[DRAFT] Member Code of Practice: Manufacture and Product Labelling of Novel Nicotine Products

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1. Acronyms and definitions

GINN	Global Institute for Novel Nicotine
QA	Quality Assurance
TRA	Toxicological Risk Assessment
TNSA	Tobacco-specific nitrosamines

2. Purpose and Scope

This Code of Practice establishes a unified framework for GINN members to ensure consistent quality, safety, and ethical standards in the manufacturing and Labelling of novel nicotine products. It aims to promote responsible practices, thereby protecting consumer or patient safety and fostering trust among stakeholders in the industry. By adhering to these principles, members demonstrate their commitment to ethical practices and regulatory compliance.

This Code applies to all members of GINN. It provides guidance on:

- Ensuring product quality and safety through rigorous manufacturing and testing practices.
- Accurate and transparent Labelling that aligns with regulatory requirements.
- Compliance with relevant local, regional, and international regulations.

The Code is designed to be adaptable, supporting members in aligning their operations with evolving scientific advancements and legal standards.

3. Introduction

The Global Institute for Novel Nicotine (GINN) is a membership-based association dedicated to advancing collaborative standards, innovation, research, and advocacy in the field of novel nicotine products. Under the leadership of Director Shem Baldeosingh, GINN supports the development and adoption of reduced-risk alternatives, such as nicotine pouches and non-combustible heated products, to engender a potentially safer choice of future products for adult consumers worldwide. GINN collaborates with consumers, policymakers, scientific and technical researchers, product innovators and the industry-at-large, to address regulatory challenges, promote harm reduction, and encourage responsible product development. Our commitment to collaboration and scientific integrity positions us as a trusted voice in the evolving landscape of tobacco harm reduction and nicotine innovation.

Regulatory requirements for the manufacture and Labelling of novel nicotine products vary significantly across jurisdictions and are continually evolving. This lack of harmonization presents challenges for organizations striving to maintain consistent quality and safety standards across different markets.

This Code of Practice does not intend to constrain the operational practices of member organizations. Instead, it provides a flexible framework to support members in applying robust, scientifically sound procedures for the manufacture of novel nicotine products.

Developed in collaboration with members and with consideration of existing standards and requirements, this Code serves as a practical tool to align organisational practices with the complexities of evolving regulatory landscapes.

This Code of Practice reflects GINN's current perspective and stance, which is expected to evolve over time in response to new regulatory developments and scientific advancements. This Code of Practice also serves as the foundation for developing additional materials that will further elaborate on GINN's position and support advocacy for regulatory advancement in the interests of consumers, patients, and GINN members.

4. Regulatory compliance

Each organisation must identify the applicable for regulatory requirements for manufacturing and labelling for its business progressions. For example, these requirements my apply to the location of manufacturing operations or to the geography relating to commercial supply.

A hierarchy for regulatory compliance is presented in Table 1.

Table 1: Regulatory compliance hierarchy

Tier	Type	Application
1	Legislation	Compliance
2	Standards	Select one, comply in full
3	Absence of guidance	Select parameter based on scientifically robust data or justification

For clarity, in the event of any discrepancies, legislation and regulatory requirements take precedence over the information provided in this document.

4.1 Legislation and regulation

All legislative requirements must be adhered to.

In some jurisdictions, novel nicotine products are regulated as medicines. These products are subject to specific and often extensive legislative and regulatory requirements. For the purposes of this Code, these requirements are not summarised but must be adhered to where applicable.

In jurisdictions where novel nicotine products are not regulated as medicines, organisations must ensure compliance with applicable consumer protection laws and regulations.

4.2 Standards

This Code of Practice recognises the following standards (Table 2).

Table 2: Standards

Group	Title
PAS 8877-2022	Tobacco-free oral nicotine pouches – Composition, manufacture and testing - specification
SIS/TS 72:2004	Teknisk Specifikation Nicotine-containing, tobacco-free oral products – Safety and quality related requirements
CORESTA (Cooperation Centre for Scientific Research Relative to Tobacco)	CORESTA Guide No. xx Technical Guide for Nicotine Pouch Safety and Quality (July 2024, Draft Rev 3)
HYAPP Group	HAYPP Marketing and Product Standards for Nicotine Containing Consumer Product. September, 2021

When compliance with particular a standard is not legally required, select one primary standard that guides all operational and manufacturing procedures. This chosen standard is followed completely.

4.3 Absence of guidance

In cases where primary standards or laws do not specify requirements for nicotine product parameters, companies should base their decisions on scientific evidence and established industry practices. This process involves:

- Identify missing regulatory parameters through careful analysis of current standards. Gather scientific evidence from peer-reviewed research, including toxicology studies and safety data. Consider conducting new studies if existing data is insufficient.

- Reference established industry practices, focusing on manufacturing processes and quality control measures that have proven effective. Consider international standards, particularly from regions with comprehensive nicotine product regulations like the FDA guidelines.

- Look to similar product categories for regulatory precedents. For example, how have authorities approached comparable parameters in nicotine pouches? Engage relevant stakeholders, including public health experts and industry specialists, to validate your approach.

- Maintain detailed documentation of all scientific data, standards, and stakeholder input used to justify your decisions. Implement a monitoring system to track new scientific findings and regulatory developments, updating your approach as needed.

Through this evidence-based methodology, companies can address regulatory gaps while ensuring product safety and compliance. This approach demonstrates commitment to responsible practice even when specific regulations are not available.

5. Manufacture

5.1 Ingredients

Manufacturers should ensure disclosure of all necessary information about ingredients from suppliers, including any flavor pre-mixture used in the production.

Disclosure of ingredient information should include but not limited to:

- Full ingredient list and quantities
- Identification numbers (e.g. CAS registry number), if available

Natural ingredients or natural extracts should be accompanied by information on source and occurrence.

Allergenic substances should be identified.

5.2 Excluded Ingredients

Manufacturers must ensure that no ingredients meeting the following criteria are used in the production of novel nicotine products:

- Carcinogenic (Category 1 or 2)
- Germ cell mutagenicity (Category 1, 1A, 1B or 2)
- Toxic to reproduction (Category 1 1A or 1B, or effects on or via lactation) (Reference: European Regulation (EC) No 1272/2008 0)

The presence of other toxic or potentially toxic ingredients must be justified by a toxicological risk assessment (see Section 5.5).

Oral formulations should be free of fermentable sugars to minimise the risk of dental caries.

5.3 Ingredients Quality

Nicotine used must comply with the relevant standards for quality, including purity. The selected standard(s) must be appropriate for the regulatory regime. For example European Pharmacopoeia, Nicotine Monograph (1452), and/or US Pharmacopoeia, Nicotine Monograph may be relevant for products regulated as medicines. Alternative nicotine formulations that demonstrate appropriate purity and safety (such as those extensively tested for TSNA-free compliance, may be appropriate for products subject to other regulatory regimes.

All ingredients must be accompanied by a certificate of analysis (CoA) and a statement of conformity to relevant legislation, regulation or standards (where applicable).

Ingredients such as those used for pouches, flavorings, and additives should be limited to substances found in food (for oral formulations) /or to those with a known and acceptable safety profile.

5.4 Supply Chain

Manufacturers should ensure all the suppliers are qualified and comply with relevant regulations.

Manufacturers and suppliers should agree on minimum specifications of the ingredients and materials.

All ingredients and materials must be supplied to the manufacturer with a unique batch code with documentation that verifies material information (e.g.) of analysis or conformity for each batch or via a general certificate of conformity from the supplier, along with a risk-based audit of the supplier by the manufacturers.

Manufacturers should apply batch numbering systems in the production process to ensure the traceability and quality of ingredients and final products. Records should ensure full traceability over the source and quantities of all ingredients and items (e.g. equipment) used during production, and that relevant procedures have been adhered to.

5.5 Toxicological Risk Assessment (TRA)

A TRA should be available for each product. A TRA should encompass all consumable components, quantities, and all packaging materials that come into contact with the consumables to determine.

The TRA considers applicable scientific data and resources, including, but not limited to:

- Exposure data – humans
- Exposure data – animals
- *In vitro* laboratory data

The TRA should be taken into account at every stage of the product's lifecycle, and usually includes the following components:

- Hazard identification
- Hazard characterization
- Exposure assessment
- Risk characterization

TRA should also consider how the manufacturing process may affect the product's composition, including contamination risks.

TRA should be reviewed regularly and updated if changes occur in:

- Ingredients or ingredient purity
- The availability of ingredient hazard data
- Consumer/patient pattern of use
- Regulatory requirements or standards

- Post-marketing complaints or reports

TRA should be conducted by a qualified toxicologist using validated procedures and documented for each commercial product.

Whilst a reputable source of regulator-allowed ingredients (e.g. the European Commission Food Additives database) may be consulted to assist in identification of suitable ingredients, a TRA for these ingredients should still be undertaken.

5.6 Final Product

The product release specification should include acceptance criteria for the following

- Nicotine content
- pH
- Water activity
- TSNAs, for products where the nicotine is derived from tobacco
- TRA considerations
- Recommended shelf-life and storage conditions
- Other parameters as appropriate, based on the product profile including nicotine origin (tobacco or synthetic), impurities, interaction of product with immediate packaging, and the potential for degradation over the product's shelf-life.

Acceptance criteria – whether defined as maximum values, minimum values or ranges – should be established in a way that guarantees product quality is consistently maintained throughout the specified limits. Ranges should be symmetrically distributed around the set nominal value e.g. 90-110% of the nominal value

If justified and documented, rotational testing of some parameters according to a defined algorithm may be justified.

Each lot should be accompanied by a Certificate of Analysis.

Analytical methods should be appropriate for use and validated according to an appropriate standard e.g. ISO 17025.

Stability data should be conducted to support the desired shelf-life and storage conditions. Parameters monitored

The release of the final product should be based on specifications that have been reviewed and approved by QA, which support use of the product throughout its shelf-life. Stability studies should encompass the following

- The accuracy of stability sample chamber conditions (temperature, humidity) should be validated.
- Product should be tested under at least two temperature/humidity combinations, one of which reflects the proposed storage conditions.

- The stability protocol should identify the test product, lot no.s (at least two batches should be tested), conditions, lot numbers, parameters and specifications
- Stability data should be available to support transport deviations and other storage deviations reasonably expected over the supply chain and the customer/patient use period.
- Parameters tested should be stability indicating, and should include
    - Nicotine
    - pH
    - Water activity
    - TSNAs, irrespective of whether the nicotine originates from tobacco or is synthetic.
    - Microbial contaminants
    - Other parameters as identified through the TRA
- Pre-marketing stability studies for new products or where significant changes to on-market products (as scientifically justified).
- Routine post-market placement of lots on stability trial, according to a pre-defined algorithm.

6. Product Packaging and Labelling

6.1 Primary and Secondary Packaging

The following definitions apply for the purposes of this Code of Practice

- Primary packing: The pack immediately surrounding /containing the product
- Secondary packaging: The pack containing the primary pack

The seal of both primary and secondary packaging shall be tamper-evident, allowing the user to easily identify if the product has been opened since manufacture

6.2 Labelling

Key labelling considerations include:

- Nicotine warning labels (e.g. “This product contains nicotine which is a highly addictive substance”) should be displayed in both primary and secondary packaging with formats following applicable regulatory requirements.
- A statement or symbol that emphasises restriction of products for adult use only should be displayed in both primary and secondary use and with formats following applicable regulatory requirements. (e.g. “keep out of reach of children or sale to persons under age 18 is prohibited”)
- The content of nicotine should be included and displayed in appropriate formats (e.g. units of mg/pouch or mg/consumable, etc.)
- Composition/ ingredient list.
- Any allergen warnings.
- Contact sensitiser categories may need to be displayed on the label based on GHS categorisation, in compliance with the relevant regulatory guidelines.
- Manufacturing information such as batch number and expiry date and details for consumer inquiries or complaints.
- Instruction for use and disposal

7. Quality Assurance

7.1 Principles

Products must be fit for their intended use and that comply with relevant requirements and standards. A QA program, commensurate with risk, must be in place with oversight of key organisational activities.

Key aspects of a QA program include, but are not limited to, the following

- A patient/consumer-centric approach
- Workflows are considered as interrelated processes
- Manufacture and batch records, including information required to support release for supply
- Fact based decision making
- Handling of complaints (including reporting safety-related reports), investigations, and recalls
- Continuous improvement
- Identification of person(s) authorised to release product for supply
- Applicable from concept through to manufacture and end of product life

7.2 Documentation and records

The creation, management, and control of records is governed within the QMS. Key requirements include

- Documents and records are clear, accurate, and contemporaneous
- Processes, procedures, and activities are in place and are approved, updated, and archived systematically.
- There is a clear process for timely and thorough handling of complaints, including mandatory reporting requirements.
- Records support traceability, ensure consistency, and demonstrate compliance with applicable legislation or standards.
- Documents and records are prepared, maintained, and updated in accordance with established data integrity principles.

8. Health and safety

8.1 Personnel

Organisations must maintain safe working environments, prioritise personnel health and safety by identifying and mitigating workplace hazards, and provide relevant training on safe practices and emergency protocols.

All personnel must be engaged in accordance with relevant legislation.

8.2 Product

Product safety principles, such as undertaking TRAs (see Section 5.5) should be embedded in the product development plan and throughout the product lifecycle.

A clear and robust process should be in place for assessment of complaints which relate to patient or consumer safety, which includes medical input as appropriate. Legislated reporting should be specified and followed. Period trends analysis of safety-related complaints should be undertaken.

9. Environmental responsibility

Organisations should uphold high standards of corporate social responsibility and environmental sustainability. This includes promoting ethical practices, fair treatment, diversity, and community development, while minimizing environmental impact through sustainable manufacturing, waste reduction, and compliance with environmental regulations. Transparency, accountability, and continuous improvement are central to ensuring long-term sustainability and positive contributions to society and the environment.

For avoidance of doubt, the following are explicitly prohibited

- Bribery, including offering, giving, receiving, or soliciting anything of value to influence decisions or gain an unfair advantage.
  Violations of child safety labour laws.

10. Supplier and partner responsibilities

Organisations should make reasonable attempts to ensure that suppliers of products or services comply with the principles outlined in this Code of Practice. This includes conducting thorough due diligence and establishing clear agreements. It can also include undertaking supplier audits.

11. Training

Relevant training requirements for each role, including the frequency of retraining where applicable, are outlined in a training matrix. All personnel must receive appropriate training, including refresher training when necessary. Training records are maintained.

12. Revision history

Version	Key changes
1	Initial version

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