for manufacturers of NHPs. ISURA requires documentation confirming current compliance with GMP and reserves the right to conduct on-site audits at its discretion.

ISURA requires all certified products to demonstrate (via documentation review and verification) traceability and up-to-date compliance with the applicable current Good Manufacturing Processes (cGMP) of the country of manufacture, including site licences and facilities registration. This documentation review includes confirming compliance, as applicable, with the following regulatory bodies:

- CFIA (Canadian Food Inspection Agency)
- FDA (United States Food and Drug Administration)
- HC (Health Canada: Natural & Non-prescription Health Product Directorate)
- TGA (Therapeutic Goods of Administration of Australia)
- USP (United States Pharmacopeia).

CONCLUSION

ISURA is committed to supporting consumer confidence in and access to safe, high quality NHPs by providing valid, reliable, robust analytical testing and certification services to the natural health product industry. As an independent, non-profit analytical testing and certification organization, ISURA is very well-placed to conduct innovative research and development for improved test methodologies and analytical equipment.

ISURA will review its Standard and certification requirements at least once a year, and will communicate any changes in its certification requirements to its clients within 30 days of the approval and issuing of such changes. ISURA will work with existing certification clients to achieve compliance with any new ISURA Standard/certification requirements within 90 days of the client being notified of such changes.

The natural health product industry is a global industry. When consumers see the ISURA Seal of Approval on the label of a NHP they can rest assured that the product is safe, has label integrity, is of proven quality and potency, and has been manufactured using Good Manufacturing Practices.

APPENDIX A

SEE THRESHOLD LIMITS APPENDIX(CES)

TABLE OF REVISIONS

Rev#	Section Changed	Reason & Description	Approval	Date
01		First issue		2016-04-14
02	Introduction page 1	Revised “ISURA laboratories meet … standards and guidelines” statement to “meet ISO 17025 laboratory standards for specific methods and ISURA is an ISO 9001 certified organization adhering to rigorous Quality Management System standards.”		2018-05-23
	Appendix A page 7	Replace “Insert safe threshold appendix(ces)” with “See Threshold Limits Appendix(ces)”		
	Page 7	Insert Table of Revisions		
	Section 1 page 2	Added to list of equipment: High Performance Thin-Layer Liquid Chromatography (HPTLC)		
	Section 2.1	Added: High Performance Thin-Layer Liquid Chromatography (HPTLC) and Nuclear Magnetic Resonance Spectroscopy (NMR) to sentence starting with: Currently, ISURA confirms identification of test samples using…		
03	Section 2.2	Replaced: “more than 400” with “about 600”		2018-08-08
	Section 2.2.2	Replaced: “more than 400” with “about 600”		
04	Section 2.2.2	Added: Plasticizers		2018-10-11
05	Appendix A: Threshold Limits: Other Contaminants:	Added after NMT 1 ppm: “for refined fish oils only - NMT 0.5 ppm”		2018-11-14

	Toxic Heavy Metals: Lead			