Final version

CASE REPORT FORM

TO BE COMPLETED BY THE INVESTIGATORR

Instructions for completing the case report form (if on paper)

- Use a black ballpoint pen.
- Write legibly, in capitals.
- Insert a single character per box and do not leave any of the boxes empty.
- If the response contains only one figure, the boxes should nevertheless be completed as follows:

  Example: for a value of 8, indicate |0|0|8|

- If the response is: "unknown", "not done", "not applicable" } Indicate ND
- Dates should be written as follows : DD/MM/YYYY
- If a date or part of a date is unknown, use ND for the unknown part, e.g.: ND/MM/YYYY ND/ND/YYYY
- Each error should be crossed out with a single line such that it remains readable and should be dated and signed:

  e.g. |~~A~~|~~B~~|~~C~~| *DR 15/11/2006*

  X Y Z

Never use correction fluid

In the case of a serious adverse effect:

All serious adverse effects occurring during the study must be reported to the Institut Pasteur in the 24 hours following the investigator becoming aware of the event (initial report), by fax (02 99 59 91 99)

Date of the visit

|__|__|/|__|__|/|__|__|__|__|

Date on which the consent form was signed

|__|__|/|__|__|/|__|__|__|__|

Inclusion criteria

		Yes	No
1*	Subject considered healthy by the investigator on the basis of medical history, clinical examination, laboratory and ECG results (blood samples for laboratory analyses and ECG carried out only after informed consent given)	☐	☐
2	Subject, that, according to the investigator, should be able to conform to the demands of the protocol and should be available for all the planned visits at the centre	☐	☐
3	Man or woman in good health and aged between 20 and 69 years (inclusive)	☐	☐
4	Of mainland French origin over at least three generations	☐	☐
5	18.5 ≤ BMC ≤ 32 kg/m² (see appendix 18.6 of the protocol)	☐	☐
6	Subject able to give written informed consent	☐	☐
7	Subject capable of understanding written and spoken French	☐	☐
8	Subject covered by French social security or a similar regime	☐	☐
9	Subject registered in the national file of people participating in biomedical research	☐	☐

If a single NO is ticked, the subject cannot be included in the study.

**** Inclusion criterion to be checked after reception of the results of the biological tests carried out at V0***

Exclusion criteria 1/3

		Yes	No
1	Volunteer for whom the status indicated in the national file of people participating in biomedical research does not allow participation in this study	☐	☐
2	Participation in another clinical study in the last three months, in which the subject received an experimental treatment (*pharmaceutical product, placebo or medical device*) or participation in another study over the same period as this study.	☐	☐
3	Volunteer related to other individuals in the study population	☐	☐
4	Travel in (sub)tropical regions in the last three months	☐	☐
5	For women: pregnant or breastfeeding or planning to become pregnant during the study or perimenopausal *Perimenopausal woman: phase of life characterised by irregular menstrual cycles:* - *Changes in menstrual cycle length of more than seven days (early perimenopause)* - *Two or more periods missed, with an interval of 60 days or more between periods (late perimenopause)*	☐	☐
6	Participation in any physical activity during the 8 hours preceding the inclusion visit (V1) and the end of study visit (V2)	☐	☐
7	Volunteer following a specific diet prescribed by a doctor or dietician for medical reasons (calorie-controlled diet or diet favouring weight loss in very overweight patients, diets to decrease cholesterol levels or volunteer with food intolerance or allergy)	☐	☐
8	Excessive alcohol consumption (*more than 50 g of pure ethanol per day; e.g. more than four 150 ml glasses of wine, more than four 250 ml glasses of beer or more than four 40 ml glasses of spirits)*	☐	☐
9	Consumption of illegal drugs or use of narcotics in the three months preceding inclusion (V1)	☐	☐
10	Neurological or psychiatric illness that the investigator considers might prevent the subject from participating in the study in a satisfactory manner, even if stable	☐	☐
11	Severe/chronic/recurrent diseases, including:		
11.1	Past or current cancer or lymphoma, with the exception of: - People with a history of cancer in complete remission, without treatment, for at least five years - Women in complete remission for at least three years following treatment for breast cancer and on long-term tamoxifen-based prophylaxis - Basal cell carcinoma or *in situ* carcinoma of the cervix	☐	☐

<u>If a single YES is ticked, the subject cannot be included in the study</u>

Exclusion criteria 2/3

		Yes	No
11.2	Personal history of organ transplantation	☐	☐
11.3	Acquired or congenital immunodeficiency (*Immunosuppressive or immunodeficiency disease, including HIV infection*)	☐	☐
11.4	Personal history of autoimmune diseases currently or previously requiring treatment (*e.g. rheumatoid arthritis, disseminated lupus erythematus, sarcoidosis, ankylosying spondlyarthritis, autoimmune haemolytic anaemia, autoimmune thrombocytopenic purpura, Crohn's disease, psoriasis, systemic sclerosis, Wegener's granulomatosis, type I diabetes, thyroiditis etc.*)	☐	☐
11.5	Splenectomy	☐	☐
11.6	Pulmonary, cardiocascular hepatic or renal disease, acute or chronic, adjudged clinically significant by the investigator on the basis of physical examination or laboratory analysis	☐	☐
11.7	History of neurological or convulsive problems considered clinically significant by the investigator	☐	☐
11.8*	Infectious diseases: - Chronic infection* (HIV, HCV, HBV etc.) - Current or past acute infection in the last three months, according to the judgement of the investigator - Rectal temperature ≥ 38.4°C, axillary temperature ≥ 37.5°C, auricular temperature ≥ 38.4°C, or buccal temperature ≥ 38°C on the day of inclusion - Subject currently on or treated in the last three months with nasal, intestinal or respiratory antibiotics or antiseptics	☐	☐
11.9	Severe arterial hypertension defined as a systolic arterial pressure ≥ 160 mmHg and/or a diastolic arterial pressure ≥ 100 mmHg (stage 2 AHT). Treated and controlled hypertension is authorised	☐	☐
11.10	Type II diabetes requiring drug treatment (diabetes treated by exercise and diet is authorised)	☐	☐
11.11	Chronic renal insufficiency, defined as: GFR <60 ml/min/1.73 m² (see ref. 8 of the protocol, National Kidney Foundation (2002))	☐	☐
11.12	Chronic bone disease treated with bisphosphonates	☐	☐
11.13	Treated depression or an episode of depression evident during the medical examination and interview	☐	☐
11.14	Any significant coagulation problem or the use of treatment derived from coumarin, heparin or anti-platelet drugs during the two months immediately preceding inclusion.	☐	☐

If a single YES is ticked, the subject cannot be included in the study.

**** Exclusion criteria to be checked on reception of the results of the biological tests carried out at V0***

Exclusion criteria 3/3

		Yes	No
11.15	Presence of any current dermatological problem sufficiently serious to prevent skin biopsy (*e.g. eczema, psoriasis, acute or chronic dermatitis*)	☐	☐
11.16	Severe acute/chronic allergy: - Severe asthma requiring a combination of two or more maintenance treatments (e.g. medium- or high-dose inhaled corticosteroids or a long-action beta stimulant or oral corticosteroids) - Severe food allergy, marked by extensive urticaria, Quincke's oedema or anaphylactic shock - Severe allergy to insect bites, marked by extensive urticaria, Quincke's oedema or anaphylactic shock - Atopic dermatitis treated with drugs	☐	☐
12	Chronic administration (*defined as more than 14 days)* of immunosuppressants or other drugs modifying the immune response in the six months preceding inclusion. For corticosteroids, this corresponds to a dose equivalent to 20 mg/day prednisone over a period of more than two weeks (*inhaled and topical steroids authorised*)	☐	☐
13	Chronic administration of NSAIDs, including aspirin: prolonged consumption *(> 2 weeks*) in the six months preceding the study or any intake in the seven days preceding the skin biopsy	☐	☐
14	Vaccination in the three months preceding inclusion or planned during the study	☐	☐
15	Subject receiving blood products or immunoglobulins in the three months preceding inclusion or requiring such treatment during the study	☐	☐
16*	Haemoglobin concentration < 10.0 g/dl for women and < 11.5 g/dl for men	☐	☐
17*	Platelet count < 120,000/mm^3	☐	☐
18*	ALAT and/or ASAT levels > 3 times the upper limit of the normal range (ULN)	☐	☐
19	Allergy to lidocaine	☐	☐

If a single YES is ticked, the subject cannot be included in the study.

**** Exclusion criteria to be checked after reception of the results of the biological tests carried out at V0***

Urinary test for pregnancy

- Result of the pregnancy test: ☐ Positive ☐ Negative ☐ NA

If the pregnancy test is positive, the subject cannot be included in the study

☞ STOP

Demographic data and vital signs

- Date of birth (MM/YYYY): |__|__|/|__|__|__|__|
- Sex: ☐ Male ☐ Female
- Weight: |__|__|__|.|__|kg
- Height: |__|__|__| cm
- BMI*: |__|__|.|__|kg/m^2
- BP* (1st reading) : |__|__|__|/|__|__|__|mmHg
  BP* (2nd reading): |__|__|__|/|__|__|__|mmHg
  *BP taken with the patient lying down
- HR: |__|__|__|bpm
- Auricular temperature: |__|__|,|__|℃
- Abdominal circumference: |__|__|__|cm
- ECG : ☐ Normal
  ☐ Abnormal, not clinically significant, describe: .....
  ☐ Abnormal, clinically significant, describe: .....

* Body mass index = (weight (kg)/(height (m) x height (m))

Physical examination

Systems	Interpretation			Comment if abnormal
	Normal	Abnormal NCS*	Abnormal CS*	
Skeletal system	☐	☐	☐	
Muscle system	☐	☐	☐	
Nervous system	☐	☐	☐	
Endocrine system	☐	☐	☐	
Cardiovascular system	☐	☐	☐	
Respiratory system	☐	☐	☐	
Integumentary system	☐	☐	☐	
Immune and lymphatic system	☐	☐	☐	
Digestive system including	☐	☐	☐	
The buccodental sphere	☐	☐	☐	
Urinary system	☐	☐	☐	
Reproductive system	☐	☐	☐	

* Abnormal NCS = Abnormal, not clinically significant
* Abnormal CS = Abnormal, clinically significant

If clinically significant, please report the abnormality in the "medical history" section.

Personal medical historv 1/4

- Antecedents and concomitant diseases

Endocrine, metabolic and nutritional diseases: ☐ Yes ☐ No							
If yes:	Yes	No	Don't know	Current		Treatment underway	
				Yes	No	Yes	No
- Hypothyroidism	☐	☐	☐	☐	☐	☐	☐
- Hyperthyroidism	☐	☐	☐	☐	☐	☐	☐
- Type 2 diabetes	☐	☐	☐	☐	☐	☐	☐
- Type 1 diabetes*	☐	☐	☐	☐	☐	☐	☐
- Hypercholesterolaemia	☐	☐	☐	☐	☐	☐	☐
- Hypertriglyceridaemia	☐	☐	☐	☐	☐	☐	☐
- Other, please specify	☐	☐	☐	☐	☐	☐	☐

Cardiovascular diseases: ☐ Yes ☐ No							
If yes:	Yes	No	Don't know	Current		Treatment underway	
				Yes	No	Yes	No
- Arterial hypertension	☐	☐	☐	☐	☐	☐	☐
- Myocardial infarction	☐	☐	☐	☐	☐	☐	☐
- Pulmonary embolism	☐	☐	☐	☐	☐	☐	☐
- Auricular fibrillation	☐	☐	☐	☐	☐	☐	☐
- Cardiac arrythmia	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:	☐	☐	☐	☐	☐	☐	☐

Respiratory diseases: ☐ Yes ☐ No							
If yes:	Yes	No		Current		Treatment underway	
				Yes	No	Yes	No
- Chronic bronchitis	☐	☐		☐	☐	☐	☐
- Emphysema	☐	☐		☐	☐	☐	☐
- Asthma	☐	☐		☐	☐	☐	☐
- Other, please specify:.....	☐	☐		☐	☐	☐	☐

If the subject presents one of the diseases followed by an asterisk, he or she cannot be included in the study.

Personal medical historv 2/4

Digestive diseases or problems: ☐ Yes ☐ No							
				Current		Treatment underway	
If yes:	Yes	No	Don't know	Yes	No	Yes	No
- Gastro-oesophageal reflux	☐	☐	☐	☐	☐	☐	☐
- Cirrhosis of the liver, chronic liver disease	☐	☐	☐	☐	☐	☐	☐
- Crohn's disease*	☐	☐	☐	☐	☐	☐	☐
- Stomatological problems	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:	☐	☐	☐	☐	☐	☐	☐

Nervous system diseases: ☐ Yes ☐ No							
				Current		Treatment underway	
If yes:	Yes	No	Don't know	Yes	No	Yes	No
- Migraines, recurrent strong headaches	☐	☐	☐	☐	☐	☐	☐
- Multiple sclerosis	☐	☐	☐	☐	☐	☐	☐
- Epilepsy	☐	☐	☐	☐	☐	☐	☐
- Alzheimer's disease	☐	☐	☐	☐	☐	☐	☐
- Parkinson's disease	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:	☐	☐	☐	☐	☐	☐	☐

Mental and behavioural problems: ☐ Yes ☐ No							
				Current		Treatment underway	
If yes:	Yes	No	Don't know	Yes	No	Yes	No
- Depression*	☐	☐	☐	☐	☐	☐	☐
- Anxiety, anxious disorders	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:.....	☐	☐	☐	☐	☐	☐	☐

Musculoskeletal problems: ☐ Yes ☐ No							
				Current		Treatment underway	
If yes:	Yes	No	Don't know	Yes	No	Yes	No
- Osteoporosis	☐	☐	☐	☐	☐	☐	☐
- Arthrosis	☐	☐	☐	☐	☐	☐	☐
- Rheumatoid arthritis*, other types of arthritis	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:	☐	☐	☐	☐	☐	☐	☐

If the subject present any of the diseases followed by an asterisk, he or she cannot be included in the study.

Personal medical historv 3/4

Childhood diseases:	☐ Yes	☐ No					
				Current		Treatment underway	
If yes:	Yes	No	Don't know	Yes	No	Yes	No
- Measles	☐	☐	☐	☐	☐	☐	☐
- Rubella	☐	☐	☐	☐	☐	☐	☐
- Chicken pox	☐	☐	☐	☐	☐	☐	☐
- Mumps	☐	☐	☐	☐	☐	☐	☐
- Exanthema subitum	☐	☐	☐	☐	☐	☐	☐
Other, please specify	☐	☐	☐	☐	☐	☐	☐
Other diseases:	☐ Yes	☐ No					
				Current		Treatment underway	
If yes:	Yes	No	Don't know	Yes	No	Yes	No
- Renal insufficiency	☐	☐	☐	☐	☐	☐	☐
- Autoimmune disease*: please specify:	☐	☐	☐	☐	☐	☐	☐
- Skin disease (eczema, psoriasis etc.)	☐	☐	☐	☐	☐	☐	☐
- Allergic disease: please specify:	☐	☐	☐	☐	☐	☐	☐
- Tumour or cancer: please specify:	☐	☐	☐	☐	☐	☐	☐
- Chronic infectious diseases* Please specify	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:	☐	☐	☐	☐	☐	☐	☐

If the subject presents a disease followed by an asterisk, he or she cannot be included in the study.

Personal medical historv 4/4

Surgical interventions: ☐ Yes ☐ No

If yes:	Yes	No	Don't know	Current		Treatment underway	
				Yes	No	Yes	No
- Splenectomy*	☐	☐	☐	☐	☐	☐	☐
- Tonsillectomy	☐	☐	☐	☐	☐	☐	☐
- Appendicectomy	☐	☐	☐	☐	☐	☐	☐
- Adenoidectomy	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:.....	☐	☐	☐	☐	☐	☐	☐
- Other, please specify:.....	☐	☐	☐	☐	☐	☐	☐

If the subject presents one of the diseases followed by an asterisk, he or she cannot be included in the study.

- Vaccinations *(please refer to the subject's vaccination records)*:

Measles ☐ Yes ☐ No

Chicken pox ☐ Yes ☐ No

Hepatitis B ☐ Yes ☐ No

Tuberculosis ☐ Yes ☐ No

Flu ☐ Yes ☐ No

Poliomyelitis ☐ Yes ☐ No

Other, please specify: ……

Has the subject been vaccinated in the last three months? ☐ Yes ☐ No

Subjects that have been vaccinated in the last three months cannot be included in the study.

Biological samples

- 20 ml blood sample taken: ☐Yes ☐No

  If yes, time at which taken (HH/MM) |__|__|/|__|__|

- Urine sample collected: ☐Yes ☐No

  If yes, time at which taken (HH/MM) |__|__|/|__|__|

- Pregnancy test carried out on urine: ☐Yes ☐No

Haematology

	Abnormal, not clinically significant	Abnormal, clinically significant
Erythrocytes	☐	☐
Haemoglobin	☐	☐
Haematocrit	☐	☐
Mean globule volume	☐	☐
Leukocytes	☐	☐
Neutrophils	☐	☐
Eosinophils	☐	☐
Basophils	☐	☐
Lymphocytes	☐	☐
Monocytes	☐	☐
Platelets	☐	☐

If the subject presents a clinically significant result, he or she cannot be included in the study.

Biochemistry

	Abnormal, not clinically significant	Abnormal, clinically significant
Sodium	☐	☐
Potassium	☐	☐
Calcium	☐	☐
Phosphate	☐	☐
Chloride	☐	☐
Bicarbonates	☐	☐
Alkaline phosphatases	☐	☐
ASAT	☐	☐
ALAT	☐	☐
Gamma GT	☐	☐
Total bilirubin	☐	☐
Urea	☐	☐
Creatinine	☐	☐
Uric acid	☐	☐
Albumin	☐	☐
Fasting glycaemia	☐	☐
Total cholesterol	☐	☐
LDL	☐	☐
HDL	☐	☐
Triglycerides	☐	☐
Total protein	☐	☐
CRP	☐	☐

If the subject presents a clinically significant result, he or she cannot be included in the study.

Serology

	Negative	Positive	Interpretation
Hepatitis B	☐	☐	☐ Prior infection ☐ Acute infection ☐ Chronic infection ☐ Vaccination ☐ Non interpretable
Hepatitis C	☐	☐	☐ Prior infection ☐ Acute infection ☐ Chronic infection ☐ Non interpretable
HIV	☐	☐	NA
CMV	☐	☐	☐ Prior infection ☐ Active infection ☐ Non interpretable
HTLV-1	☐	☐	NA

If the subject presents a positive result, he or she cannot be included in the study.

Other urine tests

- Tests of illegal substances

	Negative	Positive	Not clinically significant	Clinically significant
Cannabinoids	☐	☐	☐	☐

Subjects presenting positive results cannot be included in the study

- Proteinuria and glycosuria

	Negative	Positive
Proteinuria	☐	☐
Glycosuria	☐	☐

If the subject presents a positive, clinically significant result, he or she cannot be included in the study

Relatives

- Is the subject aware of another member of his/her family having participated in this study?

  ☐Yes ☐No

- Are the parents of the subject related? ☐Yes ☐No

  If yes: ☐ First cousins

  ☐ Second cousins

  ☐ Other, please specify: ……

If the subject is genetically related to another subject already included in the study, he or she cannot be selected.

The Nutrinet-Santé Study

- Does the subject wish to participate in the Nutrinet Santé study that has been described to him/her ☐ Yes ☐ No
- If yes, please give the number attributed by Nutrinet : |__| |__||__||__||__|

Concomitant treatments/events

- Is the volunteer currently taking any treatments or has the volunteer taken any treatments over the last three months? ☐ Yes ☐ No

  If Yes, please complete the "concomitant treatments" section, indicating all treatments (including oral contraceptives, food supplements, blood transfusions, vaccinations) received by the volunteer and check that they do not correspond to treatments prohibited by the protocol (see the protocol list).

- Did the volunteer present an adverse event at this visit?

  ☐ Yes ☐ No

  If Yes, please complete the "adverse events" section

Status of the volunteer

☐ Included ☐ Not included

If the subject is selected, please organise a new appointment for visit V1.

Date of the V1 visit

|__|__|/|__|__|/|__|__|__|__|

Confirmation of inclusion

Does the subject satisfy all the inclusion and non-inclusion criteria: ☐ Yes ☐ No

Verification of sampling constraints

		Yes	No
1	Subject fasted for at least 6 hours (only water intake permitted)	☐	☐
2	Subject has not taken part in any physical activity during the 8 hours immediately preceding inclusion	☐	☐

If a single NO is ticked, the subject cannot provide samples at V1. Please schedule a new V1 appointment.

Vital signs

- BP* (1st reading): |__|__|__|/|__|__|__|mmHg
  BP* (2nd reading): |__|__|__|/|__|__|__|mmHg
  *BP taken with the patient lying down
- HR: |__|__|__|bpm
- Auricular temperature: |__|__|.|__|℃

Physical examination

Systems	Interpretation			Comment if abnormal
	Normal	Abnormal NCS*	Abnormal CS*	
Skeletal system	☐	☐	☐	
Muscle system	☐	☐	☐	
Nervous system	☐	☐	☐	
Endocrine system	☐	☐	☐	
Cardiovascular system	☐	☐	☐	
Respiratory system	☐	☐	☐	
Integumentary system	☐	☐	☐	
Immune and lymphatic system	☐	☐	☐	
Digestive system	☐	☐	☐	
Buccodental sphere	☐	☐	☐	
Urinary system	☐	☐	☐	
Reproductive system	☐	☐	☐	

* Abnormal NCS = Abnormal, not clinically significant
* Abnormal CS = Abnormal, clinically significant

If clinically significant, please report the abnormality in the "adverse events" section.

Biological samples at V1

- 12 ml blood sample collected (baseline): ☐ Yes ☐ No
  If yes, time at which sample taken (HH/MM) |__|__|/|__|__|

- 25 ml blood sample collected (fresh blood): ☐ Yes ☐ No
  If yes, time at which sample taken (HH/MM) |__|__|/|__|__|

- 50 ml blood sample collected (TruCulture): ☐ Yes ☐ No
  If yes, time at which sample taken (HH/MM) |__|__|/|__|__|

  Were there any errors in the manipulation of the tubes? ☐ Yes ☐ No

  Specify the batch number of the tubes used: ☐ batch A ☐ batch B

- Nasal swab collected: ☐ Yes ☐ No

- Stool sample: ☐ Yes ☐ No
  If yes, date and time of collection

  Date |__| |__| / |__| |__| / |__| |__| |__| |__| time |__|__|/|__|__|

SKIN BIOPSY

Sample of skin 3 mm in diameter and 7 mm thick

- Skin biopsy carried out: ☐ Yes ☐ No ☐ NA

Serology

	Negative	Positive
Flu	☐	☐

Immunology

	Abnormal, not clinically significant	Abnormal, clinically significant
IgG	☐	☐
IgA	☐	☐
IgM	☐	☐
IgE	☐	☐

If the subject presents a clinically significant result, please reported it in the "adverse events" section.

Concomitant treatments/events

- Has there been any change in concomitant treatments (stopping, starting or modification of the prescription) since the last visit? ☐ Yes ☐ No

  If Yes, please complete the "concomitant treatments" section, indicating all treatments (including oral contraceptives and dietary supplements) taken by the volunteer, and check that none of these treatments are prohibited by the protocol (please refer to the protocol list).

- Has the volunteer presented an adverse event or a change in a concomitant disease since the last visit? ☐ Yes ☐ No

  If Yes, please complete the "adverse events" section

Nutrinet-Santé study

- Is the subject currently participating in the Nutrinet-Santé study presented to him/her at V0?

  ☐ Yes ☐ No

GENERAL QUESTIONNAIRE TO BE COMPLETED BY THE INVESTIGATOR WITH THE SUBJECT

Personal data

- Eye colour: ☐ Green ☐ Blue-grey ☐ Blue ☐ Hazel ☐ Light brown ☐ Dark brown ☐ Other, please specify:…….

- Hair colour: ☐ Black ☐ Dark brown ☐ Light brown ☐ Auburn ☐ Blonde ☐ Other, please specify:…….

- Age at which hair started greying: |__|__|years ☐ Don't know ☐ Not applicable

- Does the subject wear glasses/contact lenses: ☐ Yes ☐ No

  If yes : ☐ Glasses ☐ Contact lenses

- Place of birth (town): ……

- Place of residence until the age of 13 years (town):

  1 - ……
  2 - ……
  3 - ……
  4 - ……
  5 - ……
  6 - ……
  7 - ……
  8 - ……
  9 - ……
  10 - ……

Institut Pasteur

Inclusion visit
V1 (V0 + 4 ± 3 days)

Centre |__|

Subject |__|__|__|__|

Socio-professional information 1/2

- Level of education

  ☐ No diploma

  ☐ Primary school certificate only

  ☐ CAP, BEP, apprenticeship certificate, BEPC, *Brevet des collèges*

  ☐ Baccalaureate (general, professional or technical), technician's certificate

  ☐ Higher education, cycle one: DUT, BTS

  ☐ Higher education, second and third university cycles or equivalent (degree, *maîtrise*, DEA, Masters, PhD, engineer's diploma etc.)

- Does the subject have a steady job? ☐ Yes ☐ No
- Net monthly income of the household (€):

☐ 0 < salary ≤1000 ☐ 1000 < salary ≤ 2000 ☐ 2000 < salary ≤ 3000

☐ 3000 < salary ≤ 4000 ☐ 4000 < salary ≤ 5000 ☐ 5000 < salaire

<table>
<tr><td>If Yes: complete the next column ➔</td><td rowspan="3">Socio-professional category (INSEE)

☐ Farmer
☐ Artisans, tradesman or company director
☐ Senior executive or independent profession
☐ Middle management
☐ Employee
☐ Labourer
☐ Other categories (e.g. artist, clergy, soldier, police officer)</td></tr>
<tr><td>If No:
☐ Student
☐ Looking for first job
☐ Unemployed ➔ fill in the next column
☐ Housewife/househusband
☐ Retired ➔fill in the next column for the profession exercised for the longest period of time</td></tr>
<tr><td>For unemployed and retired subjects, how long is it since they last worked?
☐ Less than 1 year
☐ Between 1 and 3 years
☐ 3 years or more
☐ Has never worked</td></tr>
</table>

Socio-professional information 2/2

- Does the subject work:

  ☐ Exclusively during the day

  ☐ Exclusively during the night

  ☐ Without fixed hours

- Does the subject work:

  ☐ Full time

  ☐ Part time

- Is the subject on leave from work ☐ Yes ☐ No

  If yes, why?.....

- Is or has the subject been exposed to nuisances (*place a cross in the appropriate boxes*)?

	Current exposure	Past exposure	Never	Don't know
Noise				
Dust				
Silica				
Asbestos				
Benzene				
Toxic products				
Others Please specify:……..				

- Does the subject live:

  ☐ Alone with no children ☐ Alone with children

  ☐ With a partner but no children ☐ With a partner and children

- Does the subject:

  ☐ Own his/her home (or is in the process of buying it)

  ☐ Rent his/her home

- Professional physical activity:

  Does the subject's work or journey to and from work involve physical activity?

  ☐ None

  ☐ Moderate

  ☐ Considerable

If "moderate" or "considerable", please indicate the daily duration of professional physical activity:

☐ 0 to 20 minutes per day

☐ 21 to 60 minutes per day

☐ 1 to 2 hours per day

☐ More than 2 hours per day

- Physical activity during leisure time:

What is the usual level of physical activity during leisure time of the subject?

☐ Little or no physical activity

☐ Moderate physical activity

☐ Intensive physical activity (competitions)

How many days per week does the subject take part in physical activities during leisure time (0 to 7 days): |__|

How much time does the subject spend on leisure-time physical activity per day, on average: |__|__|h|__|__| min

- Voyages taken in the last three months? ☐ Yes ☐ No

  If yes, please specify:

  Country:…… Duration: |__|__|__| days

  Country:…… Duration: |__|__|__| days

  Country:…… Duration: |__|__|__| days

  Country:…… Duration: |__|__|__| days

- Has the subject donated any blood in the last six months? ☐ Yes ☐ No

If Yes, please specify the date (MM/YYYY): |__|__|/|__|__|__|__|

- Smoking:

☐ Non-smoker

☐ Smoker

☐ Cigarettes |__|__|__| /day Year started: |__|__|__|__|

☐ Cigars |__|__|__| /day Year started: |__|__|__|__|

☐ Pipe |__|__|__| /day Year started: |__|__|__|__|

☐ Ex-smoker

☐ Cigarettes |__|__|__| /day Year started/stopped: |__|__|__|__|/|__|__|__|__|

☐ Cigars |__|__|__| /day Year started/stopped: |__|__|__|__|/|__|__|__|__|

☐ Pipe |__|__|__| /day Year started/stopped: |__|__|__|__|/|__|__|__|__|

- Past exposure to second-hand smoke (home/work): ☐ Yes ☐ No

If yes, please specify: the number of years: |__|__|

The date at which exposure stopped (MM/YYYY):

|__|__|/|__|__|__|__|

- Current exposure to second-hand smoke (home/work): ☐ Yes ☐ No

If yes, please specify the number of years: |__|__|

- Substance consumption:

	Never	Rarely	Regularly
Hashish, cannabis	☐	☐	☐
Cocaine	☐	☐	☐
Heroin	☐	☐	☐
Amphetamines	☐	☐	☐
Hallucinogens	☐	☐	☐
Other, please specify: ……	☐	☐	☐

- How many hours per day does the subject sleep on average, including siestas:

|__|__| h |__|__| min Hours of sleep (over a 24-hour period, day and night)

|__| Preferred not to respond

|__| Don't know

.

- Does the subject often find it difficult to fall asleep or to remain asleep?

|__| Never
|__| Sometimes
|__| Occasionally
|__| Most of the time
|__| All the time
|__| Preferred not to respond
|__| Don't know

- On average, how much light enters the subject's bedroom while he/she is asleep?

|__| Practically none
|__| A little
|__| A lot
|__| Preferred not to respond
|__| Don't know

- During the last 12 months, has the subject experienced a stressful event, such as the loss of a loved one, a serious illness or major professional, familial or financial difficulties:
  - ☐ Yes
  - ☐ No
  - ☐ Preferred not to respond

- During the last 2 weeks, how often has the subject been bothered by the following problems?

		Never	On several days	On more than 7 days	Almost every day
A	Lack of interest or pleasure in doing things				
B	Feeling sad, depressed or despairing				
C	Difficulties falling asleep or staying asleep, or sleeping too much				
D	Feeling tired or having little energy				
E	Little or too much appetite				
F	Poor self-image, or you think that you are a loser or have not achieved your own expectations or those of your family.				
G	Difficulty concentrating on things like reading the newspaper or watching the television				
H	You move or speak so slowly that other people point it out. Or, on the contrary, you are so agitated that you move much more than normal				
i	You have thought that you would be better off dead or have considered injuring yourself in some way				

- Age at first period: |__|__|years
- Menopausal/postmenopausal: ☐ Yes ☐ No

  If yes, please specify:

  Age at last period: |__|__|years

  Hormone replacement therapy: ☐ Yes ☐ No

  Non-hormonal treatment: ☐ Yes ☐ No

  If no, please specify the method of contraception used:

  ☐ Intrauterine device

  ☐ Pill

  ☐ Male or female condom

  ☐ Tubal ligation

  ☐ Other method of contraception

  ☐ No method of contraception

- Number of pregnancies: |__|__|pregnancies
- Number of deliveries: |__|__|deliveries
- Year at the end of the last pregnancy: |__|__|__|__|
- Year of last vaginal smear {NdT : cervival??} |__|__|__|__|

- Birth:

☐ Premature. ☐ Born at term ☐ Don't know
Specify the number of weeks: ……

☐ By Caesarean section ☐Vaginal delivery ☐ Don't know

Weight at birth: |__|.|__|__|__|kg Length at birth: |__|__|.|__|cm

- Mode of feeding at birth:

☐ Formula milk. ☐ Maternal breastfeeding ☐ Don't know
Specify the duration: |__|__|__|weeks

	Yes	No	Don't know	If Yes, relationship
Arterial hypertension	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister
Myocardial infarction	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister
Diabetes	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister
Cerebral accident, haemorrhage or congestion	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister
Breast cancer	☐	☐	☐	☐ Mother ☐ Sister
Cervical cancer	☐	☐	☐	☐ Mother ☐ Sister
Cancer of the colon or rectum	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister
Other cancer, please specify: ……	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister
Allergic disease, please specify: ……	☐	☐	☐	☐ Father ☐ Mother ☐ Brother ☐ Sister

- Particular diet prescribed by a doctor or a dietician for medical reasons:

  ☐ Yes ☐ No

  If yes, please specify:

  Type of diet:…….. Reason:……..

  How long has the subject been on this diet……

- Other than on rest days, does the subject have regular mealtimes?

  ☐ Yes ☐ No

- Does the subject eat breakfast? ☐ Always ☐ Not always ☐ Never

- Does the subject eat lunch? ☐ Always ☐ Not always ☐ Never

- Does the subject eat dinner? ☐ Always ☐ Not always ☐ Never

- Does the subject eat other than at these mealtimes?

  ☐ During the morning

  ☐ During the afternoon

  ☐ During the evening or night

  ☐ No snacks

- Does the subject nibble between meals, without eating a proper snack?

  ☐ Often ☐ Sometimes ☐ Never

- Does the subject cook?

☐ Several times/week ☐ Once or twice/week ☐ Less than once/week

- Does the subject eat in restaurants (other than the canteen at work) or at friends' houses?

☐ Several times/week ☐ Once or twice/week ☐ Less than once/week

- Does the subject eat in fast-food restaurants?

☐ Several times/week ☐ Once/week ☐ Occasionally ☐ Never

- Does the subject use "light" products reduced in:

☐ Sugar ☐ Fat ☐ Salt ☐ No "light" products

- What are the subject's salt consumption habits?

☐ Often salts his/her food at table ☐ Rarely or never salts his/her food at table

- General consumption (mark a cross in the appropriate box):

	Twice per day or more	Once per day	More than twice per week	Once or twice per week	Once or twice per week	Rarely or never
Meat						
Fish						
Eggs						
Raw vegetables						
Cooked vegetables						
Starchy foods (pasta, rice, potatoes etc.)						
Dried pulses (lentils, chickpeas, split peas etc.)						
Raw fruit						
Cooked fruit (stewed fruit etc.)						
Dairy products (milk, yoghurt etc.)						
Cheese						
Cooked and cured meats (ham, salami, pate etc.)						
Sweet things (chocolate, sweets, honey, jam etc.)						
Pastries and sweet breads (croissants, brioches, pains au chocolat, etc.)						
Fried products (chips, crisps, doughnuts, nuggets, cordon bleu, etc.) or pasties/pies						
Ready meals						
Desserts (cream desserts, ice cream, cream cakes, etc.)						
Sodas and other sugary drinks (other than diet drinks low in sugar)						
Pain (one baguette ~250 g)	At least 250 g/day		Between 125 and 250 g/day		Between 50 and 125 g/day	Less than 50 g/day

- Does the subject drink alcohol:

☐ Every day ☐ Several times per week

☐ Once per week ☐ Occasionally ☐ Never

If “every day” or “once” or “several times per week”, please indicate the precise number of glasses:

Wine: |__|__|/week

Beer, cider: |__|__|/week

Spirits: |__|__|/week

- Does the subject take any dietary supplements?

	Every day	Several times/week	Several times per month	Occasionally	Rarely or never
Vitamins only, please specify:					
.....					
.....					
Minerals only, please specify:					
.....					
.....					
Multiminerals and multivitamins					
Probiotics					
Other:					

- Does the subject use essential oils?

	Every day	Several times/week	Several times/month	Occasionally	Rarely or never
Oral route					
Local application					
Diffusion into the atmosphere					

|__|__|/|__|__|/|__|__|__|__|

		Yes	No
1	Subject fasted for at least six hours (only water intake authorised)	☐	☐
2	Subject not taking part in any physical activity during the eight hours immediately preceding sampling	☐	☐

If a single NO is ticked, the V2 samples cannot be taken and a new appointment should be organised for the V2 visit.

- BP* (1st reading): |__|__|__|/|__|__|__|mmHg
  BP* (2nd reading): |__|__|__|/|__|__|__|mmHg
  *BP taken with the patient lying down
- HR: |__|__|__|bpm
- Auricular temperature: |__|__|.|__|℃

Systems	Interpretation			Comment if abnormal
	Normal	Abnormal NCS*	Abnormal CS*	
Skeletal system	☐	☐	☐	
Muscle system	☐	☐	☐	
Nervous system	☐	☐	☐	
Endocrine system	☐	☐	☐	
Cardiovascular system	☐	☐	☐	
Respiratory system	☐	☐	☐	
Integumentary system	☐	☐	☐	
Immune and lymphatic system	☐	☐	☐	
Digestive system	☐	☐	☐	
Buccodental sphere	☐	☐	☐	
Urinary system	☐	☐	☐	
Reproductive system	☐	☐	☐	

* Abnormal NCS = Abnormal, not clinically significant
* Abnormal CS = Abnormal, clinically significant

If the abnormality is clinically significant, please report it in the "adverse events" section.

- Is the biopsy zone healing normally? ☐ Yes ☐ No

If any healing problems are observed, please report them in the "adverse events" section.

- 8 ml blood sample taken (CRP): ☐ Yes ☐ No
  If yes, hour at which taken (HH/MM) |__|__|/|__|__|
- 25 ml blood sample taken (fresh blood): ☐ Yes ☐ No
  If yes, hour at which taken (HH/MM) |__|__|/|__|__|
- 50 ml blood sample taken (TruCulture): ☐ Yes ☐ No
  If yes, hour at which taken (HH/MM) |__|__|/|__|__|
  Was any error made during the manipulation of the tubes? ☐ Yes ☐ No
  Specify the batch number of the tubes used: ☐ batch A ☐ batch B
- Nasal swab taken: ☐ Yes ☐ No
- Stool sample taken: ☐ Yes ☐ No
  If yes, date and time at which taken
  Date |__| |__| / |__| |__| / |__| |__| |__| |__| time |__|__|/|__|__|
- Pregnancy test carried out on urine: ☐ Yes ☐ No

- Result of pregnancy test: ☐ Positive ☐ Negative ☐ NA

If the pregnancy test is positive, please complete a pregnancy declaration form

	Abnormal, not clinically significant	Abnormal, clinically significant
Erythrocytes	☐	☐
Haemoglobin	☐	☐
Haematocrit	☐	☐
Mean globule volume	☐	☐
Leukocytes	☐	☐
Neutrophils	☐	☐
Eosinophils	☐	☐
Basophils	☐	☐
Lymphocytes	☐	☐
Monocytes	☐	☐
Platelets	☐	☐

If the subject presents a clinically significant result, please complete the "adverse events" section.

	Abnormal, not clinically significant	Abnormal, clinically significant
CRP	☐	☐

If the subject presents a clinically significant result, please complete the "adverse events" section.

- Has there been a change in the concomitant treatments (stopping, starting or change to the prescription) since the last visit? ☐ Yes ☐ Non

  If Yes, please complete the "concomitant treatments" section, indicating all treatments (including oral contraceptives and dietary supplements) taken by the volunteer and check that none of these treatments are prohibited by the protocol (see the protocol list).

- Has the volunteer presented an adverse effect or a change in concomitant disease since the last visit? ☐ Yes ☐ No

  If Yes, please complete the "adverse events" section

- Is the subject participating in the Nutrinet Santé study and has he/she completed the questionnaires described in the protocol? ☐ Yes ☐ No

Institut Pasteur

End of the study

Centre |__||__|

Subject |__||__||__||__|

|__|__|/|__|__|/|__|__|__|__|

- Was the study carried out in accordance with the protocol and can the evaluation of the volunteer be considered valid

If the subject was randomized to the biopsy group, was the biopsy carried out at V1 and did V2 take place correctly? ☐Yes ☐ No

If no, please specify _____

If the subject was not randomised to the biopsy group, did visit V1 take place correctly? ☐Yes ☐No

If no, please specify _____

- Was the study interrupted? ☐ Yes ☐ No

If Yes, please specify the reason:

1 Decision of the volunteer ☐
Reasons: _____

2 Adverse events? *(Please complete the adverse events form)* ☐

3 Volunteer lost to follow-up ☐
(Indicate the means used to contact the volunteer, telephone calls, letters etc.)
Means used: _____

4 Decision of the promoter ☐

5 Decision of the authorities ☐

6 Decision of the investigator ☐

7 Other reason (please specify): ☐
Reasons: _____

If there are several reasons, please specify the principal reasons for leaving the study, by entering the corresponding code: |__|

I have personally checked that all the data entered on this case report form are complete and correct.

Date : |__|__|/|__|__|/|__|__|__|__| **Name and signature**

Concomitant treatments

Report in this section all **current treatments and treatments received in the last three months** (including blood transfusions, vaccinations and dietary supplements)

(R) Route of administration:

(1) Oral (per os)
(2) Parenteral (intravenous, intramusculaire, subcutaneous, periarticular)
(3) Local (cutaneous, ophthalmic, nasal, auricular, laryngal, vaginal)
(4) Transdermic
(5) Rectal
(6) Sublingual

Dose schedule: mode of treatment administration, per day, week or month, in the form of a tablet, injection, patch etc.

Dose: dose of the active ingredient of the tablet, injection etc.

If the prescription is modified, please indicate the last day before the change and complete a new line with the new prescription

Exclusion criteria/unauthorised treatments:

- Antidepressants
- Immunosuppressants or other drugs modifying the immune response (corticosteroids) used for long-term treatment in the six months preceding the study or during the study
- Chemotherapy and anticancer treatments except for tamoxifen (or similar molecules) used for long-term prophylaxis in women in complete remission for more than three years after treatment for breast cancer
- Anticoagulant (coumarin, heparin or any other antiplatelet drug) during the course of the study or in the two months preceding V0
- Non-steroidal anti-inflammatory drug, including aspirin, used for long-term treatment in the six months preceding V0 or taken as a one-off treatment during the seven days preceding V1
- Antidiabetic treatment
- Oral corticosteroids at a dose of 20 mg/day prednisone or equivalent over a period of more than two weeks
- Blood products or immunoglobulins during the course of the study or in the three months preceding V0
- Nasal, intestinal and respiratory antibiotics/antiseptics during the three months preceding V0 or during the course of the study
- Vaccination during the course of the study or in the three months preceding V0
- Trial products
- Bisphosphonates

Authorised treatments: these treatments must have begun three months before V0 and the dose must remain stable throughout the study:

- Oral contraception
- Hormone replacement therapy for the menopause