Innovation Passport (IP) Application Form

This form will be used by ILAP Partners and lay members to evaluate your application based on the ILAP selection criteria.

Refer to the ILAP Webpage for further information and guidance on the eligibility and selection criteria before completing this application.

Instructions:

- Use Arial 12-point font
- Ensure you adhere to the word count limit specified for each section
- Save this form in PDF format using the following naming convention: [Insert product name]_Innovation Passport application form_[MM-YYYY] (e.g. “myproduct_Innovation Passport application form_03-2025”

This form should be submitted through the ILAP registration portal as part of your Innovation Passport application as a PDF.

Summary

Product developer name	Vita Vitalia Ltd
Product name	Vitamin D Transport Protein (VDTP)
Active substances name(s)	Vitamin D-binding Protein
Excipient(s)	Deionised water (for solution); may vary based on format
Product type	✓ Medicine *(Biologic)*
Therapeutic indication *Only include the indication in this section (e.g. "Treatment/ Prevention of …"). Do not provide a background to the indication*. *For products under investigation in multiple indications state the lead indication for this* application*.*	Treatment of immune dysregulation in Autism Spectrum Disorder (ASD)
Route of administration *e.g., oral, intravenous, type of device to deliver medicine (if applicable)*	• *Sublingual spray* • *Oral drops* • *Topical cream*
Pharmaceutical form *e.g., powder for concentrate for solution for infusion, prolonged-release tablet, cell suspension*	*Solution: Topical emulsion*
Mode & mechanism of action *Provide a concise description that integrates the specific biochemical interactions (mechanism of action) with the broader physiological, functional, or anatomical changes (mode of action) that occur. Visual figures or diagrams are strongly encouraged for clarity.*	
VDTP (Vitamin D Transport Protein) may be derived from mammalian sources, including human plasma and bovine colostrum, both of which offer biologically compatible and ethically sourced options for therapeutic development. VDTP supports immune modulation by binding to and transporting Vitamin D, enhancing macrophage activation, modulating cytokine responses, and inhibiting immune-suppressing	

enzymes such as nagalase, potentially restoring immune competence in individuals with immune dysfunction.

Additional information

What is the global regulatory status of the product?

Marketed Territories:

- *Specify if the product is currently marketed in any territories.*
- *Provide details of the regions/countries where it is available.*

Marketing Authorisation Applications:

- *State if the product is under marketing authorisation application in any jurisdiction.*
- *Indicate whether any marketing authorisation applications have been rejected.*
- *Provide details of the jurisdictions involved and reasons for rejection, if applicable.*

Involvement in Accelerated Regulatory Pathways:

- *Indicate if the product has received any special designations.*
- *Specify involvement in pathways such as:*
  - *Orphan Drug Designation*
  - *EMA PRIME Designation*
  - *FDA Breakthrough Therapy Designation*
- *Provide details of approvals, pending applications, or rejections under these pathways.*

For Drug Device Combination products or products with an associated device (e.g. companion diagnostic) only:

Summary of the associated device
Provide an overview of the device aspect of the combination product or associated In Vitro Diagnostic (IVD) device. State, with details, if this associated device is marketed in any territories or if any clinical investigations have been approved. Furthermore, state whether the device has a CE/UKCA marking. *If referencing a competitor's device, state whether the device is being used within scope of certification or off-label. Additionally, specify whether the device is manufactured by the applicant or by a third party.*

Plain English summary

Lay members play an essential role in granting Innovation Passports by representing the views and experiences of patients and the public.

Lay members on the selection panel will use the information provided in this section to assess your application. This plain English summary will be used by lay members to assess applications.

All claimed benefits must be supported by evidence and presented in a clear and easily understandable manner.

When writing the plain English summary:

- Avoid, wherever possible, jargon, abbreviations and technical terms – if you must use them, provide a clear explanation
- Avoid complicated language or uncommon words
- Use active voice ("We will test the drug" not "The drug will be tested")
- Keep sentences short
- Explain what makes this medicine different or better than existing treatments
- Highlight the potential impact on patients' lives in practical terms
- Use numbers clearly ("2 out of 10 people" rather than "20% of patients")
- Use online tools to check the readability of your summary, and assess your language reading age
- Provide easy-to-understand explanations or analogies to help clarify complex concepts or medical terms
- Use diagrams, pictures and figures where appropriate

Word count

You must not exceed **750** words in each section. Any text that exceeds the word limit will not be assessed.

Provide a high-level overview of the indication and product, outlining the rationale behind why the product is needed by patients. *Provide an overview of the therapeutic indication and its impact on patients' lives.* *Summarise the product, explaining how it works and who it is for.* *Describe why patients need the product and what clinical unmet need it addresses. Outline the current NHS standard of care and explain where your product fits within this landscape.* *Refer to the guidance for criterion 1 for more details on what may be suitable to include.*
VDTP (Vitamin D Transport Protein) may be derived from mammalian sources, including human plasma and bovine colostrum, both of which offer biologically compatible and ethically sourced options for therapeutic development. VDTP is being developed as a **biologic therapy for Autism Spectrum Disorder (ASD)**, targeting the immune dysfunction commonly seen in autistic individuals. Research has shown that many people with autism experience chronic neuroinflammation, gut dysbiosis,

and suppressed immune markers, including low levels of activated macrophages and elevated nagalase enzyme activity. VDTP supports the immune system in a non-inflammatory, restorative manner by enhancing macrophage function and regulating cytokine response.

The therapy will be produced to **GMP (Good Manufacturing Practice)** standards via a licensed manufacturing partner in Europe. It can be formulated as a sublingual spray, dropper, or topical cream, depending on the research context. VDTP may be produced through three regulated pathways: 1) GMP-grade plasma fractionation, 2) bovine colostrum purification, or 3) recombinant protein expression. This flexibility ensures compliance with evolving regulatory requirements and supports scalable, ethical production options.

VDTP has been used in **over 500 individuals**, including children and adults with autism, under research, compassionate use, and observational conditions. In a 6-month open-label study involving 37 children, 31 participants (84%) demonstrated measurable clinical improvement, as assessed by caregiver feedback and ATEC (Autism Treatment Evaluation Checklist) scoring, based on ATEC scoring. Participants showed average improvements of 14.8% in Speech, 36.4% in Sociability, 30.7% in Sensory & Cognitive Awareness, and 46.1% in Health & Behaviour.

ATEC is a validated, caregiver-administered tool widely used to monitor changes in autism severity over time. Notable gains included the emergence of speech in previously nonverbal children, improved digestion, reduced anxiety, better emotional regulation, and increased engagement in learning and social interactions. Importantly, **no serious adverse events were reported**, and the therapy was well tolerated across all delivery formats.

The proposed indication is immune modulation in children with Autism Spectrum Disorder (ASD), with the potential to reduce inflammation, support behavioural regulation, and enhance overall developmental outcomes. The product is not a synthetic drug, but a naturally derived protein, biologically identical to what the body already produces.

This application seeks an ***Innovation Passport*** **designation** under the ILAP scheme to support the structured clinical development of VDTP in partnership with UK regulators. It is **not a request for marketing authorisation** at this stage, but an early engagement to ensure scientific and ethical alignment.

This is the first time a biologically native immune-modulating therapy will be studied under a regulated framework for autism. It could offer families access to a safe, scalable, and science-based intervention through the NHS and beyond.

We intend to work closely with NHS stakeholders to create clinician support materials, ensuring that VDTP's use aligns with best practices and patient safety frameworks.

Vita Vitalia Ltd, a UK-registered company, holds the rights to develop and market VDTP and is acting as the sponsor of this application.

Provide the word count: 482 / 750

Describe the innovative nature of the product and the significance of the innovation. Ensure comparison to existing treatments.

Describe the innovative nature of your product and how it differs from existing treatments for the specified indication.

Explain why these differences are significant and what the broader implications of the innovation are.

Outline the basis for the innovation and whether it is based on new understanding and insights into the indication, drug development or medical fields in general.

Refer to the guidance for criterion 2 for more details on what may be suitable to include.

Autism Spectrum Disorder (ASD) is widely recognised as a **seriously debilitating, lifelong neurodevelopmental condition**. It affects approximately **1 in 57 children in the UK**, with rising global prevalence. Autism can present with severe impairments in communication, behaviour, sensory processing, emotional regulation, and social interaction. Many individuals require lifelong care and support.

In its more severe forms, autism significantly impacts the quality of life and functional independence. A substantial proportion of autistic individuals are **non-verbal**, **prone to self-injury**, or suffer from **co-occurring mental health challenges** such as anxiety, depression, and obsessive-compulsive behaviours. Gastrointestinal dysfunction, sleep disruption, and sensory overload are also common.

In addition to its profound personal and family burden, ASD carries a serious **societal and economic impact**. The lifetime cost of supporting an individual with autism in the UK has been estimated at **£1.2–£1.5 million**, with the national cost of care exceeding **£32 billion annually**.

Despite its severity and prevalence, **there is no curative treatment for autism**, and very few therapies directly target the biological mechanisms now associated with the condition, such as immune dysfunction, neuroinflammation, and abnormal cytokine signalling.

VDTP offers a new and biologically grounded approach by supporting immune regulation and restoring macrophage function. Given the severity of the condition, the lifelong nature of its impact, and the absence of effective interventions, autism clearly qualifies as a **seriously debilitating condition** under ILAP Criterion 1a.

Provide the word count: 234 / 750

Explain how this product will make a meaningful difference to patients and/or the wider healthcare system.

Explain how the product will make a meaningful difference to patients and/or the wider healthcare system. Describe in simple terms the scientific rationale and reasoning behind these claims and present the evidence that supports them.

Provide a critical overview and summary of the existing NHS standard of care treatments, their limitations and how your product offers advantages. Clarify any benefits that this product could bring to the healthcare system.

Refer to the guidance for criterion 3 for more details on what may be suitable to include.

There is currently no licensed therapy that targets the immune dysregulation often seen in Autism Spectrum Disorder (ASD). While behavioural therapies and symptomatic medications are used, they do not address the underlying biological contributors to autism, such as neuroinflammation, gastrointestinal immune activation, and abnormal cytokine profiles.

The majority of available treatments focus on **managing symptoms** (e.g. antipsychotics for aggression), many of which carry significant side effects. No approved therapies exist that aim to **modulate immune function** in a way that is safe, biologically natural, and sustainable.

VDTP offers a novel mechanism of action as a native human protein that supports immune regulation through vitamin D transport, macrophage activation, and nagalase inhibition. By helping restore immune balance, it may reduce the biological drivers of autism-related symptoms, such as anxiety, gastrointestinal inflammation, and communication delays, without the risks associated with pharmaceuticals.

VDTP has already shown **meaningful improvements** in observational settings, including:

- Increased verbal communication in non-verbal children
- Improved digestion and sleep
- Better emotional regulation and engagement in learning
- Reduced reliance on pharmacological interventions

If formally validated, **VDTP could offer the first biologically targeted therapy** available for autism, addressing not just behavioural symptoms but the immune dysfunction many patients experience.

From a health system perspective, even minor improvements in function and independence can reduce the long-term burden on families, schools, and the NHS. For patients, this may mean greater autonomy, reduced suffering, and an improved quality of life.

VDTP directly addresses a **critical gap** in care and offers a safe, cost-effective, and scalable way to do so.

Provide the word count: 259 / 750

Selection Criteria

To be considered for an Innovation Passport, the product must meet all the ILAP selection criteria.

Applicants should ensure their application is concise, specific, and clear.

Figures, tables, or illustrations are encouraged and should be embedded in the text boxes below. These may be helpful when presenting details of the current treatment guidelines, mechanisms of actions and novel aspects of the product.

The overall standard and style of application should be comparable to that found in peer-reviewed journals and other regulatory submission packages.

Applicants are responsible for the content of their application. Whilst guidance is provided, it is not exhaustive, and not all examples will be relevant to the product or therapeutic area.

Evidence Requirements

Applications will be assessed solely based on the responses to the following questions.

Applicants should provide evidence to support any claims made, ensuring it is relevant, appropriate, and accurate.

Applicants are permitted to cite up to a **maximum of 5 references** in this application, focusing on those that most effectively demonstrate that the product meets the selection criteria.

These references can be provided as full text in a separate PDF file and uploaded as part of the submission form. This is optional, but advised, especially if the reference is not publicly available.

To do this, applicants must combine the full-text references into a single document and save in a PDF format, using the following naming convention:

- *[Insert product name]_Innovation Passport application references_[MM-YYYY]* (e.g. “myproduct_Innovation Passport application references_03-2025”

Examples of acceptable documents include:

- Peer reviewed journal articles
- Clinical treatment guidelines
- Health economic reports

Do not upload clinical trial protocols, investigational medicinal product dossiers (IMPDs), investigators brochures (IBs) or any other similar documents. They will not be assessed. Instead, ensure that key evidence from these documents is detailed in the relevant text boxes.

Criterion 1. The specific indication is life-threatening and/or seriously debilitating and there is a significant unmet clinical need

Both criterion 1a AND 1b must be met.

Word count:

Section 1a and 1b each have a 1500-word limit. The word limit excludes figures, figure text, and tables. You must not exceed the word limit. Any evidence that exceeds the word limit will not be assessed in your application.

Criterion 1a. The specific indication is life-threatening and/or seriously debilitating despite current NHS standard of care.
Provide evidence of how the application meets criterion 1a. *The focus should be on introducing the indication and demonstrating how it impacts patients' lives. When responding, include evidence that addresses the following:* *Epidemiology: Provide data on incidence, prevalence, survival rates, mortality, and morbidity of the indication. Referencing data relevant to the UK is encouraged.* *Symptoms: Describe the types, frequency, duration, and severity of symptoms, and how these impact a patient's quality of life, as well as their daily activities.* *Treatment: Outline the current NHS standard of care treatment strategies and where your product fits within this framework.* *Prognosis: Describe the typical progression and stages of the condition, including any potential impact on life expectancy*.
Epidemiology Autism Spectrum Disorder (ASD) is a lifelong neurodevelopmental condition that affects approximately **1 in 57 children in the UK**, with increasing prevalence globally. In England alone, more than **700,000 people** are estimated to be autistic. While autism is not itself classified as a terminal condition, it can be **seriously debilitating**, with high levels of disability and dependency. Studies show that autistic individuals have a **reduced life expectancy** of 16–30 years compared to the general population, often due to unmanaged comorbidities, lack of appropriate support, and suicide risk. Approximately 50–70% of autistic individuals also experience additional mental health conditions or neurological disorders. --- **Symptoms** ASD is characterised by impairments in **communication, social interaction, behaviour, and sensory regulation**. Many children present with: ● Non-verbal communication

- Severe anxiety
- Gut dysfunction
- Repetitive or aggressive behaviours
- Insomnia and poor emotional regulation

These symptoms are often **chronic, severe, and highly distressing** for both individuals and families. Sensory overload, meltdowns, and social exclusion can limit access to education, community life, and independence.

Parents frequently report that their children are **"locked in" — cognitively aware but unable to communicate or regulate emotions effectively.**

Treatment

There is **no curative treatment** for autism. Current NHS strategies focus on:

- Behavioural therapy (e.g. CBT, ABA)
- Speech and language support
- Occupational therapy
- In some cases, antipsychotic or anti-anxiety medications

However, these interventions are limited in scope and **do not address underlying biological contributors**, such as immune dysfunction, neuroinflammation, or gut-immune interactions.

VDTP would be the first UK therapeutic to directly target the immune system — a growing area of interest in autism research, offering a potentially groundbreaking intervention.

Prognosis

Autism is typically diagnosed in early childhood and persists across the lifespan. While some individuals improve with therapy and structured support, many continue to experience **moderate to severe disability**, including:

- Lifelong dependence on carers
- Exclusion from employment or higher education

- Co-occurring epilepsy, immune issues, and mental illness

In more severe cases, individuals may remain non-verbal, require residential care, or engage in self-injurious behaviour. **Prognosis is highly variable but often poor without meaningful biological intervention.**

Provide the word count: 347 / 1500

Criterion 1b. There is a significant unmet clinical need.
Must address a significant unmet clinical need, which means that there is no satisfactory method of prevention or treatment for the indication that has regulatory approval or, even if such a method exists, the medicinal product concerned will be of major therapeutic advantage to those affected.

Provide evidence of how the application meets criterion 1b.
Provide details of the significant unmet clinical need that the product aims to address.
Clinical unmet need, in terms of treatment, may consist of limited or ineffective treatments, significant side effects and complications associated with existing options. Other factors might be poor treatment compliance, high burden on the patient, heterogeneity in treatment response, limited accessibility due to cost or production constraints, and a lack of prevention strategies.

The Unmet Need in Autism

Autism Spectrum Disorder (ASD) affects 1 in 57 children in the UK and presents with lifelong challenges in communication, behaviour, emotional regulation, and independence. Despite its prevalence and severity, there is **no curative treatment**. Families often face years of waiting for a diagnosis, limited access to services, and few meaningful interventions.

Current NHS approaches include behavioural therapy, speech and occupational therapy, and, in some cases, antipsychotic medication. These are **symptom-focused**, not causal, and none address the biological underpinnings increasingly recognised in autism, such as **chronic neuroinflammation, gut-immune disruption, and immune suppression**.

The Role of VDTP

Vitamin D Transport Protein (VDTP) is a naturally occurring human protein with immune-modulating properties. It supports macrophage activation, facilitates vitamin D transport, and helps regulate immune responses in a restorative, non-inflammatory manner. VDTP is present in mammalian colostrum and human breast milk, making it biologically compatible and ethically sourced. It has already been used in over 500 individuals under research and observational conditions, with no serious adverse events reported, demonstrating a favourable safety profile.

In an open-label study involving 37 autistic children, 31 (84%) showed measurable clinical improvement, including:

- The emergence of speech in non-verbal children
- Improved sleep, digestion, and sociability
- Reduced anxiety and improved school engagement

This represents a **clear signal of benefit** in a population where few therapies offer even modest gains.

Supporting observational outcomes are detailed in VDTP_Innovation Passport application references_06-2025.pdf, submitted with this application.

Addressing the Gap

There is a complete absence of licensed therapies targeting immune dysfunction in autism. VDTP would be the **first intervention** to address this biological root cause in a regulated clinical setting. As a **natural protein** with established safety, it also offers an **ethical, well-tolerated** option for children with sensory and neurological sensitivities who may not tolerate pharmaceutical interventions.

Broader Healthcare System Benefits

- Improved function could reduce long-term dependence on carers, schools, and supported living.
- Early intervention may lessen the need for medication and mental health crisis services.
- NHS costs could be significantly reduced over time if biological interventions improve autonomy

In short, VDTP offers the potential for **real-world improvement** in an area where **families have had no true therapeutic options**, and the healthcare system has limited tools to address the issue.

Provide the word count: 383 / 1500

Criterion 2. The product is innovative.

Word count:

Your answers in this section must not exceed 3,000 words, excluding figures, figure text, and tables. Any content beyond this limit will not be considered in your application.

The application must fulfil one of the following (*Select only one*):	
Criterion 2a. The product is novel/ new	YES
Criterion 2b. The product is an approved medicine that is being developed in a clinically significant new indication	☐

If the product meets criterion 2a, select all that apply:	
No other product exists in clinical practice that uses the same mechanism of action (e.g. first-in-class molecule)	YES
A new chemical entity	☐
A new biological entity	YES
A novel drug-device combination	☐
A new or a novel modification of existing technologies	☐

Provide evidence of how the application meets criterion 2.
The applicant must provide strong scientific evidence for a novel/new or re-purposed product e.g. quality data, manufacturing process descriptions, active substance starting material information, licensed product where the active substance is part of etc.
The focus should be on clearly defining and demonstrating the innovative properties and potential impact of the product within current treatment paradigms and the broader scientific and technological landscape.
A detailed description of the novel aspects of the product is required, highlighting its differences from existing treatments or technologies.
It is not necessary to outline the wider impact on patient health outcomes and the health system in your response to this question as this is covered in criterion 3.
The application will be assessed based on the evidence provided regarding the product's level of innovation and impact.

Innovation Justification (Criterion 2a – New Biological Entity; First-in-Class Mechanism)

VDTP is a naturally occurring plasma protein that plays a critical role in immune modulation, vitamin D transport, and macrophage activation. It is also found in breast milk and colostrum, supporting immune development and balance, particularly in early life.

To date, **no licensed therapy or biologic has been developed using vitamin D-binding protein** as an active therapeutic substance in any indication, including autism or immune-related disorders. VDTP represents a **new biological entity** and is **first-in-class in its mechanism of action**.

Its therapeutic novelty lies in:

- **Restoring macrophage function** in immune-dysregulated individuals
- **Transporting and activating vitamin D** at the cellular level

- **Reducing nagalase enzyme activity**, which suppresses immune surveillance

Unlike conventional pharmaceutical or behavioural interventions, VDTP targets a **core immunological contributor to autism**, based on an expanding body of research linking neuroinflammation and immune suppression to behavioural outcomes. Further supporting evidence for immune modulation strategies in autism is provided in the VDTP Innovation Passport Application Full-Text References Pack June 2025.pdf (Page 13, Bradstreet et al., 2012), submitted alongside this application.

VDTP has already been used in over **500 individuals**, including children with autism, in research and observational settings, with no serious adverse events reported.

It will be manufactured under **Good Manufacturing Practice (GMP) conditions**, and the proposed ILAP application represents its **first entry into a regulated development pathway**.

The product's innovation is further strengthened by its flexible sourcing methods: while plasma-derived protein has established observational safety, recombinant and colostrum-based versions are also under active development to ensure broad accessibility, scalability, and regulatory adaptability.

However, the regulatory interpretation of these production methods, particularly recombinant human VDTP, may vary. Some authorities may consider recombinant human-derived proteins to be analogous to human blood components, even if they are not derived from plasma. This could introduce classification or approval challenges depending on jurisdiction.

Bovine-derived VDTP may offer a regulatory advantage in this respect, but could present functional differences due to cross-species variation in amino acid sequence and post-translational modifications. These distinctions are being explored, and guidance from MHRA is specifically requested to ensure optimal pathway alignment.

Provide the word count: 366 / 3000

Criterion 3. The product has the potential to offer a step change in management of the indication. It must fulfil one or more of the following:

Word count:

Your answers in this section must not exceed 4,000 words, excluding figures, figure text, and tables. Any content beyond this limit will not be assessed in your application.

The product must fulfil one or more of the following: select all that apply	
Criterion 3a. Clear and justified claimed benefits demonstrating the potential to substantially improve patient health outcomes	YES
Criterion 3b. Offers the potential of a cure where none currently exists	YES
Criterion 3c. Has the potential to substantially reduce care-related costs without negatively impacting the outcomes of patients	YES

Provide evidence of how the product meets criterion 3.

Provide scientific evidence to demonstrate how the product can significantly improve the management of the specified indication. Include an overview of the current NHS standard of care and its limitations. Demonstrate how the product offers potential solutions or improvements over the current standard of care, including patient outcomes and, if relevant, care-related cost savings. Support your statements with robust scientific reasoning and evidence.

The product will be considered based on the evidence provided. When summarising the potential impact of your product, directly reference the evidence submitted.

***Evidence for criterion 3a**. Clear and justified claimed benefits demonstrating the potential to substantially improve patient health outcomes.*

This may include improved safety, efficacy, and quality of life benefits for patients. Where possible and appropriate, justify comparisons based on quantifiable data.

Provide a critical overview and summary of the existing NHS standard of care treatment landscape for the indication targeted by your product. Describe the limitations of current standard of care treatments, and how the product offers improvements or advancements.

Summarise the potential patient health outcome improvements that your product may bring compared to existing treatments. If available and appropriate, comparisons must be based on quantifiable data such as survival, disease progression and patient-reported outcomes.

***Evidence for criterion 3b**. Offers the potential of a cure where none currently exists.*

If the product offers the potential of a cure where none currently exists, provide evidence that supports the claims that the product may offer a complete and permanent resolution of the indication, leading to the end of all indication-related symptoms, normal diagnostic test results, and a full restoration to normal function.

***Evidence for criterion 3c**. Has the potential to substantially reduce care-related costs without negatively impacting the outcomes of patients.*

Detail how the product may lead to lower treatment costs or enhanced prevention in the incidence, progression or severity of the indication. Detail how the product has the potential to reduce the service costs of delivering care through ease of administration, reduction in the length or number of hospital stays, and a transition to delivering care outside of the hospital setting. If possible, provide evidence and data to demonstrate potential cost-reductions or a strong rationale as to how the product will positively impact care-related costs.

***Evidence**:*

When providing evidence in the form of non-clinical or clinical data, only detail the necessary, relevant, and key studies and clinical trials in this section.

Provide a summary of the evidence presented to support the claims that the product meets selection criterion 3. A tabulated overview of all key studies and clinical trials presented may be included.

Clinical trial diagrams are encouraged.

For each key non-clinical study and clinical trial presented, describe the:

Objective(s)

***Study design** (randomisation, blinding, etc)*

***Population** (relevance and description of animal models or the study population, inclusion/exclusion criteria, sample size, etc)*

***Intervention** (including doses, duration of treatment, etc)*

Endpoints *(rationale for use, validity, etc)*
A clear description of the ***results and their significance****, with well-labelled accompanying tables or figures. Include statistical analysis if applicable.*
Acknowledgement of limitations*. All research inherently includes limitations, many of which are reasonable and necessary. If appropriate, applicable and relevant to evidencing criterion 3, provide a description of limitations, along with clear, justified explanations and the steps taken to mitigate them. Limitations in evidence presented may include aspects of study design, methodology, and execution e.g. the rationale behind the use of certain animal models or non-standard endpoints.*

Direct Patient Benefits

VDTP (Vitamin D-binding Protein Therapy) offers potential improvements in both core and associated features of autism, including:

- Verbal and non-verbal communication
- Emotional regulation and anxiety
- Gastrointestinal health and sleep
- Cognitive focus and social engagement

In observational settings, children receiving VDTP showed:

- Emergence of speech in previously non-verbal individuals
- Improved mood, behaviour, and attention
- Better quality of life for both children and their families

In a six-month observational study involving 37 children with autism, 31 (84%) showed measurable improvement based on ATEC scoring. Of the 37 participants, 6 showed negative or no response, 9 showed mild improvement, 13 showed moderate improvement, and 9 demonstrated significant improvement (≥50% reduction in ATEC total score). Notably, over half demonstrated moderate to significant gains, including the emergence of speech, improved social interaction, and reduced anxiety. These outcomes are supported by full charted data submitted in the accompanying summary.

ATEC Outcomes: Charted Participant Improvements (n=37)

The following visuals illustrate the observed outcomes from the six-month open-label study referenced above:

ATEC Outcome Overview

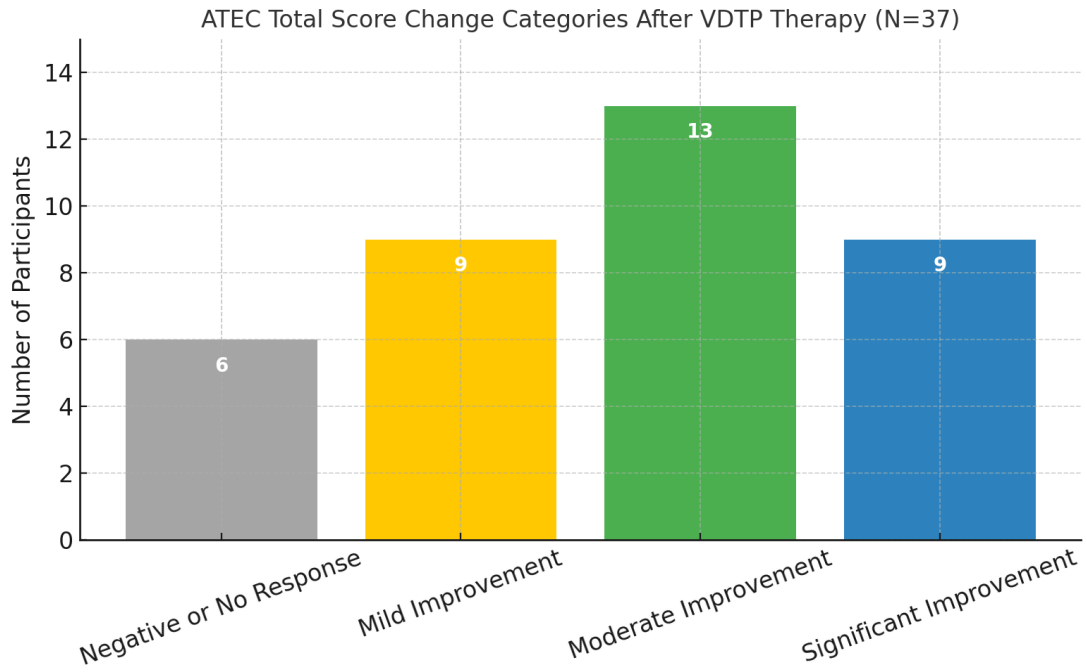

Figure 1. *Individual participant data from n=37 children with ASD. Outcome categories are based on total ATEC score reduction, grouped as No Response, Mild, Moderate, or Significant Improvement.*

Domain-Specific Average Improvements (ATEC Scores)

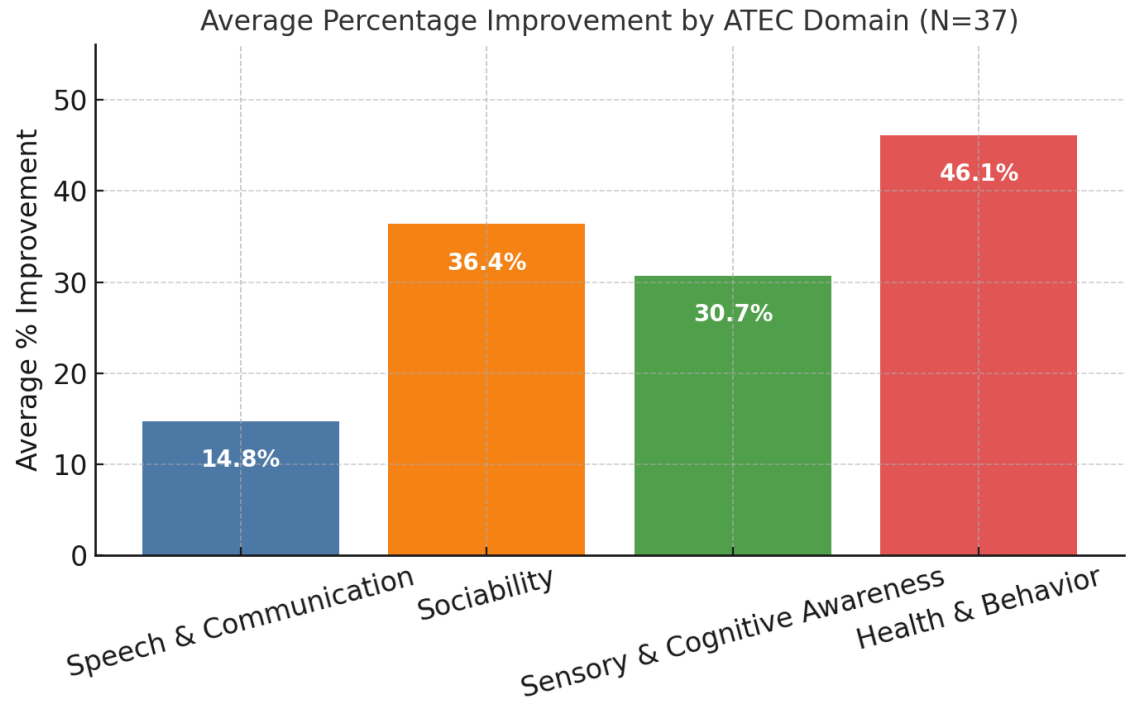

Figure 2 - Average percentage improvements across four ATEC domains *(Speech & Communication, Sociability, Sensory & Cognitive Awareness, and Health & Behaviour) following VDTP therapy.*

Table 1 - ATEC Results

Sex	Age	Diagnosis	ATEC Start	ATEC End	Change	% Change	Improvement
Male	13	ASD	3	0	-3	100.00%	Significant
Male	10	ASD	61	7	-54	88.50%	Significant
Male	6	ASD	81	13	-68	84.00%	Significant
Male	6	ASD	12	2	-10	83.30%	Significant
Male	5	ASD	31	6	-25	80.60%	Significant
Male	13	ASD	15	4	-11	73.30%	Significant
Male	5	ASD	52	18	-34	65.40%	Significant
Male	12	ASD	33	14	-19	57.60%	Significant
Male	23	ASD	46	20	-26	56.50%	Significant
Male	10	ASD	21	11	-10	47.60%	Moderate
Male	26	ASD	17	9	-8	47.10%	Moderate
Male	5	ASD	96	52	-44	45.80%	Moderate
Male	5	ASD	18	10	-8	44.40%	Moderate
Male	5	ASD	67	39	-28	41.80%	Moderate
Male	11	ASD	77	47	-30	39.00%	Moderate
Male	7	ASD	36	22	-14	38.90%	Moderate
Male	8	ASD	70	43	-27	38.60%	Moderate
Male	6	ASD	35	22	-13	37.10%	Moderate
Male	13	ASD	55	36	-19	34.50%	Moderate
Male	14	ASD	27	18	-9	33.30%	Moderate
Male	11	ASD	30	20	-10	33.30%	Moderate
Male	5	ASD	26	18	-8	30.80%	Moderate
Male	8	ASD	83	61	-22	26.50%	Mild
Male	4	ASD	36	27	-9	25.00%	Mild
Male	9	ASD	33	25	-8	24.20%	Mild
Female	6	ASD	25	20	-5	20.00%	Mild
Male	6	ASD	60	50	-10	16.70%	Mild
Male	10	ASD	84	70	-14	16.70%	Mild
Male	5	ASD	40	34	-6	15.00%	Mild
Female	6	ASD	46	43	-3	6.50%	Mild
Male	13	ASD	73	70	-3	4.10%	Mild
Male	9	ASD	34	34	0	0.00%	No Response
Male	5	ASD	74	74	0	0.00%	No Response
Male	8	ASD	39	42	+3	-8.00%	No Response
Male	10	ASD	50	53	+3	-6.00%	No Response
Male	9	ASD	25	31	+6	-24.00%	No Response
Male	5	ASD	62	72	+10	-16.00%	No Response

These outcomes were caregiver-reported, collected under Research-Use-Only conditions, and support the therapeutic potential of VDTP in ASD. The full dataset and analysis are

available in the accompanying VDTP_Innovation Passport application references_06-2025.pdf (Page 1, Banks T et al., 2012).

Positron emission tomography (PET) studies have confirmed widespread **microglial overactivation** — the brain's resident immune cells — in individuals with Autism Spectrum Disorder (ASD), particularly in the **cerebellum and prefrontal regions**. These findings support the rationale for targeting macrophage and immune pathways using VDTP as a **non-pharmaceutical immune-modulating therapy**.

If validated in trials, these outcomes would represent meaningful clinical improvements in an area with very few available therapeutic options.

Addressing a Clinical and Ethical Gap

Currently, no approved therapy addresses immune dysfunction in autism, despite a growing body of evidence linking neuroinflammation and immune imbalance to behavioural symptoms.

VDTP is the first candidate to address this through a natural, human-compatible biologic with a favourable safety profile and non-invasive delivery. It offers families a biologically sound and ethically acceptable alternative to heavy medications or lifelong behaviour-based management.

Recent studies have identified key immune-related biomarkers associated with autism, including **elevated pro-inflammatory cytokines**, **increased Nagalase activity**, and **dysregulated macrophage profiles**. VDTP's mechanism — enhancing macrophage function and restoring immune balance — directly targets these markers. Exploratory endpoints in future trials may include **serum cytokine panels** (e.g. IL-6, TNF-α), **immune activation ratios** (e.g. CD14/CD16), and **Nagalase reduction**, in addition to behavioural measures such as ATEC and CGI-I. These biomarker strategies will support both mechanism validation and personalised response profiling.

Wider System Benefits

If VDTP proves effective, it could help reduce:

- Demand on special education resources
- Carer burden and parental workforce withdrawal
- Crisis interventions and long-term residential care
- Polypharmacy and off-label drug use in vulnerable populations

These impacts align directly with **NHS Long Term Plan goals**, including:

- Personalised care

- Early intervention
- Reducing health inequality
- Support for children with complex needs

Health System Savings and Long-Term Cost Reduction

Autism imposes a substantial and lifelong financial burden on health and social care systems. In the UK, the estimated lifetime cost per individual ranges from **£1.2 to £1.5 million**, primarily due to the need for supported living, education, mental health interventions, and carer withdrawal from the workforce. VDTP offers the potential to reduce these long-term costs by promoting earlier developmental gains and reducing dependence on high-cost care structures.

A modest improvement in core functioning — such as communication, emotional regulation, or sleep — may translate to measurable reductions in educational support needs, medication use, and crisis interventions. **Economic modelling scenarios** will be incorporated into our ongoing development to quantify these savings and inform health technology assessment.

Cost Effectiveness and Scalability

VDTP is relatively low-cost to produce, highly scalable, and stable in non-invasive forms (e.g. drops, spray or cream). This supports access across community, outpatient, and potentially school-based environments, reducing the need for hospital-based or specialist delivery.

Even small improvements in independence or behaviour may reduce the overall lifetime cost of care, which currently stands at £1.2–£1.5 million per autistic individual.

Real Hope, With Real Infrastructure

VDTP will be **GMP-manufactured** and supported by a UK sponsor, Vita Vitalia Ltd. The development path is clear, the safety profile is known, and families are already waiting.

This is not a theoretical benefit. It is achievable, measurable, and overdue.

Invitation to Collaborate: Early Trial Development

We welcome engagement with academic researchers, NHS trusts, and independent investigators to co-develop early-stage clinical trials assessing VDTP. A proposed **Phase I/II study** will prioritise safety, tolerability, and immune biomarkers, using an **open-label or adaptive trial design** in a paediatric ASD population. Ethical oversight, caregiver consent, and community support will be central to this process.

The data generated will inform formal submissions to the MHRA, NICE, and international regulators. We are committed to transparency, scientific integrity, and collaboration in advancing this potentially transformative therapy.

Provide the word count: 1185 / 4000

Anticipated topics for discussion in the Target Development Profile

Specify any areas of focus or topics you would like to discuss with the ILAP Partners if your application is successful and/or any ILAP services you intend to utilise.
The points raised in this section will not influence the review of your application and are not intended to be binding.

Anticipated topics for discussion in the Target Development Profile

We welcome early engagement with MHRA and ILAP partners to explore the following topics during the TDP stage, which are central to the development and regulatory pathway for VDTP as a novel immune-modulating biologic for Autism Spectrum Disorder.

Regulatory Classification

We seek early guidance on the appropriate regulatory classification of VDTP across all proposed manufacturing pathways, including:

- Human plasma-derived protein
- Bovine colostrum-derived protein
- Recombinant human VDTP

We also request preliminary feedback on the potential feasibility of sourcing VDTP from other mammalian plasma sources, such as porcine, should this become relevant in future development.

Porcine plasma derivatives are already used in several licensed medicinal products (e.g., heparin, poractant alfa), and this precedent supports considering porcine-sourced VDTP as a viable and ethically acceptable alternative.

Guidance is requested on documentation, comparability requirements, and regulatory positioning for each manufacturing route.

Recombinant VDTP Interpretation

We seek clarification on whether recombinant human VDTP—though not plasma-derived—may be considered a human blood component under current UK regulatory definitions. This may have implications for classification, licensing strategy, and Good Manufacturing Practice (GMP) compliance.

Additionally, we would appreciate guidance on the use of bovine-derived VDTP, including the acceptability of cross-species proteins in a human therapeutic context, and the extent to which such differences may impact bioactivity, safety, and regulatory approval.

Early Trial Design

We invite collaboration on the design of an early Phase I/II clinical study targeting immune modulation in autism, with a focus on paediatric populations. Topics for discussion include:

- Selection of meaningful and measurable endpoints (e.g. ATEC scores, immunological markers, quality of life indicators)
- Potential use of open-label or adaptive trial designs
- Strategies to mitigate caregiver bias and placebo effects in neurodevelopmental trials

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Biomarker Guidance

We request input on acceptable biomarkers or clinical indicators that may support exploratory efficacy claims, particularly those linked to immune regulation and macrophage function. We are particularly interested in guidance on validated or emerging markers suitable for paediatric studies.

Safety Monitoring

We welcome advice on best practices for safety monitoring when introducing non-pharmaceutical biologics to children, particularly with novel delivery formats such as sublingual sprays, droppers or topical creams. Early input on expected safety data requirements will assist in designing an appropriately robust monitoring framework.

Patient and Family Ethics

We recognise the importance of ethical engagement when working with families affected by autism. Guidance is requested on appropriate consent procedures, safeguarding expectations, and communication strategies to ensure trust, understanding, and transparency throughout the trial process.

NICE and NHS Integration

We are committed to ensuring that future data collection supports real-world value demonstration and potential NHS access. We seek early input from NICE and NHS partners on:

- Health economic metrics related to caregiver burden, educational support, and long-term social outcomes
- Integration of trial data into future cost-effectiveness evaluations

- Alignment with NHS innovation pathways to accelerate access, if efficacy is demonstrated

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Clinician Support Materials

Finally, we anticipate the need for clinician-facing resources to support the safe and effective use of VDTP should it progress to clinical adoption. We welcome feedback on best practices for the co-development of educational materials, training tools, and clinical protocols aligned with NHS standards.

Conclusion

Our goal is to offer safe, biologically rational, and ethically sound therapeutic options to families affected by autism, where few exist today. We look forward to working in partnership with MHRA, NICE, and NHS stakeholders to ensure a responsible and well-supported path forward for VDTP.

Glossary of Terms

(Optional supporting terminology note)

Nagalase (Alpha-N-acetylgalactosaminidase):
An enzyme that degrades Gc protein (vitamin D-binding protein), preventing its conversion into the active macrophage-activating factor (GcMAF). Elevated nagalase activity has been observed in individuals with autism. By impairing macrophage activation, nagalase may contribute to broader immune suppression. VDTP (Vitamin D Transport Protein) is thought to support immune regulation, in part by mitigating the impact of this enzyme.

VDTP (Vitamin D Transport Protein):
A naturally occurring human protein involved in vitamin D transport, macrophage activation, and immune regulation. Also referred to as Gc protein or vitamin D-binding protein (DBP), VDTP plays a central role in maintaining immune balance and is present in both human plasma and mammalian colostrum, making it biologically compatible and ethically sourced for therapeutic development.

GcMAF (Gc Macrophage Activating Factor):
A biologically active form of the Gc protein (VDTP) created through enzymatic conversion. GcMAF activates macrophages and is involved in regulating immune surveillance and inflammation.

Macrophage:
A type of white blood cell that engulfs and digests pathogens, damaged cells, and foreign substances. Macrophages are essential to the innate immune response and are modulated by VDTP/GcMAF activity.

Immunomodulation:
The adjustment of immune responses to a desired level, either by stimulating or suppressing immune activity. It is a therapeutic strategy for conditions involving immune dysregulation.

ATEC (Autism Treatment Evaluation Checklist):
A widely used assessment tool designed to track changes in autism symptoms over time, including communication, social skills, sensory awareness, and physical health.

Biologic (Biological Medicine):
A medicinal product derived from living organisms or their components. Biologics, which include proteins, antibodies, and cells, are regulated differently from synthetic drugs due to their inherent complexity.

Recombinant Protein:
A protein that is produced through genetic engineering, often using bacterial, yeast, or mammalian cell systems, to replicate natural proteins in a controlled, scalable manner.

Colostrum:
The first form of milk produced by mammals post-birth is rich in antibodies and immune factors, including VDTP. Bovine colostrum is considered a potential alternative source for immune-related proteins.

Placebo Effect:
A psychological or physiological response that occurs when a patient believes they are receiving an active treatment, even if the intervention has no therapeutic value. Particularly important in trials involving neurodevelopmental conditions.

Target Development Profile (TDP):
A structured planning document used in the ILAP process to outline the regulatory, clinical, and development strategy for a novel therapy, developed in collaboration with MHRA and ILAP partners.

NICE (National Institute for Health and Care Excellence):
An independent UK organisation providing national guidance and advice to improve health and social care. NICE assesses the clinical and cost-effectiveness of health technologies for NHS use.

MHRA (Medicines and Healthcare products Regulatory Agency):
The UK regulator is responsible for ensuring medicines and medical devices work and are acceptably safe. Oversees licensing and approval of new therapeutics, including through ILAP.

ILAP (Innovative Licensing and Access Pathway):
A UK regulatory framework designed to accelerate access to promising new medicines. The pathway facilitates early dialogue, provides scientific advice, and streamlines regulatory steps.

List of References

Provide a list of the references cited in this application (maximum 5).

Any appropriate citation style (e.g. Harvard or Vancouver) is allowed. Be consistent with the citation style throughout the application

Product: *Vitamin D Transport Protein (VDTP)*
Indication: *Autism Spectrum Disorder (ASD)*
Sponsor: *Vita Vitalia Ltd*
Date: *June 2025*

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1. Banks, T et al. (2025) – Exploring Immune Modulation in Autism: The Role of Vitamin D Transport Proteins

- ***Design:*** *Open-label observational study (n=37 children with ASD).*
- ***Findings:*** *84% showed measurable improvement in ATEC scores.*

- ***Significance:*** *First real-world evaluation of VDTP, showing speech emergence, reduced anxiety, and improved behaviour.*
- ***Submitted as:*** *Exploring Immune Modulation in Autism: The Role of Vitamin D Transport Proteins (Page 1).*

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2. Bradstreet, et al. (2012) – GcMAF and Nagalase in Autism

- ***Design:*** *Open-label study examining immune modulation via Gc protein-derived macrophage activating factor.*
- ***Findings:*** *Reduced nagalase levels and clinical improvements in ASD symptoms.*
- ***Significance:*** *Supports the biological basis for macrophage-targeted therapies like VDTP.*
- ***Submitted as:*** *Initial Observations of elevated Alpha-n-Acetylgalactosaminidase Activity Associated with Autism and Observed Reductions from GC Protein—Macrophage Activating Factor Injections. (Page 13).*

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3. Suzuki, et al. (2013) – Microglial Activation in ASD

- ***Design:*** *PET imaging study of young adults with ASD.*
- ***Findings:*** *Widespread microglial overactivation in cerebellum and prefrontal cortex.*
- ***Significance:*** *Confirms neuroinflammation as a central pathology, validating the use of immune-targeted interventions.*
- ***Submitted as:*** *Microglial Activation in Young Adults With Autism Spectrum Disorders. (Page 21)*

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4. Horder, et al. (2013) – Reduced Glutamate/Glutamine in ASD ([¹H]MRS Study)

- ***Design:*** *Magnetic resonance spectroscopy in 34 adults with ASD.*
- ***Findings:*** *Reduced Glx in basal ganglia correlating with communication deficits.*
- ***Significance:*** *Highlights neurochemical imbalances that may be addressed through immune and metabolic regulation.*

- ***Submitted as:*** *Reduced subcortical glutamate/glutamine in adults with autism spectrum disorders: a [1H]MRS study. (Page 31)*

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5. *Hughes, et al. (2018)* – Immune Dysfunction and Autoimmunity as Pathological Mechanisms in Autism Spectrum Disorders

- ***Design:*** *Comprehensive review of cytokine imbalance, T-cell dysfunction, and autoimmunity in ASD.*
- ***Findings:*** *Consistent immune abnormalities linked to behavioural symptoms.*
- ***Significance:*** *Reinforces rationale for VDTP as a biologically compatible immune modulator.*
- ***Submitted as:*** *Immune Dysfunction and Autoimmunity as Pathological Mechanisms in Autism Spectrum Disorders. (Page 39)*