



Australian Government
Repatriation Medical Authority

Statement of Principles
concerning
PARKINSON'S DISEASE AND SECONDARY
PARKINSONISM
(Reasonable Hypothesis)
(No. 55 of 2016)

The Repatriation Medical Authority determines the following Statement of Principles under subsection 196B(2) of the *Veterans' Entitlements Act 1986*.

Dated 22 April 2016

The Common Seal of the
Repatriation Medical Authority
was affixed to this instrument
at the direction of:

A handwritten signature in black ink, appearing to read 'Nicholas Saunders'.

Professor Nicholas Saunders AO
Chairperson

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1 Name

This is the Statement of Principles concerning *Parkinson's disease and secondary parkinsonism (Reasonable Hypothesis)* (No. 55 of 2016).

2 Commencement

This instrument commences on 23 May 2016.

3 Authority

This instrument is made under subsection 196B(2) of the *Veterans' Entitlements Act 1986*.

4 Revocation

The Statement of Principles concerning Parkinson's disease and parkinsonism No. 65 of 2007, as amended, made under subsections 196B(2) and (8) of the VEA is revoked.

5 Application

This instrument applies to a claim to which section 120A of the VEA or section 338 of the *Military Rehabilitation and Compensation Act 2004* applies.

6 Definitions

The terms defined in the Schedule 1 - Dictionary have the meaning given when used in this instrument.

7 Kind of injury, disease or death to which this Statement of Principles relates

- (1) This Statement of Principles is about Parkinson's disease and secondary parkinsonism and death from Parkinson's disease and secondary parkinsonism.

*Meaning of **Parkinson's disease***

- (2) For the purposes of this Statement of Principles, Parkinson's disease means a neurodegenerative disease involving the progressive failure of dopaminergic transmission in the nigrostriatal system of the basal ganglia, which:

- (a) is characterised clinically by:
- (i) the presence of bradykinesia, muscular rigidity, a resting tremor and postural instability;
 - (ii) symptoms which may gradually progress;
 - (iii) a sustained response to therapy with levodopa; and

- (iv) non-motor symptoms including sleep, mood and autonomic disturbances; and
- (b) is characterised pathologically by the degeneration of dopaminergic neurons in the substantia nigra pars compacta and the presence of alpha-synuclein-associated Lewy bodies or Lewy neurite intracellular inclusions at widespread locations in the central and peripheral nervous system; and
- (c) excludes secondary parkinsonism, parkinsonism in other primary neurodegenerative diseases and Parkinson plus diseases including dementia with Lewy bodies, multiple system atrophy, progressive supranuclear palsy, frontotemporal dementia and corticobasal degeneration.

*Meaning of **secondary parkinsonism***

- (3) For the purposes of this Statement of Principles, secondary parkinsonism means an acquired movement disorder caused by exogenous factors that interfere with dopaminergic transmission in the nigrostriatal system of the basal ganglia, which:
 - (a) is characterised clinically by the presence of bradykinesia, muscular rigidity, a resting tremor and postural instability; and
 - (b) excludes Parkinson's disease, dementia pugilistica, non-parkinsonian tremors such as benign essential tremor, psychogenic parkinsonism, parkinsonism in primary neurodegenerative diseases and Parkinson plus diseases including dementia with Lewy bodies, multiple system atrophy, progressive supranuclear palsy, frontotemporal dementia and corticobasal degeneration.

*Death from **Parkinson's disease and secondary parkinsonism***

- (4) For the purposes of this Statement of Principles, Parkinson's disease or secondary parkinsonism, in relation to a person, includes death from a terminal event or condition that was contributed to by the person's Parkinson's disease or secondary parkinsonism.

Note: **terminal event** is defined in the Schedule 1 – Dictionary.

8 Basis for determining the factors

The Repatriation Medical Authority is of the view that there is sound medical-scientific evidence that indicates that Parkinson's disease or secondary parkinsonism and death from Parkinson's disease or secondary parkinsonism can be related to relevant service rendered by veterans, members of Peacekeeping Forces, or members of the Forces under the VEA, or members under the MRCA.

Note: **relevant service** is defined in the Schedule 1 – Dictionary.

9 Factors that must exist

At least one of the following factors must as a minimum exist before it can be said that a reasonable hypothesis has been raised connecting Parkinson's disease or secondary parkinsonism or death from Parkinson's disease or secondary parkinsonism with the circumstances of a person's relevant service:

(1) for Parkinson's disease only:

- (a) inhaling, ingesting or having cutaneous contact with a pesticide from the specified list of pesticides, for a cumulative period of at least 1 000 hours, before the clinical onset of Parkinson's disease;

Note: **specified list of pesticides** is defined in the Schedule 1 - Dictionary.

- (b) having moderate to severe traumatic brain injury more than 15 years before the clinical onset of Parkinson's disease;
- (c) inhaling trichloroethylene vapour in an enclosed space, or having cutaneous contact with trichloroethylene, for a cumulative period of at least 2 000 hours, at least 20 years before the clinical onset of Parkinson's disease;
- (d) an inability to undertake any physical activity greater than three METs for at least ten years within the 20 years before the clinical onset of Parkinson's disease;

Note: **MET** is defined in the Schedule 1 - Dictionary.

- (e) consuming an average of at least one litre of milk per day for at least the 15 years before the clinical onset of Parkinson's disease;
- (f) consuming an average of at least 150 grams of cheese per day for at least the 15 years before the clinical onset of Parkinson's disease;
- (g) having clinically significant depressive disorder or generalised anxiety disorder at least 15 years before the clinical onset of Parkinson's disease; or

Note: **clinically significant** is defined in the Schedule 1 - Dictionary.

- (h) in a person with a history of a regular smoking habit as specified, having not smoked for at least the five years before the clinical onset of Parkinson's disease;

Note: **regular smoking habit as specified** is defined in the Schedule 1 - Dictionary.

(2) for secondary parkinsonism only:

- (a) having an episode of acute cholinergic poisoning from exposure to an organophosphorus ester within the three months before the clinical onset of secondary parkinsonism;

Note: *acute cholinergic poisoning* and *organophosphorus ester* are defined in the Schedule 1 - Dictionary.

- (b) having moderate to severe traumatic brain injury within the one year before the clinical onset of secondary parkinsonism;
- (c) having an intracranial space occupying lesion within the three months before the clinical onset of secondary parkinsonism;
- (d) having hydrocephalus, or draining of hydrocephalus, within the three months before the clinical onset of secondary parkinsonism;

Note: *hydrocephalus* is defined in the Schedule 1 - Dictionary.

- (e) having a cerebrovascular accident, excluding transient ischaemic attack, within the five years before the clinical onset of secondary parkinsonism;
- (f) having a disease from the specified list of diseases involving the cerebral vessels, in the presence of neuroimaging findings of brain stem or cerebral white matter lesions, haemorrhage or infarction, at the time of the clinical onset of secondary parkinsonism;

Note: *specified list of diseases involving the cerebral vessels* is defined in the Schedule 1 - Dictionary.

- (g) having a subarachnoid haemorrhage within the three months before the clinical onset of secondary parkinsonism;
- (h) having an acquired cerebrovascular malformation or dural arteriovenous fistula at the time of the clinical onset of secondary parkinsonism;
- (i) having an hypoxic cerebral insult within the two years before the clinical onset of secondary parkinsonism;

Note: *hypoxic cerebral insult* is defined in the Schedule 1 - Dictionary.

- (j) having influenza within the three months before the clinical onset of secondary parkinsonism;
- (k) having encephalitis within the three months before the clinical onset of secondary parkinsonism;

Note: *encephalitis* is defined in the Schedule 1 - Dictionary.

- (l) being infected with the human immunodeficiency virus before the clinical onset of secondary parkinsonism;

- (m) having neurosyphilis at the time of the clinical onset of secondary parkinsonism;

Note: *neurosyphilis* is defined in the Schedule 1 - Dictionary.

- (n) having neurocysticercosis at the time of the clinical onset of secondary parkinsonism;
- (o) inhaling carbon disulphide vapour in an enclosed space, or having cutaneous contact with carbon disulphide, for a cumulative period of at least 500 hours, within the ten years before the clinical onset of secondary parkinsonism;
- (p) inhaling trichloroethylene vapour in an enclosed space, or having cutaneous contact with trichloroethylene, for a cumulative period of at least 2 000 hours, within the 20 years before the clinical onset of secondary parkinsonism;
- (q) inhaling or ingesting methanol or ethylene glycol, and having clinical, haematological or biochemical evidence of methanol or ethylene glycol intoxication, within the three months before the clinical onset of secondary parkinsonism;
- (r) being exposed to manganese as specified for a cumulative period of at least 250 hours, within the ten years before the clinical onset of secondary parkinsonism;

Note: *being exposed to manganese as specified* is defined in the Schedule 1 - Dictionary.

- (s) having clinical or biochemical evidence of manganese intoxication while receiving total parenteral nutrition or maintenance haemodialysis, at the time of the clinical onset of secondary parkinsonism;

Note: *total parenteral nutrition* is defined in the Schedule 1 - Dictionary.

- (t) inhaling, ingesting or having cutaneous contact with cyanide, and having clinical, haematological or biochemical evidence of cyanide intoxication, within the three months before the clinical onset of secondary parkinsonism;
- (u) having an injection containing 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) within the three months before the clinical onset of secondary parkinsonism;
- (v) using khat (*Catha edulis*), Ecstasy (3,4-methylenedioxymethamphetamine) or the drug methcathinone (ephedrone) within the three months before the clinical onset of secondary parkinsonism;

- (w) taking a drug or a drug from a class of drugs from the specified list of drugs, for a continuous period of at least seven days within the three months before the clinical onset of secondary parkinsonism;

Note: *specified list of drugs* is defined in the Schedule 1 - Dictionary.

- (x) having a disorder of calcium metabolism from the specified list of disorders of calcium metabolism at the time of the clinical onset of secondary parkinsonism;

Note: *specified list of disorders of calcium metabolism* is defined in the Schedule 1 - Dictionary.

- (y) having cirrhosis of the liver at the time of the clinical onset of secondary parkinsonism;

- (z) having chronic renal failure at the time of the clinical onset of secondary parkinsonism;

Note: *chronic renal failure* is defined in the Schedule 1 - Dictionary.

- (aa) having a disease from the specified list of autoimmune diseases at the time of the clinical onset of secondary parkinsonism; or

Note: *specified list of autoimmune diseases* is defined in the Schedule 1 - Dictionary.

- (bb) having a paraneoplastic encephalomyelitis at the time of the clinical onset of secondary parkinsonism;

- (3) inhaling, ingesting or having cutaneous contact with a pesticide from the specified list of pesticides, for a cumulative period of at least 1 000 hours, within the ten years before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *specified list of pesticides* is defined in the Schedule 1 - Dictionary.

- (4) having an episode of acute cholinergic poisoning from exposure to an organophosphorus ester within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *acute cholinergic poisoning* and *organophosphorus ester* are defined in the Schedule 1 - Dictionary.

- (5) having moderate to severe traumatic brain injury within the one year before the clinical worsening of Parkinson's disease or secondary parkinsonism;

- (6) having an intracranial space occupying lesion within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;

- (7) having hydrocephalus, or draining of hydrocephalus, within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *hydrocephalus* is defined in the Schedule 1 - Dictionary.

- (8) having a cerebrovascular accident, excluding transient ischaemic attack, within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (9) having a disease from the specified list of diseases involving the cerebral vessels, in the presence of neuroimaging findings of brain stem or cerebral white matter lesions, haemorrhage or infarction, at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *specified list of diseases involving the cerebral vessels* is defined in the Schedule 1 - Dictionary.

- (10) having a subarachnoid haemorrhage within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (11) having an acquired cerebrovascular malformation or dural arteriovenous fistula at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (12) having an hypoxic cerebral insult within the two years before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *hypoxic cerebral insult* is defined in the Schedule 1 - Dictionary.

- (13) having influenza within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (14) having encephalitis within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *encephalitis* is defined in the Schedule 1 - Dictionary.

- (15) being infected with the human immunodeficiency virus before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (16) having neurosyphilis at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *neurosyphilis* is defined in the Schedule 1 - Dictionary.

- (17) having neurocysticercosis at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (18) inhaling carbon disulphide vapour in an enclosed space, or having cutaneous contact with carbon disulphide, for a cumulative period of at least 500 hours, within the ten years before the clinical worsening of Parkinson's disease or secondary parkinsonism;

- (19) inhaling trichloroethylene vapour in an enclosed space, or having cutaneous contact with trichloroethylene, for a cumulative period of at least 2 000 hours, within the 20 years before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (20) inhaling or ingesting methanol or ethylene glycol, and having clinical, haematological or biochemical evidence of methanol or ethylene glycol intoxication, within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (21) being exposed to manganese as specified for a cumulative period of at least 250 hours, within the ten years before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *being exposed to manganese as specified* is defined in the Schedule 1 - Dictionary.

- (22) having clinical or biochemical evidence of manganese intoxication while receiving total parenteral nutrition or maintenance haemodialysis, at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *total parenteral nutrition* is defined in the Schedule 1 - Dictionary.

- (23) inhaling, ingesting or having cutaneous contact with cyanide, and having clinical, haematological or biochemical evidence of cyanide intoxication, within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (24) having an injection containing 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (25) using khat (*Catha edulis*), Ecstasy (3,4-methylenedioxymethamphetamine) or the drug methcathinone (ephedrone) within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;

- (26) taking a drug or a drug from a class of drugs from the specified list of drugs, for a continuous period of at least seven days within the three months before the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *specified list of drugs* is defined in the Schedule 1 - Dictionary.

- (27) having a disorder of calcium metabolism from the specified list of disorders of calcium metabolism at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;

Note: *specified list of disorders of calcium metabolism* is defined in the Schedule 1 - Dictionary.

- (28) having cirrhosis of the liver at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;

- (29) having chronic renal failure at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;
- Note: *chronic renal failure* is defined in the Schedule 1 - Dictionary.
- (30) an inability to undertake any physical activity greater than three METs for at least the five years before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- Note: *MET* is defined in the Schedule 1 - Dictionary.
- (31) having a disease from the specified list of autoimmune diseases at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;
- Note: *specified list of autoimmune diseases* is defined in the Schedule 1 - Dictionary.
- (32) consuming an average of at least one litre of milk per day for at least the five years before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (33) consuming an average of at least 150 grams of cheese per day for at least the five years before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (34) having a paraneoplastic encephalomyelitis at the time of the clinical worsening of Parkinson's disease or secondary parkinsonism;
- (35) having clinically significant depressive disorder or generalised anxiety disorder for at least the five years before the clinical worsening of Parkinson's disease or secondary parkinsonism;
- Note: *clinically significant* is defined in the Schedule 1 - Dictionary.
- (36) in a person with a history of a regular smoking habit as specified, having not smoked within the ten years before the clinical worsening of Parkinson's disease and secondary parkinsonism;
- Note: *regular smoking habit as specified* is defined in the Schedule 1 - Dictionary.
- (37) inability to obtain appropriate clinical management for Parkinson's disease or secondary parkinsonism.

10 Relationship to service

- (1) The existence in a person of any factor referred to in section 9, must be related to the relevant service rendered by the person.
- (2) The factors set out in subsections 9(3) to 9(37) apply only to material contribution to, or aggravation of, Parkinson's disease or secondary parkinsonism where the person's Parkinson's disease or secondary parkinsonism was suffered or contracted before or during (but did not arise out of) the person's relevant service.

11 Factors referring to an injury or disease covered by another Statement of Principles

In this Statement of Principles:

- (1) if a factor referred to in section 9 applies in relation to a person; and
- (2) that factor refers to an injury or disease in respect of which a Statement of Principles has been determined under subsection 196B(2) of the VEA;

then the factors in that Statement of Principles apply in accordance with the terms of that Statement of Principles as in force from time to time.

Schedule 1 - Dictionary

Note: See Section 6

1 Definitions

In this instrument:

acute cholinergic poisoning means symptoms and signs due to the inhibition of acetylcholinesterase enzyme activity which occur within the 24 hours following exposure. These symptoms and signs are acute paralysis, overwhelming bronchial secretions, bradycardia, gastrointestinal distress, miosis, lacrimation or diarrhoea.

being exposed to manganese as specified means:

- (a) working in the mining or smelting of ores containing manganese; or
- (b) welding with rods containing manganese; or
- (c) inhaling dust containing manganese.

chronic renal failure means:

- (a) having a glomerular filtration rate of less than 15 mL/min/1.73 m² for a period of at least three months; or
- (b) a need for renal replacement therapy (dialysis or transplantation) for treatment of complications of decreased glomerular filtration rate which would otherwise increase the risk of morbidity and mortality; or
- (c) undergoing chronic dialysis.

clinically significant means sufficient to warrant ongoing management, which may involve regular visits (for example, at least monthly), to a psychiatrist, counsellor or general practitioner.

encephalitis means a viral, bacterial or protozoal infection of the brain parenchyma, manifested clinically by acute febrile illness, confusion, behavioural abnormalities, altered level of consciousness, and focal or generalised epileptic seizures, or demonstrated by neuroimaging or laboratory studies.

hydrocephalus means a condition characterised by dilation of the cerebral ventricles and accompanied by accumulation of excess cerebrospinal fluid within the skull. This definition includes obstructive and non-obstructive hydrocephalus, idiopathic normal pressure hydrocephalus or traumatic hydrocephalus.

hypoxic cerebral insult means an event which results in either a decreased rate of cerebral blood flow or decreased oxygen content of cerebral arterial blood for a sustained period.

MET means a unit of measurement of the level of physical exertion. 1 MET = 3.5 ml of oxygen/kg of body weight per minute, 1.0 kcal/kg of body weight per hour or resting metabolic rate.

MRCA means the *Military Rehabilitation and Compensation Act 2004*.

neurosyphilis means infection of the central nervous system with *Treponema pallidum*.

organophosphorus ester means an agent used to inhibit acetylcholinesterase, and includes the organophosphate pesticides chlorpyrifos, dichlorvos, EPN, leptophos, methamidophos, mipafox (diisopropyl phosphorofluoridate), omethoate, parathion, TOCP (tri-ortho-cresyl phosphate), trichlorfon and trichlorfonat.

Parkinson's disease—see subsection 7(2).

regular smoking habit as specified means having smoked at least three pack-years of cigarettes or the equivalent thereof in other tobacco products.

relevant service means:

- (a) operational service under the VEA;
- (b) peacekeeping service under the VEA;
- (c) hazardous service under the VEA;
- (d) British nuclear test defence service under the VEA;
- (e) warlike service under the MRCA; or
- (f) non-warlike service under the MRCA.

secondary parkinsonism—see subsection 7(3).

specified list of autoimmune diseases means:

- (a) antiphospholipid syndrome;
- (b) Behçet's disease;
- (c) nonvasculitic autoimmune inflammatory meningoencephalitis;
- (d) Sjogren's syndrome; or
- (e) systemic lupus erythematosus.

specified list of diseases involving the cerebral vessels means:

- (a) Binswanger's disease;
- (b) cerebral amyloidosis;
- (c) cerebral arteriolosclerosis (fibrinoid necrosis, lipohyalinosis, microatheroma microaneurysms, segmental arterial disorganisation);
- (d) cerebral venous thrombosis;
- (e) hippocampal sclerosis;
- (f) inflammatory or immunologically mediated vasculitis;
- (g) intravascular lymphomatosis;
- (h) laminar cortical necrosis; or
- (i) Moyamoya disease.

specified list of disorders of calcium metabolism means:

- (a) Fahr's disease;
- (b) hyperparathyroidism;
- (c) hypoparathyroidism; or
- (d) pseudohypoparathyroidism.

specified list of drugs means:

(a)	5-fluorouracil;
(b)	alizapride;
(c)	alpha-methyldopa;
(d)	amiodarone;
(e)	amlodipine;
(f)	amoxapine;
(g)	amphotericin B;
(h)	antipsychotic drug;
(i)	aprindine;
(j)	bethanechol (intraspinal or intracranial);
(k)	bupropion;
(l)	buspirone;
(m)	butyrophenones;
(n)	captopril;
(o)	cephaloridine;
(p)	chloroquine;
(q)	cimetidine;
(r)	cinnarizine;
(s)	cisapride;
(t)	clebopride;
(u)	clopamide-pindolol combination;
(v)	cyclophosphamide;
(w)	cyclosporine;
(x)	cytosine arabinoside;
(y)	diltiazem;
(z)	disulfiram;
(aa)	domperidone;
(bb)	donepezil;
(cc)	doxorubicin;
(dd)	droperidol;
(ee)	etoposide;
(ff)	flunarizine;
(gg)	flurbiprofen;
(hh)	indeloxazine;
(ii)	interferon-alpha;
(jj)	itopride;
(kk)	lithium;
(ll)	lorazepam;
(mm)	mandipine;
(nn)	methotrexate;
(oo)	metoclopramide;
(pp)	metopimazine;
(qq)	mexiletine;
(rr)	molindone;
(ss)	naproxen;
(tt)	nifedipine;
(uu)	pentoxifylline;

(vv)	pethidine;
(ww)	phenelzines;
(xx)	phenothiazine;
(yy)	phenylamine;
(zz)	phenytoin;
(aaa)	pimozide;
(bbb)	pregabalin;
(ccc)	procaine;
(ddd)	propiverine;
(eee)	pyridostigmine;
(fff)	reserpine;
(ggg)	selective serotonin reuptake inhibitor;
(hhh)	sodium valproate (valproic acid);
(iii)	tacrine;
(jjj)	tacrolimus;
(kkk)	tetrabenazine;
(lll)	thiethylperazine;
(mmm)	thioxanthenes;
(nnn)	tiapride;
(ooo)	trimetazidine;
(ppp)	veralipride;
(qqq)	verapamil; or
(rrr)	vincristine plus Adriamycin.

specified list of pesticides means:

- (a) a dithiocarbamate-based fungicide;
- (b) an organochlorine insecticide;
- (c) an organophosphorus ester;
- (d) paraquat;
- (e) rotenone; or
- (f) the phenoxy acid herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) or 2,4,5-trichlorophenoxyacetic acid (2,4,5-T).

terminal event means the proximate or ultimate cause of death and includes the following:

- (a) pneumonia;
- (b) respiratory failure;
- (c) cardiac arrest;
- (d) circulatory failure; or
- (e) cessation of brain function.

total parenteral nutrition means continuous intravenous drip feeding with no feeding via mouth or gut.

VEA means the *Veterans' Entitlements Act 1986*.