



Australian Government
Repatriation Medical Authority

Statement of Principles
concerning
HYPOGONADISM
(Reasonable Hypothesis)
(No. 73 of 2021)

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

Dated 21 May 2021

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

Professor Nicholas Saunders AO
Chairperson

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1 Name

This is the Statement of Principles concerning *hypogonadism (Reasonable Hypothesis)* (No. 73 of 2021).

2 Commencement

This instrument commences on 21 June 2021.

3 Authority

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

4 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.

5 Definitions

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

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

- (1) This Statement of Principles is about hypogonadism and death from hypogonadism.

Meaning of hypogonadism

- (2) For the purposes of this Statement of Principles, hypogonadism:
- (a) means deficient production of testosterone from the testis or estrogen from the ovary, or deficient production of ova (eggs) or sperm, where any such deficiency is associated with clinical symptoms and signs or a requirement for treatment; and
 - (b) includes:
 - (i) primary hypogonadism;
 - (ii) secondary hypogonadism (also known as central hypogonadism and hypogonadotropic hypogonadism); and
 - (iii) infertility due to endocrine or gonadal pathology; and
 - (c) excludes heritable and congenital forms of hypogonadism, compensated hypogonadism, diminished ovarian reserve, naturally occurring menopause and abnormal semen analysis.

Note 1: Associated clinical symptoms and signs of hypogonadism may include loss of secondary sexual characteristics, loss of sexual function and loss of reproductive function (endocrine or gonadal infertility).

Note 2: *infertility* is defined in the Schedule 1 - Dictionary.

Death from hypogonadism

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

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

7 Basis for determining the factors

The Repatriation Medical Authority is of the view that there is sound medical-scientific evidence that indicates that hypogonadism and death from hypogonadism 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: *MRCA*, *relevant service* and *VEA* are defined in the Schedule 1 - Dictionary.

8 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 hypogonadism or death from hypogonadism with the circumstances of a person's relevant service:

- (1) having hypopituitarism involving deficiency of follicle stimulating hormone or luteinising hormone at the time of the clinical onset of hypogonadism;
- (2) having hyperprolactinaemia at the time of the clinical onset of hypogonadism;
- (3) for males only, having a spinal cord injury resulting in paraplegia or tetraplegia before the clinical onset of hypogonadism;
- (4) having blunt or penetrating trauma to:
 - (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;sufficient to cause gonadal atrophy before the clinical onset of hypogonadism;
- (5) having surgical excision of:
 - (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;before the clinical onset of hypogonadism;

- (6) undergoing a course of therapeutic radiation for cancer, where:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- were in the field of radiation before the clinical onset of hypogonadism;
- (7) having infection with human immunodeficiency virus before the clinical onset of hypogonadism;
- (8) having infection with *Mycobacterium leprae* before the clinical onset of hypogonadism;
- Note: *Mycobacterium leprae* is the organism that causes leprosy.
- (9) having infection with *Trypanosoma brucei* before the clinical onset of hypogonadism;
- Note: *Trypanosoma brucei* is the organism that causes African sleeping sickness (trypanosomiasis).
- (10) having mumps orchitis as an adult affecting:
- (a) both testes; or
 - (b) a single functional testis, where there is only one functional testis;
- before the clinical onset of hypogonadism;
- (11) for males only, having rheumatoid arthritis or granulomatosis with polyangiitis before the clinical onset of hypogonadism;
- (12) having Addison disease before the clinical onset of hypogonadism;
- (13) having an infiltrative disease from the specified list of infiltrative diseases of:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- before the clinical onset of hypogonadism;
- Note: *specified list of infiltrative diseases* is defined in the Schedule 1 - Dictionary.
- (14) for males only, having a testicular varicocele before the clinical onset of hypogonadism;

- (15) having infarction of:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- within the 1 year before the clinical onset of hypogonadism;
- (16) having sickle-cell disorder before the clinical onset of hypogonadism;
- (17) having a bone marrow or stem cell transplant before the clinical onset of hypogonadism;
- (18) having cirrhosis of the liver at time of the clinical onset of hypogonadism;
- (19) having chronic kidney disease at time of the clinical onset of hypogonadism;
- Note: *chronic kidney disease* is defined in the Schedule 1 - Dictionary.
- (20) having anorexia nervosa at the time of the clinical onset of hypogonadism;
- (21) taking a course of systemic cytotoxic drugs for treatment of a malignant neoplasm before the clinical onset of hypogonadism;
- (22) taking gonadotrophin releasing hormone agonists or antagonists as androgen or estrogen deprivation therapy for at least 1 year within the 2 years before the clinical onset of hypogonadism;
- (23) having active epilepsy before the clinical onset of hypogonadism;
- Note: *active epilepsy* is defined in the Schedule 1 - Dictionary.
- (24) taking a drug from the Specified List 1 of drugs before the clinical onset of hypogonadism;
- Note: *Specified List 1 of drugs* is defined in the Schedule 1 - Dictionary.
- (25) taking an immune checkpoint inhibitor within the 1 year before the clinical onset of hypogonadism;
- Note: *immune checkpoint inhibitor* is defined in the Schedule 1 - Dictionary.
- (26) taking a drug from the Specified List 2 of drugs, which cannot be ceased or substituted, at the time of the clinical onset of hypogonadism;
- Note: *Specified List 2 of drugs* is defined in the Schedule 1 - Dictionary.

- (27) taking a drug which cannot be ceased or substituted and which is associated in the individual with the clinical onset of hypogonadism during drug therapy and either:
- (a) the improvement of hypogonadism within 2 months of discontinuing or tapering drug therapy; or
 - (b) the redevelopment of hypogonadism on rechallenge with the same drug; and

where taking the drug continued for at least the 30 days before the clinical onset of hypogonadism;

- (28) inhaling fumes from a metal from the specified list of metals or a compound containing a metal from the specified list of metals:
- (a) for a cumulative period of at least 2,000 hours before the clinical onset of hypogonadism; and
 - (b) if that exposure has ceased before the clinical onset of hypogonadism, then that onset occurred within 2 years of cessation;

Note: *fumes* and *specified list of metals* are defined in the Schedule 1 - Dictionary.

- (29) inhaling, ingesting or having cutaneous contact with a chemical agent from the specified list of chemical agents:
- (a) for a cumulative period of at least 2,000 hours before the clinical onset of hypogonadism; and
 - (b) if that exposure has ceased before the clinical onset of hypogonadism, then that onset occurred within 2 years of cessation;

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

- (30) for females only, inhaling, ingesting or having cutaneous contact with a chemical agent contaminated by 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD):
- (a) for a cumulative period of at least 1,000 hours, within a consecutive period of 10 years before the clinical onset of hypogonadism; and
 - (b) if that exposure has ceased before the clinical onset of hypogonadism, then that onset occurred within 25 years of cessation;

Note: *inhaling, ingesting or having cutaneous contact with a chemical agent contaminated by 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD)* is defined in the Schedule 1 - Dictionary.

- (31) for females only, having smoked tobacco products:
- (a) in an amount of at least 5 pack-years before the clinical onset of hypogonadism; and
 - (b) if smoking has ceased before the clinical onset of hypogonadism, then that onset occurred within 10 years of cessation;

Note: *one pack-year* is defined in the Schedule 1 - Dictionary.

- (32) having alcohol use disorder before the clinical onset of hypogonadism;
- (33) being obese for at least the 5 years before the clinical onset of hypogonadism;

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

- (34) for females only, being underweight for at least the 5 years before the clinical onset of hypogonadism;

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

- (35) for females only, being nulliparous at the time of the clinical onset of hypogonadism;

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

- (36) for parous women only, an inability to breast feed for a cumulative period of at least 6 months before the clinical onset of hypogonadism;

Note: The period of breastfeeding could be cumulative over a number of pregnancies.

- (37) having diabetes mellitus before the clinical onset of hypogonadism;
- (38) for males only, having obstructive sleep apnoea at the time of the clinical onset of hypogonadism;
- (39) having hypopituitarism involving deficiency of follicle stimulating hormone or luteinising hormone at the time of the clinical worsening of hypogonadism;
- (40) having hyperprolactinaemia at the time of the clinical worsening of hypogonadism;
- (41) for males only, having a spinal cord injury resulting in paraplegia or tetraplegia before the clinical worsening of hypogonadism;

- (42) having blunt or penetrating trauma to:

- (a) both ovaries or testes; or
- (b) a single functional ovary or testis, where there is only one functional ovary or testis;

sufficient to cause gonadal atrophy before the clinical worsening of hypogonadism;

- (43) having surgical excision of:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- before the clinical worsening of hypogonadism;
- (44) undergoing a course of therapeutic radiation for cancer, where:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- were in the field of radiation before the clinical worsening of hypogonadism;
- (45) having infection with human immunodeficiency virus before the clinical worsening of hypogonadism;
- (46) having infection with *Mycobacterium leprae* before the clinical worsening of hypogonadism;
- Note: *Mycobacterium leprae* is the organism that causes leprosy.
- (47) having infection with *Trypanosoma brucei* before the clinical worsening of hypogonadism;
- Note: *Trypanosoma brucei* is the organism that causes African sleeping sickness (trypanosomiasis).
- (48) having mumps orchitis as an adult affecting:
- (a) both testes; or
 - (b) a single functional testis, where there is only one functional testis;
- before the clinical worsening of hypogonadism;
- (49) for males only, having rheumatoid arthritis or granulomatosis with polyangiitis before the clinical worsening of hypogonadism;
- (50) having Addison disease before the clinical worsening of hypogonadism;
- (51) having an infiltrative disease from the specified list of infiltrative diseases of:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- before the clinical worsening of hypogonadism;
- Note: *specified list of infiltrative diseases* is defined in the Schedule 1 - Dictionary.

- (52) for males only, having a testicular varicocele before the clinical worsening of hypogonadism;
- (53) having infarction of:
- (a) both ovaries or testes; or
 - (b) a single functional ovary or testis, where there is only one functional ovary or testis;
- within the 1 year before the clinical worsening of hypogonadism;
- (54) having sickle-cell disorder before the clinical worsening of hypogonadism;
- (55) having a bone marrow or stem cell transplant before the clinical worsening of hypogonadism;
- (56) having cirrhosis of the liver at time of the clinical worsening of hypogonadism;
- (57) having chronic kidney disease at time of the clinical worsening of hypogonadism;
- Note: *chronic kidney disease* is defined in the Schedule 1 - Dictionary.
- (58) having anorexia nervosa at the time of the clinical worsening of hypogonadism;
- (59) taking a course of systemic cytotoxic drugs for treatment of a malignant neoplasm before the clinical worsening of hypogonadism;
- (60) taking gonadotrophin releasing hormone agonists or antagonists as androgen or estrogen deprivation therapy for at least 1 year within the 2 years before the clinical worsening of hypogonadism;
- (61) having active epilepsy before the clinical worsening of hypogonadism;
- Note: *active epilepsy* is defined in the Schedule 1 - Dictionary.
- (62) taking a drug from the Specified List 1 of drugs before the clinical worsening of hypogonadism;
- Note: *Specified List 1 of drugs* is defined in the Schedule 1 - Dictionary.
- (63) taking an immune checkpoint inhibitor within the 1 year before the clinical worsening of hypogonadism;
- Note: *immune checkpoint inhibitor* is defined in the Schedule 1 - Dictionary.
- (64) taking a drug from the Specified List 2 of drugs, which cannot be ceased or substituted, at the time of the clinical worsening of hypogonadism;
- Note: *Specified List 2 of drugs* is defined in the Schedule 1 - Dictionary.

- (65) taking a drug which cannot be ceased or substituted and which is associated in the individual with the clinical worsening of hypogonadism during drug therapy and either:
- (a) the improvement of hypogonadism within 2 months of discontinuing or tapering drug therapy; or
 - (b) the clinical worsening of hypogonadism on rechallenge with the same drug; and

where taking the drug continued for at least the 30 days before the clinical worsening of hypogonadism;

- (66) inhaling fumes from a metal from the specified list of metals or a compound containing a metal from the specified list of metals:
- (a) for a cumulative period of at least 2,000 hours before the clinical worsening of hypogonadism; and
 - (b) if that exposure has ceased before the clinical worsening of hypogonadism, then that worsening occurred within 2 years of cessation;

Note: *fumes* and *specified list of metals* are defined in the Schedule 1 - Dictionary.

- (67) inhaling, ingesting or having cutaneous contact with a chemical agent from the specified list of chemical agents:
- (a) for a cumulative period of at least 2,000 hours before the clinical worsening of hypogonadism; and
 - (b) if that exposure has ceased before the clinical worsening of hypogonadism, then that worsening occurred within 2 years of cessation;

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

- (68) for females only, inhaling, ingesting or having cutaneous contact with a chemical agent contaminated by 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD):
- (a) for a cumulative period of at least 1,000 hours, within a consecutive period of 10 years before the clinical worsening of hypogonadism; and
 - (b) if that exposure has ceased before the clinical worsening of hypogonadism, then that worsening occurred within 25 years of cessation;

Note: *inhaling, ingesting or having cutaneous contact with a chemical agent contaminated by 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD)* is defined in the Schedule 1 - Dictionary.

- (69) for females only, having smoked tobacco products:
- (a) in an amount of at least 5 pack-years before the clinical worsening of hypogonadism; and
 - (b) if smoking has ceased before the clinical worsening of hypogonadism, then that worsening occurred within 10 years of cessation;

Note: *one pack-year* is defined in the Schedule 1 - Dictionary.

- (70) having alcohol use disorder before the clinical worsening of hypogonadism;

- (71) being obese for at least the 5 years before the clinical worsening of hypogonadism;

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

- (72) for females only, being underweight for at least the 5 years before the clinical worsening of hypogonadism;

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

- (73) for females only, being nulliparous at the time of the clinical worsening of hypogonadism;

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

- (74) for parous women only, an inability to breast feed for a cumulative period of at least 6 months before the clinical worsening of hypogonadism;

Note: The period of breastfeeding could be cumulative over a number of pregnancies.

- (75) having diabetes mellitus before the clinical worsening of hypogonadism;

- (76) for males only, having obstructive sleep apnoea at the time of the clinical worsening of hypogonadism;

- (77) inability to obtain appropriate clinical management for hypogonadism.

9 Relationship to service

- (1) The existence in a person of any factor referred to in section 8, must be related to the relevant service rendered by the person.
- (2) The factors set out in subsections 8(39) to 8(77) apply only to material contribution to, or aggravation of, hypogonadism where the person's hypogonadism was suffered or contracted before or during (but did not arise out of) the person's relevant service.

10 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 8 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 5

1 Definitions

In this instrument:

abnormality of kidney structure or function means:

- (a) having a glomerular filtration rate of less than 60 mL/min/1.73 m²; or
- (b) having kidney damage, as evidenced by renal biopsy, imaging studies, albuminuria, urinary sediment abnormalities or other markers of abnormal renal function; or
- (c) having had a kidney transplant.

active epilepsy means having at least one epileptic seizure per year.

being nulliparous means never having experienced a gestation period of at least 20 weeks.

being obese means having a Body Mass Index (BMI) of 30 or greater.

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

being underweight means having a Body Mass Index (BMI) of 18.5 or less.

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

BMI means W/H^2 where:

- (a) W is the person's weight in kilograms; and
- (b) H is the person's height in metres.

chronic kidney disease means an abnormality of kidney structure or function that has been present for at least 3 months.

Note: ***abnormality of kidney structure or function*** is also defined in the Schedule 1 - Dictionary.

fumes means combustion products, aerosols, vapours or dust arising through industrial processes or from workplace practices that involve the refining, manufacture or use of the stated material.

hypogonadism—see subsection 6(2).

immune checkpoint inhibitor means a form of cancer immunotherapy that uses monoclonal antibodies targeting the immune checkpoint proteins. Examples include ipilumab, tremelimumab, nivolumab and pembrolizumab.

infertility means inability to conceive a pregnancy after 12 months of unprotected sexual intercourse, use of assisted reproductive technology or azoospermia in males.

inhaling, ingesting or having cutaneous contact with a chemical agent contaminated by 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD) means:

- (a) decanting or spraying;
- (b) cleaning or maintaining equipment used to apply;
- (c) being sprayed with;
- (d) handling or sawing timber treated with;

- (e) being in an environment shrouded in dust from timber treated with;
- (f) using cutting oils contaminated with;

one of the following chemicals:

- (i) 2,4,5-trichlorophenoxyacetic acid;
- (ii) 2,4,5-trichlorophenoxypropionic acid;
- (iii) 2,4,5-trichlorophenol;
- (iv) 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate;
- (v) o,o-dimethyl-o-(2,4,5-trichlorophenyl)-phosphorothioate;
- (vi) pentachlorophenol;
- (vii) 2,3,4,6-tetrachlorophenol;
- (viii) 2,4,6-trichlorophenol;
- (ix) 1,3,5-trichloro-2-(4-nitrophenoxy)benzene;
- (x) 2,4-dichloro-1-(4-nitrophenoxy)benzene; or
- (xi) 2,4-dichloro-1-(3-methoxy-4-nitrophenoxy)-benzene.

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

one pack-year means the amount of tobacco consumed in smoking 20 cigarettes per day for a period of 1 year, or an equivalent amount of tobacco products.

Note 1: An equivalent amount of tobacco products is 7,300 grams of smoking tobacco by weight, either in cigarettes, pipe tobacco or cigars, or a combination of same. For pipe tobacco, cigars or combinations of multiple tobacco types, 1 gram of tobacco is considered to be equal to one cigarette.

Note 2: Pack-years are calculated by dividing the number of cigarettes smoked per day by 20 and multiplying this number by the number of years the person has smoked. For example, smoking 10 cigarettes per day for 10 years is equal to 5 pack-years, and smoking 40 cigarettes per day for 10 years is equal to 20 pack-years.

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.

Note: *MRCA* and *VEA* are also defined in the Schedule 1 - Dictionary.

Specified List 1 of drugs means:

- (a) alkylating agents including busulphan, carmustine, chlorambucil, cyclophosphamide, dacarbazine, lomustine, melphalan (phenylalanine mustard), nitrogen mustard (mechlorethamine), procarbazine and ifosfamide (isophosphamide);
- (b) anthracycline antibiotics including daunorubicin, doxorubicin, epirubicin and idarubicin;
- (c) etoposide;
- (d) ibiraterone;
- (e) platinum compounds including cisplatin and carboplatin.

Specified List 2 of drugs means:

- (a) androgens;

- (b) antipsychotics;
- (c) bevacizumab for females only;
- (d) dutasteride for males only;
- (e) estrogens for males only;
- (f) finasteride for males only;
- (g) flutamide for males only;
- (h) glucocorticoids;
- (i) ketoconazole for males only;
- (j) opioids;
- (k) progestins for males only;
- (l) sirolimus for males only;
- (m) spironolactone for males only;
- (n) steroidal antiandrogens (including cyproterone acetate) for males only;
- (o) sulfasalazine for males only; or
- (p) vismodegib for females only.

specified list of chemical agents means:

- (a) 2-bromopropane;
- (b) carbon disulphide for females only; or
- (c) dibromochloropropane for males only.

specified list of infiltrative diseases means:

- (a) amyloidosis;
- (b) endometriosis;
- (c) haemochromatosis;
- (d) a primary or secondary malignant neoplasm; or
- (e) sarcoidosis.

specified list of metals means:

- (a) cadmium;
- (b) lead; or
- (c) mercury.

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.

VEA means the *Veterans' Entitlements Act 1986*.