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MNZH MAKE NEW ZEALAND HEALTHY

Pause Drafting of the Medical Products Bill. Restart Consultation.

THE PROBLEM: The Government is progressing a Medical Products Bill to replace the current Medicines Act. While it has been stated that 'consultation will be included in the process of development of new legislation' there has been no recent publicly visible consultation on the substance of the Bill, nor updated policy reassessment to support its development. The Bill is understood to be in drafting and expected to be introduced this year.

Government documents indicate that the framework will be 'risk proportionate', yet existing policy material shows that many foundational issues remain outside official consideration. With pre-policy consultation limited, any broader consultation will occur only once the draft Bill is released. By that stage, the underlying assumptions, core direction, and regulatory architecture will largely be settled. Consultation will therefore be constrained to technical amendments, with limited ability for lay or expert stakeholders to influence the fundamental design of the legislation.

Policy documents suggest an insufficient evidential and analytical foundation. Key scientific, clinical, and regulatory questions have not been examined during the policy formulation phase and are unlikely to be addressed in the draft legislation. Current signals suggest that several issues central to contemporary medical practice and public health in New Zealand have not been adequately considered. Officials appear likely to rely on existing regulatory assumptions and international templates, often reflecting World Health Organization norms, without sufficient scrutiny of global best practice or whether these frameworks adequately address the realities of chronic illness, multimorbidity, and nutritional medicine in New Zealand.

These omissions directly affect whether the future regulatory system will be capable of recognising real-world health outcomes at a population level. They include:

- Under-recognition of the extent of multiple-medicine prescribing and associated risks.
- Under-recognition of adverse drug events, such as non-serious, clinically significant harms.
- Absence of policy analysis on the distinct risk profiles of biologic medicines.
- Evidence that emerging biologics and clinical trials may be insufficiently regulated.
- Risk that natural health products will be captured as medicines due to therapeutic' triggers.
- Lack of graded risk classification frameworks for natural health products.
- Absence of transparency regarding subject matter experts informing policy development.
- Limited consideration of drug–drug interactions, pharmacovigilance, and polypharmacy.
- Insufficient evaluation of international regulatory models, including European frameworks.

THE SOLUTION: Cease drafting. Return to broad, transparent public consultation, extending beyond undisclosed officials, to establish evidence-based policy foundation prior to Bill drafting.

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MNZH POLICY RECOMMENDATIONS

A temporary moratorium should be placed on the legislative process, with the policy framework returned to a full consultation phase. This would enable the development of a proportionate, risk-based regulatory model that aligns legal definitions with biological reality and ensures that medicines law is directed to substances and products that genuinely warrant that level of control.

It is essential that a broad spectrum of foundational issues is clearly articulated before drafting proceeds. These matters determine the architecture of the regulatory system and directly affect the health and safety of New Zealanders. In particular, clarity is required on how substances are classified, how risk is defined, including drug–drug interaction risk, and where the legal boundary is drawn between food, nutrients, natural health products, and medicines. Key issues requiring resolution include:

- Declaration of officials and advisors, including relevant expertise, informing policy and legislation.
- Substantive, evidence-based review of biologic medicines and their distinct risk profiles.
- Clear statutory principles for regulatory decision-making.
- Evaluation of international best practice in medicines regulation and clinical trial design.
- Systemic challenges in adverse-event reporting, including under-reporting and the exclusion of non-serious but clinically meaningful harms.
- Evaluation of polypharmacy and interaction risk, including harms arising from two-drug combinations.
- Streamlined access to Pharmac funding for nutrients with a long history of safe use.
- Development of an appropriate regulatory framework for natural health products.
- Consideration of risk-based classification models for nutrients.
- Assessment of disproportionate penalties applied to low-risk substances.

A central concern is that the current pharmacovigilance system captures only a partial picture of harm. Non-serious but clinically significant adverse effects, including interaction-related harms, withdrawal phenomena, and impacts on quality of life, are not routinely visible in public datasets. Nor are risks consistently stratified by age, sex, or vulnerability. Without statutory reform, safety monitoring will remain incomplete, limiting informed consent, clinical decision-making, and early detection of emerging risks.

Official materials also indicate limited evaluation of the evolving risk profile of biologic and advanced therapeutic products. These products, including monoclonal antibodies, gene therapies, and other biologics, raise distinct challenges, such as immunogenicity, manufacturing variability, contamination risk, and long-term safety uncertainty. They require robust, transparent post-market surveillance systems capable of detecting cumulative and subgroup-specific harms.

If these matters are not resolved at the outset, there is a significant risk that the legislation will entrench existing conceptual errors, including the overbroad ‘therapeutic purpose’ trigger, and extend medicines regulation into domains more appropriately governed by food and public health frameworks. This would constitute a fundamental flaw in the statute, with long-term consequences for proportionality, access, and scientific coherence.

A modern regulatory framework must therefore apply greater precision and intensity to high-risk biologics, while avoiding unnecessary extension of medicines-level controls to low-risk nutritional or traditionally used substances. Without a scientifically grounded, risk-based classification system, regulatory burden risks being misallocated, diluting oversight where it is most needed and over-regulating where it is not.

For these reasons, proceeding with drafting in the absence of a coherent, evidence-based framework, risks producing legislation that is internally inconsistent, scientifically misaligned, and difficult to administer in practice.

A further concern is that current regulatory pathways create barriers to the evaluation and inclusion of nutrients within Pharmac funding. Access is often contingent not on evidence or safety, but on whether a sponsor is able and willing to navigate the system. This creates an uneven system that favours commercially backed products over equally evidence-supported alternatives. If left unaddressed, this bias will continue to result in low-risk, evidence-supported interventions being overlooked, while resources are directed toward products that align with the existing commercial model.

For these reasons, proceeding with drafting in the absence of a coherent, evidence-based framework risks producing legislation that is internally inconsistent, scientifically misaligned, and difficult to administer in practice. The appropriate course is to pause the drafting process and return to broad, independent public consultation, supported by transparent disclosure of the evidential base and meaningful input from a full range of disciplines, including toxicology, pharmacology, nutrition science, and public health.

A minimally adequate foundation for natural health products legislation would require:

- ✓ A clear, risk-based classification framework grounded in toxicology and dose–response.
- ✓ Explicit analysis of the distinction between physiological function and pharmacological effect.
- ✓ A proportionality assessment linking regulatory burden to demonstrable risk.
- ✓ transparent identification of expert inputs across relevant disciplines, including nutrition and public health.
- ✓ Full accounting of alternative regulatory models, including those that avoid overbroad capture.
- ✓ Require comprehensive interrogation of the scientific literature, including mechanistic, clinical, observational, and toxicological evidence when undertaking evaluations.
- ✓ Pathways for Pharmac funding that flexibly incorporate evidence drawn from the broader scientific literature.

Absent these elements, proceeding to legislation carries a substantial risk of entrenching the current overinclusive and conceptually flawed regulatory regime, rather than correcting it.

BACKGROUND TO THIS POLICY

The available documentation suggests a discernible policy orientation toward facilitating pharmaceutical development and clinical trials, yet the evidential basis for this emphasis is not clearly set out. It remains unclear what analyses, submissions, or stakeholder inputs have

informed this direction, and whether equivalent consideration has been given to alternative frameworks, particularly those relevant to natural health products and nutritional science. In the absence of disclosure, there is a reasonable concern that policy development may have been influenced by undisclosed stakeholder engagement, including potential industry input, without corresponding transparency.

Key questions of concern:

Absence of evidence of best-practice review. No clear evidence that officials have systematically reviewed or applied international best practice to inform the regulatory framework.

Overbroad 'therapeutic purpose' definition. The current Medicines Act 1981 definition has reinforced a policy environment in which pharmaceutical toxicology dominates regulatory thinking, while the biological role of nutrition remains marginalised.

Inadequate treatment of biologic risk. Limited evidence that policy development has substantively addressed the distinct and evolving risk profile of biologic and advanced therapeutic products, or the need for tailored regulatory responses.

An insufficiently integrated and sensitive approach to adverse events and drug–drug interactions. This limits the system's ability to detect, assess, and respond to clinically meaningful harms arising from real-world medicine use.

Failure to operationalise uncertainty. Although uncertainty is implicitly acknowledged in policy documents, it is not articulated as a guiding regulatory principle. A modern framework should embed adaptive, uncertainty-responsive governance within the purpose clause, enabling proportionate responses as scientific understanding evolves.

The scientific literature now leaves little doubt that micronutrients function as integral components of cellular regulation and systemic resilience. Their safety is evaluated primarily through nutritional toxicology and exposure thresholds such as upper intake levels, rather than through pharmaceutical risk paradigms. The continued use of a regulatory trigger based on 'therapeutic action' therefore lacks a rational risk threshold and fails to reflect contemporary scientific understanding of human physiology.

Retaining this definitional model in future legislation would perpetuate a regulatory framework that conflates nutrition with pharmacology and extends medicines regulation beyond its legitimate risk-based purpose.

A modern statutory framework must instead establish a clear distinction between nutritional substances that sustain physiological function and pharmacological agents intended to modify disease processes. Correcting this overbroad statutory trigger is essential to ensure that regulatory authority is exercised proportionately, coherently, and in alignment with both scientific evidence and the proper limits of medicines legislation.

There is little evidence that officials have reviewed the European framework, prior to commencing work on draft legislation. The European Union framework illustrates a more differentiated, albeit imperfect, approach to regulating substances at the interface of food and medicine. Rather than

relying on a single, overbroad statutory trigger, the EU system is anchored to the food–medicine distinction, with food supplements regulated under food law and herbal medicinal products regulated under medicines law.

[1] KEY POLICY QUESTIONS THAT REQUIRE REVIEW

The problems that are identified below suggest that the policy foundations of the proposed legislation remain incomplete and that policy formulation has been poor or non-existent.

These issues indicate that the policy framework underpinning the proposed legislation has not adequately reconciled the scientific realities of pharmacology, nutritional biology, and modern health risk assessment. Without addressing these deficiencies, the legislation risks entrenching a regulatory architecture that simultaneously under-recognises pharmaceutical risk while over-extending regulatory control over low-risk nutritional substances.

If officials proceed directly to a draft Bill, and this is suspected, this risks the locking in of deficient and improperly formulated regulatory assumptions that have not been tested against the current scientific literature, clinical realities, or the evolving role of nutrition and multimorbidity in modern health systems.

Once legislative architecture is set, correcting these issues becomes significantly more difficult.

1. Lack of transparency regarding the expertise informing policy development

There is a material absence of transparency concerning the sources of advice and influence shaping the underlying policy framework for the proposed legislation. The policy papers do not identify the officials, advisers, or external contributors involved in developing the positions that will inform the draft Bill.

The policy papers and briefing materials supporting the proposed legislation do not clearly identify the subject-matter experts whose advice informs the regulatory recommendations. This lack of transparency is particularly concerning in light of four major issues:

i. Biologic medicines including gene therapies are major new classes of medical drug, yet their risks, which include challenges concerning contamination and degradation have not been discussed.
ii. Biologic medicines regulation in foreign jurisdictions, including in Europe has not bee reviewed.
iii. Case studies suggest that decision-makers have struggled to evaluate substances, such as micronutrients, that have long histories of safe human use and well-characterised physiological roles.
iv. Contracted organisations seem to lack expertise on the scientific and technical issues that they have been contracted to review.

Where advisory processes lack expertise in nutritional biochemistry and human physiology, biological activity may be misinterpreted through a pharmaceutical regulatory lens. The result is a risk that uncertainty regarding biological mechanisms is treated as evidence of potential hazard rather than interpreted within the established scientific understanding of nutritional exposure ranges and safety.

2. Absence of substantive policy analysis concerning biologic medicines

Biologic medicines present distinct regulatory challenges that differ fundamentally from those associated with small-molecule pharmaceuticals. These include immunogenicity, complex manufacturing variability, and long-term immune or systemic effects that may only become apparent after extended population exposure.

Despite these well-recognised characteristics, no review has been undertaken to analyse the risks of biologic medicines and to discern whether any proposed legislative framework adequately addresses these known and unknown issues. The absence of such analysis raises concerns that the regulatory architecture may insufficiently differentiate between categories of medicines whose safety monitoring and regulatory oversight requirements differ substantially.

3. Disproportionate policy emphasis on protecting pharmaceutical innovation.

Policy development for the proposed legislation has placed substantial emphasis on ensuring that regulatory frameworks do not impede pharmaceutical innovation or clinical trials. While regulatory efficiency in this area is legitimate, the disproportionate attention given lowering barriers for development and trials, particularly as little risk analysis has been undertaken, risks creating an imbalance in the statutory framework.

This is particularly concerning when 'innovative' biologic drugs are considered that include the risk characteristics of biologic drugs, which are yet to be considered in any official documentation, and the implications for the safety of laboratory staff and clinical trial participants.

Medicines regulation exists primarily to safeguard public health and ensure that therapeutic products are managed in accordance with demonstrable risk. A regulatory system that prioritises facilitating market entry and research activity without equivalent attention to long-term safety monitoring, polypharmacy risk, and population-level health outcomes risks misaligning regulatory priorities with the statutory purpose of medicines legislation.

4. Historic under-recognition of adverse drug events.

The current adverse event reporting framework captures only a narrow subset of medicine-related harms, typically those classified as 'serious' within formal reporting thresholds with so-called less serious events that have been reported, retained in the drug sponsor's reporting systems. However, these lower level adverse events do not get summarised and regularly reported back on, so that the public may understand the extent of adverse events by age and gender.

Many adverse drug effects that materially affect patient wellbeing, functional capacity, and long-term health outcomes fall outside this threshold and therefore remain invisible to the public health surveillance system. The result is a consistent under-reporting of adverse drug events, with significant portions of safety-relevant data retained within pharmaceutical sponsor datasets rather than incorporated into publicly accessible pharmacovigilance systems. This arrangement weakens the evidentiary base available to regulators and clinicians and undermines the capacity of the regulatory system to assess medicine-related harms at the population level.

5. Systematic under-recognition of polypharmacy risk

Current regulatory norms frequently define polypharmacy as the use of more than four prescription medicines. This definition is difficult to defend scientifically. Clinically meaningful

drug–drug interaction risk begins with two or more medicines, and this has long been recognised in pharmacology and clinical toxicology.

Without explicit reference to the recognition of a drug risk from two or more medicines, if the higher regulatory threshold is required, the policy framework enforces a systematic under-recognition of interaction risk within the safety monitoring system itself. The consequence is a regulatory architecture that underestimates medicine-related harm in real-world populations. A medicines regulatory regime that fails to recognise the risks inherent in multi-drug prescribing from the point at which interactions become biologically plausible cannot credibly claim to provide comprehensive pharmacovigilance or population-level safety oversight.

6. Replacement natural health products regulatory framework.

There is no public discussion of how a new regulatory framework might operate without a trigger that categorises natural health products as medicines. The policy documentation does not adequately address the longstanding problem identified within the Medicines Act 1981: the overbroad statutory definition of 'therapeutic purpose' that captures substances influencing physiological, metabolic, or immunological pathways. These pathways are the fundamental mechanisms through which nutrition operates.

Retaining this definitional trigger without modification perpetuates a regulatory framework that conflates nutritional biology with pharmacological intervention. Such an approach fails to recognise the scientific distinction between nutrients that sustain normal physiological function and drugs designed to modify disease processes. In effect, the statutory trigger remains misaligned with the actual risk profile of the substances captured by it.

Officials have contracted an external organisation to review the risks of natural health products, and the regulatory frameworks of foreign jurisdictions.

7. Absence of a risk-based classification framework for nutrients

The policy framework does not establish any clear toxicological or risk-based threshold that would justify categorising a nutrient or natural health product as a pharmaceutical medicine. In modern regulatory science, classification thresholds are typically anchored to intrinsic hazard, pharmacological potency, or demonstrable risk of harm. In the absence of such criteria, regulatory decisions concerning nutrient classification risk becoming discretionary and precautionary rather than evidence-based. Without a defined risk-grading framework, the regulatory system lacks the rational risk threshold required to distinguish between substances that warrant pharmaceutical regulation and those that fall within the domain of nutritional support.

8. Disproportionate penalty regimes applied to low-risk substances

Proposed offence and penalty provisions appear to apply broadly across substances classified as medicines under the Act. If natural health products or nutrient formulations are captured by the overbroad statutory trigger discussed above, manufacturers of products with minimal intrinsic toxicity could be exposed to enforcement provisions designed for pharmacologically potent medicines capable of causing serious harm. Such an outcome would represent a disproportionate exercise of regulatory authority, applying punitive regulatory tools to substances whose risk profiles differ fundamentally from those of pharmaceutical drugs. A regulatory framework

grounded in proportionality must ensure that enforcement mechanisms correspond to the actual hazard posed by the substances being regulated.

9. Failure to disclose lobbying and policy inputs

Published policy papers and documents do not disclose the materials, submissions, or stakeholder engagements that have been relied upon in reaching those positions. This lack of disclosure is inconsistent with basic principles of administrative law, which require that regulatory decision-making be transparent, traceable, and capable of scrutiny.

This concern is compounded by the omission of relevant materials from the declared policy record. For example, a policy proposal white paper dated 22 August 2025, provided to Ministry of Health officials, does not appear among the documents identified as informing the policy process. [1] The absence of such material from the official record raises questions as to whether the full evidential and advisory base has been made available for scrutiny, and whether decision-makers have had regard to a sufficiently broad range of perspectives.

In public law terms, a regulatory framework developed on the basis of undisclosed inputs and unidentified advisory sources risks lacking procedural integrity. Where the origins of policy positions are not transparent, it is not possible to assess whether decision-making has been balanced, evidence-based, or unduly influenced by particular interests. This is particularly significant in a context where the legislation will determine the boundary between pharmaceutical regulation and the governance of nutrition and natural health products.

A democratically robust legislative process requires that all material inputs, stakeholder engagements, and advisory contributions be clearly disclosed, and that the expertise informing policy development, particularly in areas such as nutritional science, be explicitly identified. Without such transparency, the legitimacy of the policy framework is undermined, and the resulting legislation risks reflecting unexamined assumptions rather than a robust and accountable evidential foundation.

10. Barriers to Pharmac funding for nutrients

Current regulatory and funding pathways rely on formal, sponsor-driven processes that create barriers to the evaluation and inclusion of nutrients. This limits the ability to incorporate metabolically and immunologically important nutrients into the Pharmaceutical Schedule, even where there is a strong safety profile and supporting evidence. A more appropriate model would enable flexible, evidence-based assessments, allowing such interventions to be considered on a public-health basis rather than contingent on commercial sponsorship.

[2] BRIEF OUTLINE: NEW ZEALAND'S REGULATORY SCHEME

New Zealand's current regulatory framework for medicines, food, and dietary supplements is best understood as a fragmented and overlapping system rather than a single coherent architecture.

[1] Natural Health Alliance (August 22, 2025). Towards Regulatory Excellence: Learning from Experience A Policy Proposal Regarding the Future Regulation of Natural Health Products. https://www.naturalhealthalliance.co.nz/wp-content/uploads/2025/12/A-Policy-Proposed-Natural-Health-Products-Regulatory-Reform-2025-Merged-Document-02.pdf

Medicines Regulations

The Medicines Act 1981 and associated Regulations govern therapeutic products, with classification based primarily on 'therapeutic purpose' or the presence of pharmacological, immunological, or metabolic effects. This definition is broad and can capture substances irrespective of dose.

Under the Act's secondary legislation sits the Medicines Regulations 1984. These regulations classify or schedule certain substances as medicines by default, meaning that their inclusion in a product, regardless of dose, context, or route of exposure, can automatically trigger regulation under the Medicines Act.

Part 1 *Prescription medicines* lists nutrients that are automatically categorised as a medicine. Lithium salts are a clear example: although lithium is naturally present at trace levels in food and water, its listing as a medicinal substance means that products containing it may be captured as medicines even where exposure is within physiological or nutritional ranges. This reflects a broader issue within the Regulations, where classification is substance-based rather than risk- or dose-based. Other ingredients that may warrant review on this basis include melatonin (1260), high-dose vitamin D, certain amino acids, and herbal constituents with recognised pharmacological activity (e.g. St John's Wort), where the current framework may not adequately distinguish between traditional use, nutritional function, and higher-risk pharmacological dosing.

Food and Dietary Supplements Regulations

Alongside the medicines and medical devices regulations sit the Food Act 2014 and the Food Standards Code, administered through the Ministry for Primary Industries. This regime is designed to ensure food safety at a population level, focusing on contaminants, permitted ingredients, and exposure thresholds, rather than efficacy. However, the boundary between food and medicine is not determined by intrinsic risk or dose, but by claims and perceived function. Where a product makes therapeutic claims, it may be shifted out of the food regime and into medicines regulation, even where the underlying substance is nutritionally or physiologically normal.

The Dietary Supplements Regulations 1985 occupy an intermediate and increasingly unstable position within this framework. They define supplements broadly, covering vitamins, minerals, amino acids, and herbs, but operate as a legacy regime with no pre-market approval process and limited modern risk assessment capability. As a result, supplements are neither regulated with the rigour of medicines nor integrated into the food safety system, leaving a demonstrable gap in oversight, particularly for chronic or cumulative exposure.

Institutionally, regulatory responsibility is distributed across multiple agencies. Medsafe, within the Ministry of Health, oversees medicines, including classification decisions and adverse event monitoring through the Centre for Adverse Reactions Monitoring. Its orientation is toward clinical safety and efficacy, reflecting a pharmaceutical approach to regulation.

In contrast, the Ministry for Primary Industries and New Zealand Food Safety regulate food, focusing on contamination and population-level risk. The Environmental Protection Authority manages hazardous substances and environmental exposures, but with limited integration into human health risk assessment across food and supplement pathways.

There is no single agency responsible for assessing cumulative exposure across these domains.

This institutional separation is mirrored by differences in risk assessment approaches.

- Medicines are evaluated through clinical trial evidence and pharmacovigilance systems, which are suited to higher-dose, shorter-term exposures.
- Food is regulated through threshold-based models aimed at population safety.
- Dietary supplements, by contrast, lack a modern, structured risk assessment framework.

Critically, there is no integrated model that accounts for cumulative exposure from multiple sources, dose–response relationships across a continuum, or the effects of chronic low-level exposure, particularly during sensitive developmental periods.

The classification system that underpins this framework is therefore not anchored in toxicology or exposure science, but in intended use and perceived biological effect.

This creates a situation in which the same substance may fall under entirely different regulatory regimes depending on how it is described or marketed. More fundamentally, it collapses the distinction between normal physiological function and pharmacological intervention, as both are captured under the concept of 'therapeutic effect'.

This gives rise to what can be described as a scientifically questionable classification problem, whereby substances integral to human biology may be drawn into medicines regulation without a corresponding assessment of risk or proportionality.

Lithium provides a clear illustration of this issue. It is present in the natural environment and consumed at low levels through diet and water and can be in natural supplements, not as a stand-alone ingredient, but as a component of another food-based ingredient. However, under the current framework it is exclusively positioned within a therapeutic context, despite the absence of a clear legal distinction between physiological and pharmacological exposure.

The current system does not provide a coherent framework for managing this continuum. Low-level exposure is effectively unregulated within the food system, moderate exposure through supplements sits in a weakly governed space, and higher-dose use is tightly controlled as a medicine. There is no integrated approach that recognises or governs the transition across these exposure levels.

In sum, New Zealand's regulatory system does regulate substances, but not in a manner that is coherent across dose, exposure, and biological function. It relies on categorical distinctions driven by claims and legacy statutory definitions rather than a unified, risk-based framework grounded in toxicology, physiology, and cumulative exposure. This creates gaps, inconsistencies, and the potential for both over- and under-regulation, particularly for substances that exist across a spectrum from nutritional to pharmacological use.

[3] PHARMACOVIGILANCE & ADVERSE-EVENT REPORTING

(a) Absence of Evaluation in Policy Formulation: Pharmacovigilance

External oversight of whether the pharmacovigilance system is itself performing effectively appears limited, and the budget for adverse-event monitoring is not transparently disclosed as a distinct line item. As a result, it is difficult to assess whether the system is adequately resourced,

whether reports are processed in a timely manner, and whether interaction-related harms are being systematically captured.

This lack of visibility is reflected in current policy formulation. Regulatory Impact Statements (RIS/RIAs) for the proposed Medical Products Bill do not appear to evaluate the effectiveness, limitations, or performance of the existing pharmacovigilance system. In particular, there is no structured assessment of under-reporting, subgroup safety monitoring, or the system's ability to detect drug–drug interactions. The absence of such analysis means that the parent legislation risks being developed without a clear understanding of the safety infrastructure it is intended to govern.

The New Zealand framework for adverse-event reporting follows standard international definitions. A 'serious' adverse reaction is defined as one resulting in death, life-threatening outcome, hospitalisation, significant disability, congenital anomaly, or a medically important event. Serious events must be reported to the national pharmacovigilance system (Medsafe/CARM), typically within defined timeframes.

By contrast, non-serious adverse reactions are not routinely submitted to the national database. Instead, they are retained within industry sponsor-held pharmacovigilance systems for internal signal detection and evaluation. While the legacy framework aligns with international norms, it creates a bifurcated system in which only a subset of harms is centrally visible.

Data held within sponsor pharmacovigilance systems does not appear to be routinely incorporated into New Zealand Formulary guidance or other publicly accessible safety and efficacy materials. Product data sheets likewise do not typically disclose the extent or pattern of these non-serious adverse events.

Oversight of safety signals is provided by the Medicines Adverse Reactions Committee (MARC), established under the Medicines Act 1981,and tasked with reviewing reported events and providing expert advice. However, MARC operates within the Medsafe system and does not constitute an independent audit of system performance.

A publicly disclosed pharmacovigilance budget for Medsafe/CARM is difficult to identify. Broader Medsafe financial information is available, such as the Ministry's 2022/23 annual report, where the Medsafe memorandum account shows about NZ$10.166 million revenue and NZ$10.610 million expenditure for that year. However, this covers Medsafe more broadly, not pharmacovigilance alone.

There is no evidence of a separate, routine, independent performance-review mechanism that audits the effectiveness of the pharmacovigilance system as a whole, including whether current resourcing is adequate. This is a material gap. Publicly available financial information suggests that the total budget for medicines regulation, encompassing Medsafe and associated functions such as CARM and MARC, is modest (on the order of ~NZ$10–11 million annually), and not disaggregated to show dedicated pharmacovigilance capacity.

In the absence of transparent budget lines, it is not possible to assess whether sufficient funding is allocated to core system requirements, including data infrastructure, staffing, and specialist

expertise. This modest budget contrasts with Pharmac's Combined Pharmaceutical Budget (CPB) which is often described as around NZ$1.5-1.8 billion annually.[2]

A properly functioning oversight mechanism would be expected to evaluate system performance indicators such as under-reporting rates, timeliness of triage, completeness of follow-up, subgroup capture (including age and gender), and adequacy of public reporting. Without such independent review, there is no clear basis for determining whether the system is operating effectively or is appropriately resourced to detect and respond to emerging safety signals. As a result, while expert review of individual safety issues is undertaken, there is little visible scrutiny of the performance and capacity of the pharmacovigilance system itself.

(b) Downplaying of non-serious events and under-reporting

The distinction between serious and non-serious events results in an insensitive scheme that does not articulate the extent of adverse events experienced by one person, or at the level of a sub-population or population. Many adverse effects that are clinically meaningful do not meet the regulatory threshold of seriousness but nonetheless affect quality of life, treatment adherence, and long-term outcomes. These include neuropsychiatric effects, gastrointestinal symptoms, withdrawal phenomena, and moderate interaction effects.

Because non-serious events are not routinely captured in the national system, they remain largely invisible in public data. With industry sponsors holding this information, but not routinely 'feeding back' this data for public access, there is limited transparency regarding their frequency, duration, and cumulative impact on quality of life, leaving clinicians and patients without a clear understanding of the full benefit–risk profile of medicines.

This limitation is compounded by well-established under-reporting in spontaneous reporting systems. International evidence suggests that the majority of adverse drug reactions are not reported, particularly those that are gradual, ambiguous, or socially sensitive.

Akathisia provides a clear example of how the current pharmacovigilance framework can obscure clinically important harm. In its milder and more common forms, restlessness, agitation, and internal distress, it is typically classified as a non-serious adverse event and therefore not routinely captured in the national reporting system. Yet these symptoms can be profoundly distressing, impair functioning, and alter treatment trajectories. In more severe cases, akathisia may escalate to a medically important event, including acute agitation or suicidal ideation, at which point it may finally meet the threshold for central reporting. This creates a structural blind spot: the system captures the endpoint of harm but not its earlier, more prevalent manifestations.

This limitation is particularly concerning for young people, who are frequently prescribed SSRIs and SNRIs during critical developmental periods. Akathisia is also recognised as a withdrawal or dose-change phenomenon, meaning it can arise not only at initiation but during attempts to discontinue treatment. When these earlier or sub-threshold symptoms are not systematically recorded or communicated, they may be misinterpreted as relapse or worsening illness. This can lead to dose escalation or prolonged prescribing, with some individuals remaining on medication

[2] Pharmaceutical Management Agency. Annual Report 2023/2024. ISSN 2382-0799 (Online)

for significantly longer than intended. The result is a hidden cycle in which adverse effects contribute to continued exposure, while the underlying pattern of harm remains largely invisible within formal regulatory systems.

The result is a system that preferentially captures acute, severe harms while under-representing cumulative, functionally impairing, and interaction-driven effects.

(c) Failure to capture two-drug interaction risk

A central gap in the current framework is the failure to systematically capture drug–drug interaction risk arising from two or more medicines. Pharmacologically, interaction risk begins as soon as two medicines are used together. Even a single interacting pair can alter pharmacokinetics or pharmacodynamics in ways that produce clinically significant harm. Ten-year-old primary-care guidance notes that defining polypharmacy purely by an arbitrary number is limited, because the risk varies greatly by the actual drugs involved.[3]

However, regulatory and policy discussions often focus on polypharmacy thresholds of four or more medicines. These thresholds function as administrative indicators of regimen complexity but do not reflect the underlying biology of interaction risk. As a result, a substantial proportion of real-world harm arising from two-drug interactions is not systematically identified, analysed, or reported.

In practice, only severe interaction outcomes, such as serotonin syndrome requiring hospitalisation, are likely to be captured as 'serious' events, while disabling events that do not require hospitalisation but are traumatic. The much more common moderate interaction effects, which may impair function or treatment response, are not visible within the central system.

In an era where modern health-data systems and computational tools are capable of analysing large-scale prescribing patterns and interaction networks, relying on coarse numerical thresholds is increasingly difficult to justify scientifically.

(d) Absence of stratified data by age, gender, and vulnerability

The lack of systematic data publication by age, gender, and exposure context further limits the usefulness of the current system. While individual case reports may include such identifiers, they are not consistently aggregated or publicly reported in a way that allows independent assessment of subgroup risk.

This is particularly significant for vulnerable populations, including:

- Children and adolescents.
- Young adults (under 25).
- Pregnant women.
- People with complex comorbid conditions.

Publicly accessible analyses, such as the HQSC polypharmacy Atlas, are largely confined to older populations and high medicine counts. Its methodology does analyse the older population by ethnicity, age band, and gender, but that is still an older-adult dispensing framework, not a

[3] BPAC (2014). Polypharmacy in primary care: Managing a clinical conundrum https://bpac.org.nz/bpj/2014/october/polypharmacy.aspx?

pharmacovigilance map of interaction harms across the life course. It does not address children, adolescents, pregnant women, or younger adults with complex comorbidities, and it does not provide a broader epidemiology of two-drug or three-drug interaction injury beyond the limited sentinel combination it tracks.

The Ministry's broader strategy and review documents do not appear to fill that gap. The Pharmacy Action Plan 2016–2020 is framed around medicines management, pharmacist roles, and service integration, but the document does not appear to discuss pregnancy, adolescence, or interaction epidemiology in any systematic way. The same is true of the Medicines Strategy Scoping Briefing 2024, which is a high-level system overview, and the PHARMAC Review Final Report 2022, which reviews medicines policy and institutions but does not appear to set out a drug–drug interaction epidemiology framework or a subgroup safety architecture for pregnant women, adolescents, or patients with complex multimorbidity. In short, these documents discuss the medicines system, but they do not appear to map the real-world burden of interaction-related harm across vulnerable groups.

As a result, patients and clinicians lack access to clear, stratified information on how risks vary across age, sex, and physiological state, despite these factors being central to safe prescribing.

The features outline above, result in a pharmacovigilance system that lacks coherence and transparency. The system captures a narrow subset of serious events but does not provide a comprehensive account of medicine-related harm in real-world settings.

There is a disconnect between:

- what is experienced by patients and clinicians
- what is visible in regulatory datasets
- and what is reflected in policy analysis

This limits the ability of:

- regulators to identify emerging risks
- Pharmac to make fully informed funding decisions
- clinicians to understand benefit–risk profiles
- patients to give informed consent

In effect, the current system does not provide a sufficiently complete or accessible evidence base to support safe and transparent decision-making.

The current pharmacovigilance system does not provide a complete or reliable account of medicine-related harm. It under-captures non-serious but clinically meaningful effects, does not systematically identify drug–drug interaction risks, lacks stratified data by age and sex, and is not subject to independent performance review. These are institutional limitations that go to the core purpose of medicines regulation and cannot be addressed through guidance alone. They require explicit statutory direction.

The Medical Products Bill should establish a mandatory, low-friction reporting system embedded within prescribing and dispensing workflows. Reporting obligations must extend beyond serious

adverse reactions to include clinically significant interaction events, discontinuation syndromes, pregnancy exposures and outcomes, and harms in children, adolescents, and young adults. Without this, the system will continue to capture only a narrow and delayed subset of harms.

The Bill should also require routine publication of de-identified, aggregated safety data, stratified by medicine, event type, age, sex, pregnancy status, and interaction class. Transparency of this kind is essential for informed consent, clinical decision-making, and early signal detection. A system that does not make these patterns visible cannot support safe and evidence-based care.

Vulnerable populations must be explicitly addressed. Pregnancy, childhood, adolescence, and early adulthood are periods of heightened biological sensitivity, yet pre-market evidence is often limited. The Bill should therefore require subgroup-tagged reporting, active follow-up of emerging safety signals, and publication of stratified summaries to identify whether harms are clustering in specific populations.

Finally, the legislation should require independent evaluation of pharmacovigilance system performance, including under-reporting rates, timeliness, follow-up completeness, and adequacy of public reporting. Given the scale of national expenditure on medicines relative to the comparatively small and opaque resourcing of safety monitoring, Parliament should ensure that the pharmacovigilance function is both adequately resourced and transparently assessed.

Without these reforms, safety monitoring will remain partial and reactive. A modern Medical Products Act should instead ensure that the full spectrum of medicine-related harm is visible, measurable, and actionable, so that regulatory decisions, clinical practice, and patient consent are grounded in a complete and accessible evidence base.

[4] EVIDENCE FOR INADEQUATE POLICY FORMULATION IN MINISTERIAL DOCUMENTS

(i) Biologic Medicines

Biologic medicines present distinct and often irreducible uncertainties compared with conventional small-molecule drugs. Their effects can depend not only on the active substance but on complex biological processes involved in manufacturing, cellular expression, and host response, meaning that variability, immunogenicity, long-tail adverse effects, and process-related changes may only become apparent over time or through post-market observation.

These characteristics make uncertainty itself a central feature of biologic regulation. For this reason, it is important that the parent legislation explicitly recognise these uncertainties and provide clear statutory direction enabling regulators to act precautionarily where evidence is incomplete. These expectations can be drafted as principles and explicit considerations relating to uncertainty, post-market evidence generation, and transparency in the parent Act, in order to help ensure that officials have both the authority and the obligation to require stronger disclosure, monitoring, and scrutiny in the public interest as scientific understanding evolves.

The publicly released Cabinet papers, Regulatory Impact Statements and associated briefings which currently inform the establishment of the proposed Medical Products Bill do not identify any systematic review of the scientific literature addressing the risk profile of biologic medical products (biologics). While the documents recognise biologics as a category of product and propose flexible, risk-proportionate regulatory pathways, they do not demonstrate that the

underlying policy design has been informed by an in-depth appraisal of the scientific evidence relating to the distinctive hazards associated with biologics, such as manufacturing complexity, biological heterogeneity, immunogenicity, or process-related impurities.

This absence of a documented evidence review raises a concern that the drafting of the Bill may not fully reflect the complexity of biologic drug regulation. Although it may be assumed that these issues will be addressed in secondary legislation, the published material provides no indication that regulatory frameworks will be established that would ensure that recognised categories of biologics risk are systematically considered. At a minimum, the parent legislation could articulate high-level principles and specify key domains of risk, through indicative lists or statutory considerations, to ensure that the known scientific and regulatory challenges of biologic medicines are explicitly traversed when developing subordinate rules and regulatory standards.

The Medical Products Bill material recognises:

- Biologics and innovative therapies as distinct product types requiring tailored regulatory pathways and risk management.
- The intention that risk-proportionate regimes (both for clinical trials and for product authorisations) will be in place.
- That regulatory flexibility and future-proofing will be drafted into the Bill's architecture via secondary legislation and bespoke pathways because innovation inherently involves technical uncertainty.

What remains mostly absent from current public material. None of the released documents yet:

- Spell out biologics hazard taxonomies (e.g., immunogenicity, residual DNA/RNA, aggregate/particle controls, heterogeneity metrics, etc.).
- Embed uncertainty quantification frameworks (e.g., uncertainty ranges, evidence quality gradation, decision thresholds).
- Require specific lifecycle evidence obligations for biologics beyond general risk pathways.

Those details are still expected to be developed in secondary legislation and regulatory standards because Cabinet/RIS deliberately delegated technical specifics to rules and regulations that the Bill will enable.

Risk categorisation from the identification of detectable fragments to where a biologic will result in a meaningful clinical hazard remains a contested issue, due to the variation in biologic medicines, including between samples supplied to secure regulatory approval and commercial releases, and between batches released across specific regions.

Not all biologics have genome-level or heritability-type risks. Those are primarily concerns for gene therapies / genome editors / integrating viral vectors, rather than for most recombinant proteins or monoclonal antibodies.

The regulator (and delegated legislation) to explicitly address, for each biologic class, at least:

- ✓ Cell substrate / template controls (cell banks, plasmid/template controls, traceability)

- ✓ Adventitious agent strategy (testing + validated clearance)
- ✓ Process impurity specifications (HCP, residual DNA/RNA, endotoxin, particulates/aggregates)
- ✓ Platform-specific impurities (e.g., dsRNA for IVT mRNA)
- ✓ Stability/cold chain obligations (degradation, potency drift, in-use stability)
- ✓ Traceability by batch number
- ✓ Biodistribution/persistence + pharmacovigilance triggers (including subgroup monitoring where plausible)

1) Prone to non-RNA/DNA contamination (incl. reagents, particulates/nanoparticles). Some impurities are immunogenic (can trigger unwanted immune responses). Particulates/aggregates in the formulation can alter potency and reactogenicity. These issues have been a recurring quality challenge in biologics manufacturing.

Biologics are manufactured using complex biological systems and multi-step processes (cell culture/fermentation; purification; formulation; fill-finish). That creates exposure to process-related impurities and particulates (e.g., host cell proteins, media components, chromatography leachables, endotoxin, protein aggregates, and other particulates).

2) Prone to RNA/DNA contamination (residual nucleic acids).

Residual DNA/RNA can arise from cell substrates (for cell-derived biologics) or from templates/reagents (e.g., plasmid DNA templates for IVT mRNA manufacturing). Regulators treat residual nucleic acids as a known, controllable impurity class.

There are longstanding expectations to reduce residual DNA to very low levels; WHO and regulators have historically used benchmarks such as ≤10 ng DNA per dose (context-dependent) and additional considerations around fragment size and biological activity, however the safety of these levels remain contested.

There is a live technical dispute in the literature and public arena about the measurement, interpretation, and significance of residual DNA fragments in some testing claims related to COVID-19 mRNA vaccines. Some reviews note that whether any detected plasmid DNA fragments have clinical significance 'remains to be defined', while regulators (e.g., Australia's TGA) have published testing summaries indicating batches tested met WHO limits.

3) Breakdown / decay (stability, degradation products, potency drift).

Many biologics are inherently less stable than small molecules. They can degrade (chemical modifications, deamidation/oxidation), aggregate, or lose functional conformation; nucleic-acid products can undergo hydrolysis; delivery systems (like LNPs) can change with storage. This makes cold chain, shelf-life, and in-use stability central to risk control.

Degradation can change dose delivered, immunogenicity, and effect duration.

4) Exposure extent and duration (biodistribution, persistence, and variability)

For biologics, 'dose' is often not the whole story, distribution into tissues, persistence, and immune activation can differ by age, sex, immune status, co-morbidities, and product platform.

For mRNA–LNP products specifically, the literature highlights remaining gaps around biodistribution and the biology of the platform (what cells take it up; how long components persist; how innate sensing contributes to both efficacy and reactogenicity).

The variability in expression/persistence is a plausible research and surveillance concern. Regulators generally try to address this through platform characterization, nonclinical packages, pharmacovigilance, and batch release controls.

5) Heritability / intergenerational risk (DNA/RNA & epigenetic)

Gene therapies and advanced therapy medicinal products, especially integrating viral vectors, genome editors, or therapies with durable genetic changes, because the hazard pathway includes insertional mutagenesis, off-target edits, long-term expression, and (in some cases) theoretical germline exposure concerns that are managed by specific nonclinical and long-term follow-up expectations. Gene therapies include mRNA vaccines, yet regulators have generally classified these as non-replicating, and considered that their heritability risk is generally treated as theoretically remote. However, the persistence of, for example, the vaccine derived spike protein, has resulted in ongoing questions about impurities, biodistribution, and persistence, which necessarily entails ongoing study and surveillance of these agents.

6) Adventitious agents (viral, microbial, prion/TSE risks)

Biologics can be exposed to adventitious viruses or other agents via raw materials, cell banks, or process failures; this is a foundational biologics risk addressed through cell bank control, testing, and viral clearance validation.

7) Immunogenicity and hypersensitivity (including anti-drug antibodies)

Biologics can provoke immune responses against the product (neutralising antibodies, loss of efficacy, immune-mediated adverse events). This is a core differentiator from many small molecules. Biologic platforms may have distinctive rare serious risks that require tailored surveillance and risk management, yet these might not be detected in smaller clinical trials.

8) Platform-related innate immune activation (not just "side effects")

For nucleic-acid platforms, impurities like dsRNA and aspects of formulation can drive innate sensing and inflammation; manufacturing and purification strategies explicitly target these impurities.

9) Lot-to-lot variability and comparability after manufacturing changes

Biologics are sensitive to process changes ("the process is the product"). Small manufacturing changes can alter glycosylation patterns, folding, impurity profiles, or potency, hence the heavy emphasis on comparability exercises and specifications.

10) Delivery-system toxicology (for complex formulations)

Where delivery vehicles are used (e.g., LNPs), the carrier itself can contribute to reactogenicity/toxicology and influence tissue targeting, relevant for risk-proportionate controls.

(ii) Natural Health Products

Natural health product policy development, as reflected in currently disclosed Ministry of Health materials, does not provide a sufficiently robust scientific or legal foundation for legislative reform.[4]

The documents available do not demonstrate a structured approach to risk assessment, nor do they adequately address the central regulatory task: determining when medicines-level regulation is justified.

Evidence base is largely descriptive while lacking analytical substance. Reports such as the Sapere reviews catalogue regulatory approaches and instances of harm but do not apply a coherent framework grounded in toxicology, dose–response relationships, or exposure assessment. Critically, they do not distinguish between fundamentally different categories of risk, including intrinsic toxicity, product contamination, misuse, or interaction with pharmaceuticals. These distinctions are essential for proportionate regulatory design. Without them, heterogeneous risks are treated as a single regulatory problem, leading to overgeneralised conclusions.

Key omission: The failure to interrogate the statutory trigger of 'therapeutic purpose'. This definition, which captures substances influencing physiological, metabolic, or immunological processes, has long driven the classification of natural health products as medicines. However, these processes are intrinsic to normal human biology and nutrition. The absence of analysis on whether this trigger remains scientifically valid or legally proportionate means that the policy framework does not adequately test whether it risks systematically over-capturing low-risk substances.

No clear demonstration that officials have applied a proportionality framework. Modern regulatory systems distinguish between levels and types of risk and align regulatory burden accordingly. The current materials do not assess whether medicines-level controls are justified for natural health products, nor do they explore alternative tiered models based on toxicology and exposure science. This creates a material risk that regulatory responses will be disproportionate to actual harm.

Treatment of adverse events highlights current system limitations. While harms are identified, the analysis does not calibrate their significance. Case reports, heterogeneous datasets, and uncertainty regarding under-reporting are presented without resolving their relevance to regulatory thresholds. Without a comprehensive scientifically robust evaluation of evidence quality, dose, substance specificity, and co-exposures, it is not possible to determine whether observed harms justify product-specific controls, broader category restrictions, or non-regulatory interventions.

The comparative regulatory analysis is similarly incomplete. Although international approaches are described, there is no evaluation of whether these frameworks are sufficiently integrative, scientifically grounded, or proportionate for New Zealand from 2026 and beyond. In particular, the European approach, where classification is linked to pharmacological effect and dose rather than mere biological activity, is not substantively examined. As a result, the materials

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[4] Ministry of Health (2025). Documents on natural health products. https://www.health.govt.nz/regulation-legislation/medicines-legislation/regulating-medicines-medical-devices-and-natural-health-products/documents-on-natural-health-products. https://www3.parliament.nz/en/pb/sc/submissions-and-advice/document/53SCHE_ADV_130084_HE45248/ministry-of-health-departmental-report-appendix-6

document regulatory diversity but do not extract principles capable of informing New Zealand legislation.

Unresolved issues of transparency and evidential completeness. The absence of clear disclosure of expert inputs, combined with the omission of relevant materials from the declared policy record, raises concerns as to whether the policy process has been sufficiently rigorous, balanced, and open to scrutiny. Where legislation is developed on a partial or undisclosed evidential base, it risks failing to take into account relevant considerations and may lack procedural integrity.

As the Ministry-sponsored reviews discussed below reveal, the current policy materials do not provide a sufficiently robust foundation for legislative design. They do not resolve the key questions of classification, proportionality, or scientific coherence that are central to regulating natural health products. Without addressing these issues, there is a significant risk that new legislation will perpetuate existing conceptual errors, extend medicines regulation beyond its proper scope, and fail to align regulatory control with actual risk.

Sapere Review: Evidence of harm in relation to the use of natural health products (2023).

The Sapere review: *Evidence of harm in relation to the use of natural health products A rapid literature review* (April 2023)[5], functions as a catalogue of reported harms rather than a scientifically rigorous risk assessment. It does not apply a toxicological framework, does not differentiate between types of risk, and does not engage with the core regulatory question of proportionality.

This report was released as Appendix Six to the Ministry of Health's Departmental Report to the Health Committee on the Therapeutic Products Bill, and has been incorporated as a commissioned report for use in development of natural health products regulation.[6]

As a result, it provides an incomplete and potentially misleading account of the challenges that many countries, including European regulatory systems have sought to address, and it is not, on its own, a sufficient basis for designing or justifying regulatory reform.

It does not provide a sufficiently robust basis for policy design.

The report itself signals important methodological constraints which are not meaningfully carried through into the analysis. It is explicitly a rapid review, does not formally assess the robustness of included studies, and acknowledges definitional inconsistency across jurisdictions. These limitations are not incidental; they go directly to the reliability and comparability of the evidence base. Yet the report proceeds to draw generalised conclusions about risk without stratifying evidence quality, distinguishing between study types, or resolving definitional ambiguity. The result

[5] Sapere review: Evidence of harm in relation to the use of natural health products A rapid literature review (April 2023),
[6] Ministry of Health (2025). Documents on natural health products. https://www.health.govt.nz/regulation-legislation/medicines-legislation/regulating-medicines-medical-devices-and-natural-health-products/documents-on-natural-health-products. https://www3.parliament.nz/en/pb/sc/submissions-and-advice/document/53SCHE_ADV_130084_HE45248/ministry-of-health-departmental-report-appendix-6

is an aggregated narrative of harm that lacks the intelligence required for regulatory decision-making.

The paper identifies four broad categories of harm: adverse events, interactions with medicines, manufacturing and contamination risks, and substitution for clinical care. These categories are valid at a descriptive level. However, the analysis does not progress to risk calibration. There is no systematic attempt to distinguish between intrinsic toxicity, dose-dependent effects, product quality failures, or misuse. These are analytically distinct categories with materially different regulatory implications. Their conflation leads to an implicit framing in which heterogeneous risks are treated as a single regulatory problem, rather than as a set of differentiated issues requiring targeted responses.

This becomes particularly evident in the treatment of adverse events. The report acknowledges that serious adverse events are generally low in incidence, but then introduces uncertainty around underreporting without resolving its magnitude or implications. Similarly, the discussion of hepatotoxicity draws heavily on case reports and heterogeneous datasets but does not disentangle dose, compound specificity, co-administration with pharmaceuticals, or contamination.

From a toxicological and regulatory perspective, these omission are significant. Without a dose–response framework or substance-specific analysis, it is not possible to determine whether observed harms justify product-specific controls, broader category restrictions, or non-regulatory interventions.

Critically, the review does not engage with the central issue that has shaped European regulatory debates: the boundary between food, supplement, and medicine. European frameworks have developed around the principle that classification should depend on pharmacological effect and dose, not merely on biological activity. This reflects an attempt to preserve proportionality, ensuring that regulatory burdens correspond to demonstrable risk.

The Sapere paper does not address this problem. It notes international inconsistency in definitions but does not analyse how or why those distinctions are made, nor does it consider the consequences of collapsing them.

The paper also conflates distinct regulatory domains. Risks arising from contamination, adulteration, or poor manufacturing practice are presented alongside risks arising from intrinsic properties of substances and from patterns of consumer behaviour. In practice, these are governed through different mechanisms: manufacturing standards and enforcement for contamination; dose limits and classification for intrinsic toxicity; labelling and clinical guidance for interactions; and public health interventions for substitution behaviours. By grouping these together, the report implicitly supports a generalised precautionary stance rather than a proportionate, risk-differentiated framework.

The treatment of regulatory responses is correspondingly underdeveloped. While the report notes calls in the scientific literature for greater oversight, testing, and education, it does not examine whether the identified harms necessitate medicines-level regulation or whether they could be addressed through more targeted measures.

The key policy question, whether regulatory intensity is proportionate to risk, is not engaged with. Instead, the logic tends toward an unexamined assumption that the presence of harm justifies an escalation of regulatory control.

In this respect, the review does not adequately reflect the European experience, where over-regulation concerns arise precisely from the difficulty of maintaining proportionality in the face of biological complexity and heterogeneous evidence. The European approach has been shaped by attempts to avoid classifying all biologically active substances as medicines while still managing genuine risks. That tension, central to the policy debate, is largely absent from the Sapere analysis.

International approaches to Natural Health Product regulations: Regulatory scan (2024).

The Sapere report: International approaches to Natural Health Product regulations: Regulatory scan[7] provides a competent survey of international regulatory arrangements. However, it does not engage with the core scientific, legal, and policy questions necessary to inform legislative design. The *Regulatory Scan* catalogues how systems operate but does not evaluate whether they are coherent, proportionate, or grounded in an appropriate understanding of biological function and risk. As such, it is insufficient as a stand-alone basis for policy formulation in this area.

The *Regulatory Scan* provides a useful descriptive overview of how different jurisdictions approach the regulation of natural health products. It maps the diversity of international frameworks, outlining how products may be classified as foods, medicines, or other categories depending on factors such as claims, composition, format, and history of use. It also usefully documents the range of regulatory mechanisms in place, including listing and licensing systems, monographs, traditional use pathways, and manufacturing and labelling requirements, and highlights the existence of 'interfaces' and 'grey areas' between regulatory regimes. In this respect, the report succeeds as a comparative inventory of regulatory approaches and illustrates the practical complexity faced by regulators and industry across jurisdictions.

However, the report does not progress beyond description into substantive analysis of the underlying regulatory problem. While it acknowledges that classification is complex and inconsistent across jurisdictions, it does not interrogate the causes or consequences of that inconsistency. In particular, it does not examine whether the widespread reliance on 'function' or 'claims' as a classification trigger is scientifically or legally coherent, nor whether this approach results in the systematic over-capture of substances, such as nutrients, that act through normal physiological pathways. The report therefore records the existence of definitional ambiguity but does not assess whether that ambiguity reflects a deeper underlying defect in regulatory design.

Critically, the report does not engage with the central question of proportionality. It outlines varying degrees of regulatory control, from minimal oversight of food supplements in some jurisdictions to more stringent authorisation pathways for certain products, but does not evaluate whether these differing levels of control are justified by corresponding differences in risk. There is no attempt to distinguish between intrinsic toxicity, dose-dependent effects, manufacturing quality failures, or patterns of misuse, nor to align regulatory responses with these distinct

[7] Sapere. 2024. International approaches to Natural Health Product regulations: Regulatory scan. Wellington: Ministry of Health. https://www.health.govt.nz/system/files/2024-06/international_approaches_to_nhp_regulations.pdf

categories of risk. Without such a framework, the report does not provide a basis for determining when medicines-level regulation is warranted and when it is not.

The absence of a clear scientific framework is particularly evident in the treatment of biological activity. The report adopts, without critique, definitional approaches that classify products as medicinal where they exert pharmacological, immunological, or metabolic effects. It does not distinguish between pharmacological intervention and normal physiological or nutritional function, despite this being a central issue in contemporary regulatory debates. As a result, it implicitly reinforces a categorisation model that risks conflating nutrition with pharmacology, without assessing whether such an approach is scientifically defensible or proportionate.

Further, although the report identifies 'grey areas' at the interface between foods, medicines, and other product categories, it does not evaluate whether the criteria used to resolve these boundaries, such as claims, presentation, or perception, are capable of producing consistent and predictable outcomes. Nor does it consider whether such criteria may introduce arbitrariness or allow regulatory scope to expand beyond its intended limits. The implications of this for legal certainty, administrative consistency, and the proper scope of regulatory authority are not addressed.

Finally, the report does not examine the institutional or evidential foundations of the regulatory approaches it describes. There is no discussion of the expertise informing these systems, no assessment of whether nutritional science is adequately represented in policy development, and no consideration of whether existing frameworks are disproportionately shaped by pharmaceutical paradigms. In the absence of such analysis, the report cannot assess whether current regulatory models are appropriately calibrated to the substances they govern.

[5] NUTRITIONAL SCIENCE AND THE DEFINITION OF 'THERAPEUTIC PURPOSE'.

The statutory definition of "therapeutic purpose" in the Medicines Act 1981 permits a substance to be classified as a medicine where it is intended to influence physiological, metabolic, or immunological processes. While administratively convenient in the context of pharmaceutical products, this formulation is overbroad in legal and scientific terms, as it captures substances whose biological activity reflects normal physiological function rather than pharmacological intervention.

Regulatory Trigger Blind to Biological Processes Essential for Human Health

The effect of the current definition is to establish a regulatory trigger that does not distinguish between endogenous biological processes essential to health and exogenous pharmacological interventions intended to modify disease states. By treating the mere presence of biological activity as evidence of therapeutic pharmacology, the statute collapses a fundamental scientific distinction and extends the scope of medicines regulation beyond its proper domain. This conflation creates a material risk of systematic misclassification, particularly in relation to low-risk substances.

As a matter of scientific principle, this definitional approach conflates two distinct categories. Nutrients, including vitamins, minerals, and related compounds, operate through physiological, metabolic, and immunological pathways because these are the biochemical systems that sustain life. Their functions include enzyme cofactor activity, mitochondrial energy production, immune

regulation, gene expression, and endocrine signalling. These roles are intrinsic and constitutive of normal biological function, not indicative of pharmacological intervention.

By contrast, pharmaceutical agents are designed to exert targeted effects on specific receptors or pathways in order to alter pathological processes. They act by modulating, inhibiting, or overriding biological systems, often at doses that exceed physiological norms. The failure to distinguish between these modes of action, supporting physiological sufficiency versus inducing pharmacological change, results in a category error that lacks scientific justification.

Accordingly, a regulatory trigger based on the existence of physiological or metabolic activity captures the defining characteristics of nutrition itself, rather than identifying substances that present pharmacological risk. Contemporary biomedical science, including nutritional biochemistry and systems biology, recognises that micronutrients function as integral components of complex regulatory networks governing cellular metabolism, redox balance, immune competence, and gene regulation. These are not incidental effects; they are the primary biological roles of these compounds.

If Ministry officials elected to retain the 'therapeutic action' as the operative criterion for classification would perpetuate an error which has improperly extended the scope of medicines regulation for decades. It would fail to align regulatory scope with established scientific understanding and would risk extending medicines control to substances whose effects are foundational to normal human physiology.

Definitions Not Based on Real Risk via Toxicology and Risk Assessment

The current definition of a medicine which applies a 'therapeutic purpose' definition is not grounded in toxicology or risk assessment. In toxicological science, regulatory attention is typically triggered by evidence of intrinsic hazard, dose-dependent toxicity, or demonstrable potential to cause serious harm to human health.

The definition has had systemic consequences for health governance. Micronutrients at nutritional or moderate supplemental levels generally operate within established physiological ranges and are evaluated using safety frameworks such as upper intake levels rather than drug toxicity paradigms.

The Medicines Act 'therapeutic action' trigger is not linked to hazard or dose–response risk; it is linked only to biological effect. Because biological effect is intrinsic to all nutrients, the regulatory threshold becomes detached from scientifically meaningful measures of risk.

Misleading Risk Signals

A scientific and health-based consequence has involved the creation of misleading risk signals within the regulatory system. When a micronutrient product is categorised as a medicine, the classification implicitly associates that product with the pharmaceutical risk framework used for drugs, including assumptions regarding adverse drug reactions, side-effect monitoring and prescription oversight. Yet the safety evaluation of nutrients is based on nutritional physiology and exposure ranges rather than pharmacological toxicity.

The classification has communicated regulatory status rather than scientific hazard, potentially distorting clinical and public understanding of risk. Clinicians have recently advised patients that a nutrient supplement with an excellent safety profile, that was recently recategorized as a medicine due to 'therapeutic purpose' that they were unwilling to prescribe this now-medicine, as it must have carried a medical risk.

Finally, the definitional model is inconsistent with contemporary scientific understanding of health and disease, which increasingly recognises nutrition as a foundational determinant of biological resilience and disease prevention. A regulatory system that treats nutrients as medicines solely because they influence physiological or metabolic pathways risks embedding a pharmaceutical paradigm into areas of health that are fundamentally governed by nutritional biology. From a scientific standpoint, a modern regulatory framework should instead distinguish clearly between nutritional regulation of physiological systems and pharmacological intervention in disease processes, ensuring that classification thresholds reflect mechanism, dose–response relationships and genuine toxicological risk.

[6] INDUSTRY / SECTOR ADVOCACY

Medicines, Including Biologic Products

There is no published declaration or transparency regarding the extent of private communications with sector lobbyists or advisors who may have informed the current policy formulation. However, given that the policies emphasise reducing barriers for innovative medicines and clinical trials, it is reasonable to infer that there has been some involvement from experts within the pharmaceutical and biologics sectors.

Natural Health Products

The natural health products sector has not been invited to meet with Ministry of Health officials in order to discuss new regulatory options for natural health products.

In August 2025 a *Natural Health Alliance document Towards Regulatory Excellence: Learning from Experience,* made a clear and practical case that New Zealand's current and proposed regulatory settings for natural health products are not fit for purpose. [8]

It identified that the existing framework, particularly the reliance on 'therapeutic' classification, created uncertainty, that it restricted access, and risked inappropriately capturing low-risk products within medicines regulation.

The *Towards Regulatory Excellence* paper's central aim appears to be the establishment of a stand-alone, proportionate regulatory regime for natural health products, distinct from medicines, and capable of supporting both domestic access and export growth. It emphasises the economic importance of the sector, the need for regulatory certainty, and the removal of barriers created by inappropriate classification, particularly where products are captured under medicines frameworks due to their perceived 'therapeutic' effects.

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[8] Natural Health Alliance (August 22, 2025). Towards Regulatory Excellence: Learning from Experience A Policy Proposal Regarding the Future Regulation of Natural Health Products. https://www.naturalhealthalliance.co.nz/wp-content/uploads/2025/12/A-Policy-Proposed-Natural-Health-Products-Regulatory-Reform-2025-Merged-Document-02.pdf

The paper highlighted international approaches that provide more flexible mechanisms, such as listing systems, monographs, and traditional use pathways.

It draws attention to the potential consequences of misaligned regulation, including reduced consumer access, constraints on practitioners, and diminished competitiveness for New Zealand manufacturers in export markets.

In this respect, the document aligns with a legitimate and widely recognised problem: the current system is fragmented, outdated, and not well calibrated to the characteristics of natural health products.

The document identifies practical regulatory constraints. These include overly restrictive permitted ingredient lists, labelling requirements that exceed international norms, and the risk that New Zealand becomes an outlier jurisdiction that discourages product availability and export participation. The concern that regulatory settings may be more restrictive than comparator jurisdictions is particularly relevant, and reflects a genuine risk of regulatory isolation in a small market.

The emphasis on enabling access to products at 'therapeutic' doses also reflects a real tension in the current system, where classification rules can limit availability even where risk is low.

The document contributed a useful, practice-oriented perspective on the operational challenges faced by the sector and underscores the need for a more proportionate and workable regulatory model. It is not published on the Ministry of Health website.

As with current papers listed on the Ministry of Health website, the Natural Health Alliance paper does not clearly articulate a coherent alternative classification framework grounded in dose, exposure, risk and biological context. Nor does not resolve the central issue of how to distinguish between physiological (nutritional) effects and pharmacological effects. This paper therefore risks leaving intact the same definitional ambiguity that underpins the current 'therapeutic category trap'.

[7] NAVIGATING NATURAL HEALTH PRODUCT RISK: HEPATOTOCITY, ENDOCRINE, & DRUG INTERACTION RISK

The existence of hepatotoxicity signals, endocrine activity, or interaction potential does not justify default classification as a medicine. These risks are, in most cases, amenable to standard risk management tools used across food and public health systems.

While some botanicals and isolates can cross into pharmacological territory at higher doses or specific formulations, a regulatory framework that requires nutrient-based or traditionally used substances to undergo full medicines regulatory processes in the absence of clear pharmacological hazard constitutes a disproportionate extension of regulatory power and reinforces the same overbroad definitional problem identified in the Medicines Act.

Across the main areas of concern, which are included in the Sapere report[9], hepatotoxicity, endocrine effects, and pharmacological interaction risk, the scientific literature does not support a default escalation of natural health products into full medicines regulation.

Rather, these risks are dose-dependent, context-dependent, and in many cases well characterised within existing nutritional and toxicological frameworks.

In each of these domains, the appropriate regulatory response is not automatic classification as a medicine, but the application of proportionate, risk-based controls, including:

- clearly defined upper safe intake levels or dose limits
- quality assurance and standardisation (identity, purity, contaminants)
- evidence-based labelling and contraindications
- post-market monitoring where appropriate

This approach is entirely consistent with how other widely consumed substances are managed. Alcohol, food additives, and even common dietary components such as sugar carry well-established risks at excessive intakes, yet they are not regulated as medicines. The presence of risk at high exposure does not, in itself, justify pharmaceutical regulatory treatment.

From a scientific and regulatory standpoint, the critical distinction is between:

- manageable, dose-dependent risk within a known safety envelope, and
- intrinsic pharmacological hazard requiring medical supervision

Where a substance has a long history of safe human use, a well-characterised safety profile, and risks that are predictable and controllable through conventional safety measures, escalation into medicines regulation represents a disproportionate regulatory response.

Hepatotoxicity, while a serious endpoint, is typically associated with specific extracts, high-dose preparations, contaminants, or idiosyncratic reactions, rather than the intrinsic properties of botanicals or nutrients used within established exposure ranges. Similarly, endocrine activity (e.g. phytoestrogens) reflects normal biological signalling interactions, not inherently hazardous pharmacology. Interaction risks, such as those seen with St John's Wort, are well described and manageable through labelling, contraindications, and clinical guidance.

This is particularly important in the case of nutrients or naturally derived compounds that have been isolated or standardised. Isolation does not, in itself, transform a substance into a pharmacological agent. The relevant questions remain:

i. Does the substance exhibit pharmacological potency at the proposed dose?
ii. Is there evidence of serious or unpredictable harm?
iii. Does its use require medical supervision to manage risk?

Absent such characteristics, requiring compliance with a medicines regulatory regime reflects an overextension of pharmaceutical regulatory frameworks into domains more appropriately governed by food and nutritional safety law.

[9] Sapere review: Evidence of harm in relation to the use of natural health products A rapid literature review (April 2023),

[8] BARRIERS TO INCLUSION OF NUTRIENTS ON THE PHARMAC SCHEDULE

The current regulatory pathway to securing funding under the Pharmac Schedule does not prevent nutrients from being funded, but it does not systematically enable their evaluation or inclusion.

Current legislation does not recognise nutrients as a distinct category, nor provide tailored assessment frameworks, and permit decision-makers to consider a broader evidential base, including mechanistic, clinical, observational, and long-term use data.

As a result, access to funding is often contingent not on evidence or safety, but on whether a sponsor is able and willing to navigate the system.

At its core, the current framework does not support a public-health–driven approach to funding decisions, rather than one dependent primarily on the presence of a commercial sponsor.

(a) Legislative architecture: An application-driven system favouring medicines

New Zealand's parent medicines legislation does not establish a clear or distinct pathway for the inclusion of nutrients within the publicly funded Pharmaceutical Schedule. The Medicines Act 1981 regulates approval, classification, and supply, but does not address funding. Funding decisions are instead made by Pharmac under the Pae Ora (Healthy Futures) Act 2022, through administrative policies and processes rather than through explicit statutory direction.

This separation creates barriers to the inclusion of nutrients that are frequently lower cost and not patent-protected, and raises questions about whether the current framework is capable of supporting a truly risk-proportionate model, in which regulatory and funding intensity are aligned with actual risk profiles.

While medicines regulation is codified in primary legislation, the inclusion of substances, including nutrients, within the funded Schedule is governed by lower-order policy instruments, including Pharmac's Operating Policies and Procedures and advisory committee processes. There is no statutory mechanism requiring the system to identify, evaluate, or fund nutrients on a public-health basis.

Entry into the Pharmaceutical Schedule is application-driven. The system prioritises interventions that are supported by commercial infrastructure, rather than those supported by public-health need or evidential sufficiency.

Although applications can technically be made by any party, most originate from pharmaceutical suppliers with the resources to prepare regulatory dossiers, generate or synthesise evidence, and engage with the assessment process. This creates barriers for nutrients and low-margin formulations as they:

- Are typically not patent-protected.
- Lack dedicated commercial sponsors.
- Do not carry embedded marketing or regulatory budgets.

As a result, even where there is a substantial scientific literature and a long history of safe use, these products may never be formally evaluated for funding.

(b) Cost barriers and Alignment with Clinical Evidence Norms

The preparation of a funding application requires significant technical, regulatory, and evidential work. While official fee schedules relate primarily to regulatory approvals rather than funding applications per se, they illustrate the broader point: the system is designed around resource-intensive evaluation pathways.

Pharmac's assessment framework draws on health technology assessment principles, including clinical benefit, cost-effectiveness, and budget impact. These frameworks are well suited to conventional pharmaceuticals developed through formal trial pipelines. However, they are less well aligned with:

- Nutrients and non-patentable substances
- Interventions supported by mechanistic, observational, and cohort data
- Products with a long history of safe use at therapeutic dose levels

Without explicit direction to consider these forms of evidence, the system risks undervaluing interventions that fall outside the standard pharmaceutical development model.

The limitations of the current framework are illustrated by several examples. While oral vitamin C is listed in the Pharmaceutical Schedule, there is no clear pathway for systematic evaluation or funding of intravenous vitamin C in hospital contexts, despite ongoing international research and clinical use. Melatonin has achieved funded status, but only through a narrow, highly restricted listing for specific paediatric neurodevelopmental conditions, reflecting a conventional pharmaceutical pathway rather than a broader nutrient framework.

Broad-spectrum multinutrient formulations (e.g. Hardy Nutritionals), despite a growing scientific literature and clinical application, have no clear route into funding in the absence of a sponsoring entity. Similarly, magnesium, an essential nutrient with a well-established safety profile at therapeutic doses and substantial evidence across neuromuscular, metabolic, and cardiovascular domains, lacks any systematic pathway for evaluation or inclusion.

Taken together, these examples demonstrate a consistent pattern: low-risk, evidence-supported interventions remain excluded not due to lack of evidence, but due to the absence of a sponsor-driven pathway within the current system.

(c) Off-patent medicines and off-label purposes

An important contrast arises with off-patent medicines used for non-indicated (off-label) purposes. New Zealand law permits such use, and the Pharmaceutical Schedule can fund medicines for uses that are not formally approved indications. This demonstrates that the system is capable of recognising clinical utility beyond the original approval pathway while supporting funded access in the absence of new proprietary evidence.

However, there is no equivalent approval pathway for nutrients. Substances with comparable or stronger safety profiles, and with supportive literature, may not be considered for funding unless they are carried through the same sponsor-driven application process. This creates disproportionate access pathways where conventional pharmaceuticals can be repurposed and funded, while biologically-relevant nutrients remain unassessed and unfunded, despite evidence of benefit.

(d) Consequences and implications for legislative reform.

The absence of a clearly delineated pathway for nutrients has several implications:

- Missed opportunities to support low-cost, low-risk interventions
- Over-reliance on pharmaceutical pathways, even where alternative approaches may be appropriate
- Misalignment between evidence and access, particularly where evidence exists but is not translated into funding decisions
- Inequity in system responsiveness, favouring commercially backed products over public-health interventions

These issues have resulted in an uneven system that favours commercially backed products over equally evidence-supported alternatives. If left unaddressed, officials will continue to operate across a regulatory and funding environment in which low-risk, evidence-supported interventions are overlooked, while resources and attention are disproportionately directed toward products that align with the existing commercial and regulatory model.

A modern Medical Products Act should address these gaps directly. At a minimum, it should enable non-sponsor-initiated evaluations of substances with strong safety profiles and credible evidence bases, recognising that not all clinically valuable interventions will be advanced by commercially resourced applicants.

Without such provisions, there is a significant risk that the new legislative framework will perpetuate an application-dependent system that does not fully reflect scientific evidence, biological reality, or public-health need.

[9] EUROPEAN FRAMEWORKS AS A GUIDE

The European Union operates a differentiated regulatory framework for substances at the interface of food, nutrition, and medicine. The EU model demonstrates a graduated, risk-sensitive approach to regulation, in which:

- ✓ foods and nutrients are governed by safety and exposure thresholds
- ✓ herbal and traditional products are accommodated through simplified pathways
- ✓ medicinal products are subject to more stringent controls where justified by risk

Rather than applying a single, over-inclusive definition, the EU system is structured around a clear legal distinction between food and medicinal products, with separate statutory pathways, evidential standards, and regulatory objectives for each domain.

While not without limitations, this framework provides a more proportionate and scientifically grounded model than systems that rely on broad definitions of biological activity to trigger medicines regulation.

1. Legislative Objectives and Regulatory Anchoring

The EU framework is anchored in two principal regulatory domains:

1) Food law, including food supplements and novel foods

2) Medicines law, including herbal medicinal products

The overarching objectives are to:

a. ensure a high level of protection of human health
b. safeguard consumer information and prevent misleading claims
c. support the functioning of the internal market
d. apply proportionate regulatory controls aligned to risk

Food supplements are regulated under Directive 2002/46/EC and related instruments, while medicinal products are governed by Directive 2001/83/EC, including the Traditional Herbal Medicinal Products Directive (2004/24/EC). This dual structure ensures that products are regulated according to their function, risk profile, and intended use, rather than through a single definitional trigger.

2. Risk Framework: Dose, Effect and Toxicological Assessment

The EU framework incorporates both risk-based and effect-based assessment, with different approaches applied across regulatory domains.

Within food law, risk is managed through:

- toxicological assessment, including evaluation of safety margins
- establishment of tolerable upper intake levels (ULs) for nutrients
- restrictions or prohibitions on substances where safety concerns arise
- assessment of exposure across the population

Within medicines law, classification as a medicinal product by function requires evidence that a substance exerts a sufficiently significant pharmacological, immunological, or metabolic action, taking into account:

- composition and potency
- dose and route of administration
- intended use and target population
- known risks and safety profile

This approach ensures that biological activity alone is not determinative; rather, the magnitude and nature of effect and associated risk are central to classification.

3. Dynamic Risk Assessment: Monographs, Registers and Jurisprudence

The EU framework evolves over time through a combination of scientific, regulatory, and judicial mechanisms.

Key instruments include:

- ✓ EMA (HMPC) herbal monographs and list entries, which compile evidence on safety, use, and conditions of use for herbal substances
- ✓ EFSA scientific opinions, which evaluate safety and substantiate health claims
- ✓ the EU Register of Nutrition and Health Claims, which records authorised and rejected claims
- ✓ Union lists for novel foods and permitted substances

- ✓ case law of the Court of Justice of the European Union, which clarifies the boundary between food and medicines

This system allows regulatory decisions to be updated in light of emerging evidence, ensuring that classification and control remain responsive to scientific developments.

4. Proportionality and Tiered Regulatory Pathways

A defining feature of the EU framework is the application of proportionality through tiered regulatory pathways.

- ➢ Food supplements are subject to safety, composition, and labelling requirements, but do not require demonstration of clinical efficacy
- ➢ Health claims must be substantiated through scientific evidence and authorised at EU level
- ➢ Traditional herbal medicinal products are eligible for a simplified registration pathway, based on long-standing use and safety, without requiring full clinical trial data
- ➢ Full medicines authorisation is required for products making stronger therapeutic claims or presenting higher risk

This graduated approach aligns regulatory burden with risk and intended use, avoiding unnecessary application of medicines-level controls to low-risk products.

5. Novel Foods Pathway

The EU provides a distinct regulatory mechanism for innovation through the Novel Foods Regulation (EU) 2015/2283.

This pathway applies to foods and ingredients not consumed to a significant degree within the EU prior to May 1997 and requires:

- ➢ assessment of composition and production processes
- ➢ evaluation of toxicology, allergenicity, and nutritional impact
- ➢ estimation of anticipated intake and exposure

Where appropriate, a simplified pathway exists for traditional foods from third countries with a documented history of safe use. The novel foods pathway enables new substances to be assessed within a food safety framework, rather than defaulting to medicines regulation.

6. Residual Uncertainty and Ongoing Disputes

Despite its structured and multi-layered design, the EU framework continues to experience boundary disputes and regulatory inconsistency, particularly in relation to botanicals.

- Classification of certain substances remains non-harmonised across Member States
- The same botanical may be treated as a food in one jurisdiction and a medicine in another
- Evaluation of botanical health claims remains incomplete, with some claims held in abeyance
- Borderline determinations continue to rely on case-by-case assessment

These challenges reflect the inherent complexity of regulating substances that sit between nutrition and pharmacology. However, the EU framework addresses this complexity through an

integrative criteria, scientific guidance, and judicial oversight, rather than by collapsing categories into a single regulatory regime.

[10] ROBUST EVALUATION AND ASSESSMENT – EUROPEAN EXAMPLE

Publicly disclosed documents relating to the policy formulation of a future Medical Products Bill do not demonstrate that officials have undertaken a systematic review of international regulatory practice beyond proximate jurisdictions such as the Australian Therapeutic Goods Administration.

Policy development for primary legislation should be grounded in comparative best practice, drawing on multiple competent regulatory systems and assessing their strengths, limitations, and relevance to New Zealand's context. In the absence of evidence that such comparative analysis has been undertaken, it is difficult for the public to have confidence that the proposed legislation will be fit for purpose and aligned with current scientific, legal, and regulatory standards.

This absence of comparator analysis raises a further concern. New Zealand frequently relies on, or aligns with, decisions made by overseas regulators. However, without transparent evaluation of which jurisdictions represent best available practice, and why their approaches are appropriate to adopt, such reliance risks becoming uncritical. This undermines confidence in decision-making, particularly where foreign regulatory positions are incorporated without clear justification or assessment of their applicability to New Zealand conditions.

European Regulations: Biologic Medicines

Biologic medicines are not regulated as if they were ordinary small-molecule drugs, and uncertainty is drafted into the legal architecture of the European Commission, as biologic medicines which carry a distinct range of risks.

EU drafts biologics regulation around five key issues. First, category differentiation: advanced biologics get bespoke statutory treatment. Second, risk-based uncertainty management: the required evidence is tailored to the product's identified risks and updated over time. Third, contamination and infectious-risk control: cell substrates, raw materials, viral testing, and clearance are built into quality requirements. Fourth, immunogenicity as a distinct hazard class: immune responses are treated as a central regulatory issue, not a side note. Fifth, traceability and post-market follow-up: long-tail uncertainty is managed through statutory pharmacovigilance and follow-up obligations.

For New Zealand, the implication upon reviewing the European approach is that a parent Act can do more than simply say 'risk-proportionate'. It can expressly require that biologics regulation address, at minimum, source-material risk, manufacturing-process variability, adventitious contamination, immunogenicity, traceability, and post-market evidence generation under uncertainty. The EU model shows that those matters can be signalled at a high level in the legislation, while leaving the technical detail to guidelines and secondary instruments.

In the EU, biologic medicines are not regulated as if they were ordinary small-molecule drugs. The framework is drafted on the premise that biologics are process-sensitive, heterogeneous, and uncertainty-laden, so risk control is spread across the parent legislation, ATMP-specific legislation where relevant, and detailed EMA/Commission guidelines. For conventional biologics, the legal base sits in Directive 2001/83/EC plus EMA quality/safety guidance. For advanced biologics such as gene therapies, somatic cell therapies and tissue-engineered products, the EU adds a bespoke

layer through Regulation (EC) No 1394/2007 and the ATMP amendments to Annex I of Directive 2001/83/EC. That is already an important lesson for New Zealand: the EU does not assume one generic medicines code is enough.

The clearest drafting device for uncertainty is the EU's risk-based approach for ATMPs. The amended Annex I to Directive 2001/83/EC allows the extent of quality, non-clinical and clinical data to be adapted to the identified risks of the product, and it expressly points to risk factors such as the origin of the cells, whether they are autologous/allogeneic/xenogeneic, their ability to proliferate or initiate an immune response, the level of cell manipulation, the combination with bioactive molecules or structural materials, the site of administration, and the duration of functionality and activity in target tissues. In other words, uncertainty is not treated as an afterthought; it is built into the legal architecture as something that must be analysed product by product.

That same risk-based logic is carried into current EMA guidance for investigational ATMPs. EMA states that, throughout development, a sponsor can adapt the quality, non-clinical and clinical dataset to the identified potential risks, based on an initial risk analysis that considers, for example, cell origin, vector type, genetic-modification method, manufacturing process, non-cellular components, and intended therapeutic use. EMA also says that this risk analysis should be updated throughout the product life cycle as new data become available. That is a sophisticated uncertainty model: not 'approve and forget', but iterative reassessment as knowledge changes.

On contamination and adventitious-agent risk, the EU framework is unusually explicit. For biotechnology-derived products from human or animal cell lines, the EMA-adopted ICH Q5A(R2) guideline requires testing and evaluation of viral safety, including data on cell-line qualification, testing for the presence of viruses, and virus-clearance measures. For investigational biologics, EMA states that viral safety is assured by three complementary approaches: selecting and testing cell lines and raw materials, testing the capacity of the manufacturing process to clear or inactivate viruses, and testing the product at appropriate stages of production. For ATMPs derived from tissues and cells, EU law also links back to the separate EU quality-and-safety framework for human tissues and cells.

The EU also drafts for manufacturing variability and contamination-like process risks by treating biologics as products in which the process is part of the product. EMA's comparability guidance says that when the manufacturing process changes, the manufacturer must generate evidence showing the change has no adverse impact on quality, safety or efficacy. For biosimilars, the quality guideline requires attention to manufacturing processes, analytical methods, physicochemical characterisation, biological activity, purity, and specifications. This is the legal-technical answer to heterogeneity: the system does not assume that a changed process or a "similar" biological can simply be inferred to be equivalent. It must be demonstrated.

On immunologic risk, the EU framework is also explicit. EMA's guideline on immunogenicity assessment of therapeutic proteins starts from the premise that, unlike most small molecules, therapeutic proteins can induce unwanted immune responses, including anti-drug antibodies that may affect safety, efficacy, and pharmacokinetics. The guideline requires an integrated

immunogenicity programme and specifically includes sections on risk factors, risk management, and pharmacovigilance. That is important because the law is not just looking for overt toxicity; it is designed to detect the distinct biologic problem of the body responding immunologically to the product itself.

The EU also builds post-authorisation uncertainty management into ATMP legislation itself. Regulation 1394/2007 contains express chapters on post-authorisation follow-up of efficacy and adverse reactions, and risk management, and on traceability. The point is that for advanced biologics, pre-market evidence is not treated as the whole story. The law anticipates that some risks, durability issues, delayed harms, and effectiveness questions will only become clear after use in real patients, so follow-up and traceability are statutory requirements, not merely optional guidance.

At the pharmacovigilance level, EMA's GVP module for biological medicinal products adds another biologics-specific protection: product traceability. It explicitly links biological pharmacovigilance to immunogenicity, manufacturing comparability, biosimilarity, and process validation, because safety signals in biologics can depend on the precise product, batch, and manufacturing history. That is a more exacting model than a generic adverse-event regime.

European Regulations: Natural Health Products

Within the European Commission framework, risk assessment for natural health products is conducted through a broad, integrative review of the scientific literature, rather than a narrow or single-tier evidential test. This work is primarily undertaken by the European Food Safety Authority (EFSA) for food supplements and by the European Medicines Agency (EMA), particularly its Committee on Herbal Medicinal Products (HMPC), for herbal medicines. The approach is explicitly weight-of-evidence based, drawing on multiple streams of data to assess safety, plausibility, and risk.

Classification as a medicine 'by function' requires an evaluation of whether a product exerts a sufficiently significant pharmacological effect. This is assessed case by case, taking into account composition, dose, use, and risk, and is informed by both scientific evidence and jurisprudence.

Within the food domain, risk is managed through toxicological thresholds, including tolerable upper intake levels and substance-specific restrictions, rather than treating physiological activity as inherently therapeutic. The framework is dynamic, evolving through EMA herbal monographs, EFSA scientific opinions, Union registers, and court decisions.

Proportionality is achieved through tiered regulatory pathways, including simplified registration for traditional herbal medicines based on long-standing use, and a distinct novel foods pathway for new substances assessed primarily on safety. While inconsistencies remain across Member States, the EU model demonstrates a more graduated and risk-sensitive approach than systems that treat any physiological effect as sufficient to trigger medicines regulation.

At its core, the EU approach involves a comprehensive interrogation of the scientific literature. Mechanistic evidence is routinely considered, including data on biochemical pathways, receptor interactions, enzyme activity, immune modulation, and metabolic processes. These data are used to establish biological plausibility, but are not determinative on their own; they are interpreted alongside human and safety data.

Human evidence forms a central pillar of assessment. This includes not only randomised controlled trials, but also cohort studies, case–control studies, epidemiological data, and population exposure information. The evidential threshold varies by pathway: EFSA emphasises demonstration of cause–effect relationships for health claims, while EMA allows reliance on long-standing human use where clinical data are limited, provided safety is adequately characterised.

Safety assessment also incorporates case-based evidence, including adverse event reports, case series, pharmacovigilance data, and poison centre records. These sources are particularly important for identifying rare, delayed, or interaction-related effects, and are routinely synthesised within EMA monographs.

Toxicological evaluation is a further core component, including hazard identification, dose–response assessment, and establishment of safe intake levels or margins of exposure. Consideration is given to cumulative exposure and to vulnerable populations, such as children and pregnant women. EFSA applies standard toxicological methodologies, while EMA integrates toxicology with clinical and traditional use data.

A distinctive feature of the EU system is the formal recognition of traditional use as longitudinal human evidence. Documented use over decades contributes to assessments of safety and plausibility, particularly where modern clinical data are limited, and is incorporated alongside other evidence streams.

These different forms of evidence are not applied in isolation but are integrated into a coherent assessment, weighing consistency, plausibility, and overall evidence convergence. This enables regulatory decisions even where evidence is incomplete, provided the risk profile is sufficiently understood.

In summary, the EU approach is characterised by:

- ✓ Comprehensive literature review, including mechanistic, clinical, and observational evidence
- ✓ Integration of case reports and pharmacovigilance data for safety signals
- ✓ Application of toxicology and dose–response principles
- ✓ Recognition of long-standing human use as supportive evidence
- ✓ A weight-of-evidence methodology rather than reliance on a single evidential hierarchy

This results in a multi-layered, scientifically grounded risk assessment process, which aligns regulatory decisions with both biological mechanisms and real-world patterns of use, rather than defaulting to a purely pharmacological or trial-centric model.

CONCLUSION

The Medical Products Bill is progressing through drafting and is expected to be introduced this year. However, there has been no recent publicly visible consultation on the substance of the Bill, nor any updated policy reassessment to support its development. The available evidence indicates that the current policy foundation is insufficiently developed, raising concerns that the drafting process is proceeding without a robust evidential and analytical base. This creates a material risk that the resulting legislation will be ineffective or misaligned with scientific and

regulatory realities. The limited transparency surrounding the policy and drafting process further compounds this concern, as the public is not informed of the stage of development or the basis on which key decisions are being made.