罕見疾病個案通報審查標準

疾病名稱	審查條件	附件
多發性硬化症 (Multiple Sclerosis, MS)	符合 McDonald 診斷準據，且符合 DIT 及 DIS 的要件者。	需附臨床相關的兩次發病之病歷紀錄及中樞神經系統之影像報告。
結節硬化症 (Tuberous Sclerosis Complex, TSC)	(1)符合 TS 臨床診斷準據之臨床表徵中二項主要表徵者。 或(2)結節硬化症基因檢查具有突變，且臨床有任何一項診斷準據之表徵者。	符合(1)者，需附相關病歷紀錄及影像報告。 符合(2)者，需附基因檢查報告。
脊髓肌肉萎縮症 (Spinal Muscular Atrophy, SMA)	符合脊髓肌肉萎縮的肌肉無力表徵，且 SMA 基因檢查具突變者。	需附 SMA 的基因報告及臨床症狀及徵兆的病歷紀錄。
肌肉萎縮側索硬化症 (Amyotrophic Lateral Sclerosis, ALS)	符合 ALS 之臨床表現及神經學身體診查，且神經學影像檢查及肌電圖標準檢查也符合者。	(1)需附臨床症狀及徵兆的病歷紀錄及檢驗報告。 (2)肌電圖要原始檢驗報告數據。
粒線體疾病(Mitochondrial Disease) 共包含 5 項疾病： 1.Kearns-Sayre 氏症候群 2.Leigh 氏童年期腦脊髓病變 3.MELAS 症候群 4.MNGIE 症候群 5.粒線體缺陷	(1)符合症候群性粒線體疾病(Syndromic MD)，且相關致病基因檢查具突變者。 或(2)符合症候群性粒線疾病，且其組織切片病理檢查符合細胞粒線病變者或其酵素檢查異常者。 或(3)非症候群粒線體疾病(non-syndromic MD)之臨床表現符合粒線體診斷準據(Bernie’s criteria 2002 Neurology)之二項主要準據或一項主要及二項次要準據者，且其組織切片病理檢查符合細胞粒線體病變或其酵素檢查異常者。	符合(1)(2)者，需附症候群粒線疾病之臨床症狀及徵兆的病歷紀錄及檢查報告(包括基因報告)。 符合(3)者，需附非症候群粒線體疾病之臨床症狀及徵兆的病歷紀錄及相檢驗報告。
原發性肺動脈高壓 (Idiopathic pulmonary arterial hypertension)	臨床上具肺動脈高壓之症狀及徵兆，且心臟超音波及心導管檢查符合肺動脈高壓，並排除次發性肺動脈高壓之原因。	(1)需附臨床症狀及徵兆之病歷紀錄。 及(2)需附心臟超音波及心導管檢查報告，並具有肺動脈壓的數據。 及(3)需附排除次發性肺動高壓相關原因之檢驗報告。

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(審查資料表)

-多發性硬化症[Multiple Sclerosis, MS]-

1. ☐ 病歷摘要中包含足以佐證之臨床資料及實驗室數據。
2. ☐ MRI 報告或 MRI 之重點影像足以佐證。
3. ☐ 無更適合的解釋(no better explanation) 。
4. 符合 McDonald criteria (2010)。

	Clinical Presentation	Additional Data Needed for MS Diagnosis
☐	≧2 attacks ; objective clinical evidence of ≧2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack	None[c]
☐	≧2 attacks ; objective clinical evidence of 1 lesion	Dissemination in space, demonstrated by: ≧1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) ; or Await a further clinical attack implicating a different CNS site
☐	1 attack ; objective clinical evidence of ≧2 lesions	Dissemination in time, demonstrated by: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack
☐	1 attack ; objective clinical evidence of 1 lesion (clinically isolated syndrome)	Dissemination in space and time, demonstrated by: For DIS: ≧1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) ; or Await a second clinical attack implicating a different CNS site; and For DIT: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of

		its timing with reference to a baseline scan; or Await a second clinical attack
☐	Insidious neurological progression suggestive of MS (PPMS)	1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria: 1. Evidence for DIS in the brain based on ≧1 T2 lesions in the MS-characteristic (periventricular, juxtacortical, or infratentorial) regions 2. Evidence for DIS in the spinal cord based on ≧2 T2 lesions in the cord 3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index)
☐	**備註**(病人為非典型之表現，不完全符合以上之診斷標準，但仍診斷為此疾病之理由)	

參考文獻:

1. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol. 2011 Feb;69(2):292-302.
2. Swanton JK, Rovira A, Tintore´ M, et al. MRI criteria for multiple sclerosis in patients presenting with clinically isolated syndromes: a multicentre retrospective study. Lancet Neurol 2007;6:677–686.
3. Swanton JKFernando K, Dalton CM, et al. Modification of MRI criteria for multiple sclerosis in patients with clinically isolated syndromes. J Neurol Neurosurg Psychiatry 2006;77:830–833.
4. Montalban X, Tintore´ M, Swanton J, et al. MRI criteria for MS in patients with clinically isolated syndromes. Neurology 2010;74: 427–434.

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(送審標準表)

行政院衛生福利部國民健康屬「罕見疾病個案通報審查標準機制」(送審資料表)

-多發性硬化症[Multiple Sclerosis, MS]-

1. □病歷摘要中包含足以佐證之臨床資料及實驗室數據。(必要)
2. □ 附上 MRI 報告或 MRI 之重點影像。(必要)
3. □ 無更適合的解釋(no better explanation) 。
4. 勾選 McDonald criteria (2010)之項目 。(必要)

	Clinical Presentation	Additional Data Needed for MS Diagnosis
□	≧2 attacks ; objective clinical evidence of ≧2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack	None[c]
□	≧2 attacks ; objective clinical evidence of 1 lesion	Dissemination in space, demonstrated by: ≧1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) ; or Await a further clinical attack implicating a different CNS site
□	1 attack ; objective clinical evidence of ≧2 lesions	Dissemination in time, demonstrated by: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack
□	1 attack ; objective clinical evidence of 1 lesion (clinically isolated syndrome)	Dissemination in space and time, demonstrated by: For DIS: ≧1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) ; or Await a second clinical attack implicating a different CNS site; and For DIT: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of

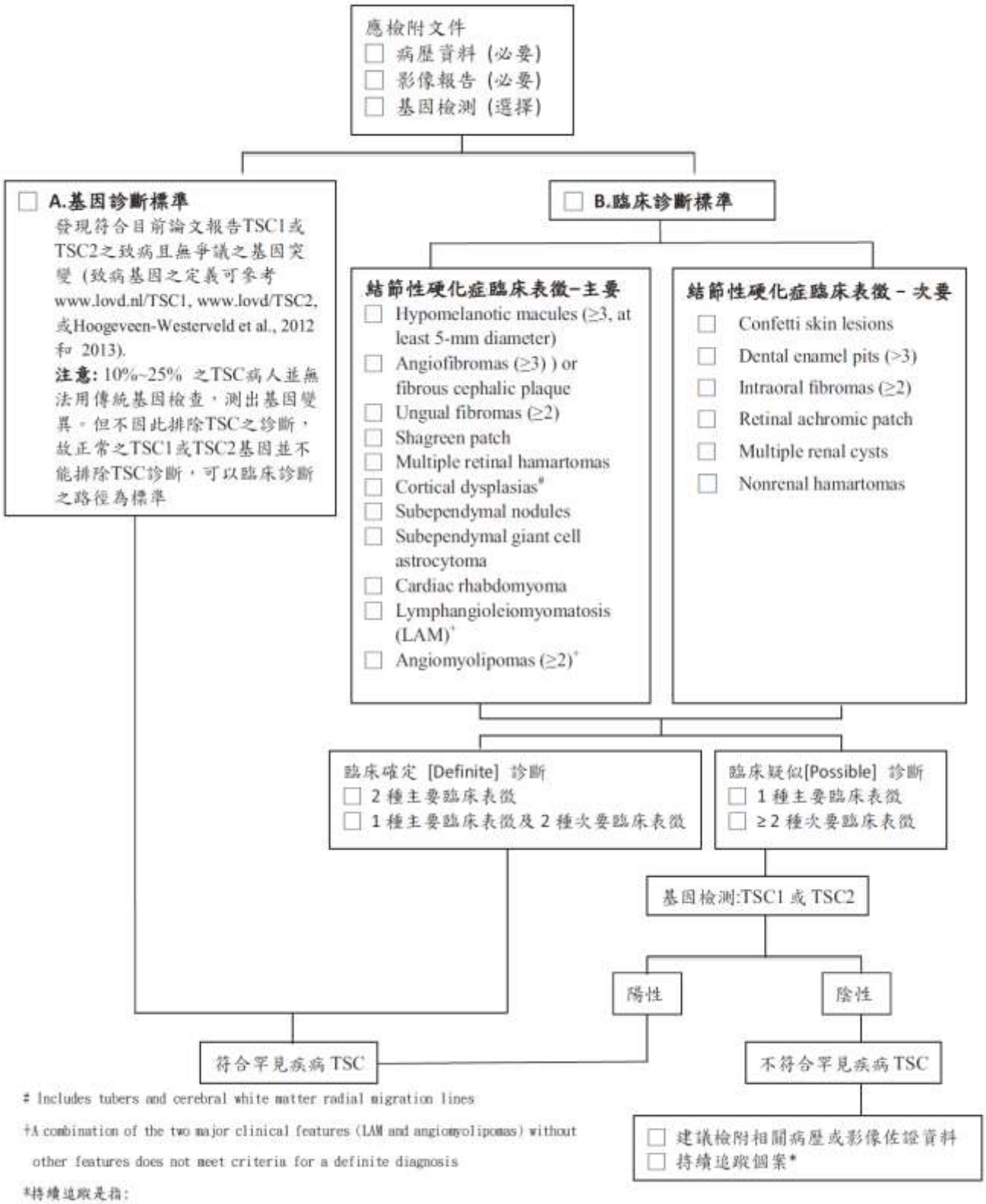
		its timing with reference to a baseline scan; or Await a second clinical attack
☐	Insidious neurological progression suggestive of MS (PPMS)	1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria: 1. Evidence for DIS in the brain based on ≧1 T2 lesions in the MS-characteristic (periventricular, juxtacortical, or infratentorial) regions 2. Evidence for DIS in the spinal cord based on ≧2 T2 lesions in the cord 3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index)
☐	**備註**(病人為非典型之表現，不完全符合以上之診斷標準，但仍診斷為此疾病之理由)	

參考文獻:

1. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol. 2011 Feb;69(2):292-302.
2. Swanton JK, Rovira A, Tintore´ M, et al. MRI criteria for multiple sclerosis in patients presenting with clinically isolated syndromes: a multicentre retrospective study. Lancet Neurol 2007;6:677–686.
3. Swanton JKFernando K, Dalton CM, et al. Modification of MRI criteria for multiple sclerosis in patients with clinically isolated syndromes. J Neurol Neurosurg Psychiatry 2006;77:830–833.
4. Montalban X, Tintore´ M, Swanton J, et al. MRI criteria for MS in patients with clinically isolated syndromes. Neurology 2010;74: 427–434.

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(審查資料表)

-結節性硬化症[Tuberous Sclerosis Complex, TSC] -



Includes tubers and cerebral white matter radial migration lines

†A combination of the two major clinical features (LAM and angiomyolipomas) without other features does not meet criteria for a definite diagnosis

*持續追蹤是指:

1)臨床是否出現結節性硬化症相關症狀，或

2)影像學出現病灶，影像學的追蹤包括腦部核磁造影檢查、心臟超音波檢查、腹部超音波檢查或肺部高層次電腦斷層檢查(適用於成人女性)

Northrup H, Krueger DA , et al. Pediatric Neurology 49 (2013) 243-254

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(送審標準表)

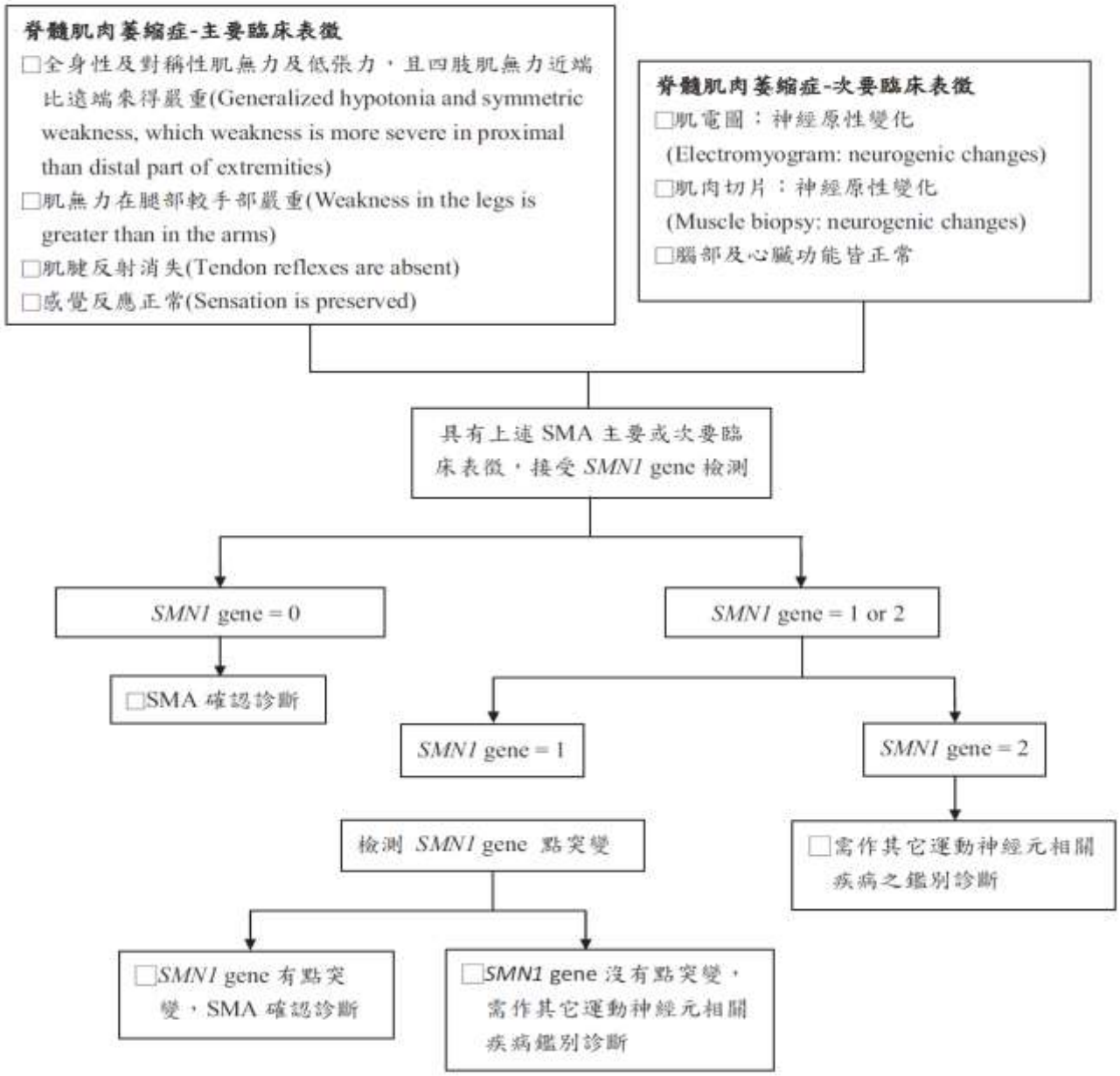
-結節性硬化症[Tuberous Sclerosis Complex, TSC]-

項目	填寫部分
A.病歷資料	
1. 主要病史	
2. 臨床表徵-主要	☐ Hypomelanotic macules (≧3, at least 5-mm diameter) ☐ Angiofibromas (≧3) or fibrous cephalic plaque ☐ Ungual fibromas (≧2) ☐ Shagreen patch ☐ Multiple retinal hamartomas ☐ Cortical dysplasias ☐ Subependymal giant cell astrocytoma ☐ Cardiac rhabdomyoma ☐ Lymphangioleiomyomatosis (LAM) ☐ Angiomyolipomas(≧2)
3. 臨床表徵-次要	☐ Confetti skin lesions ☐ Dental enamel pits (>3) ☐ Intraoral fibromas (≧2) ☐ Retinal achromic patch ☐ Multiple renal cysts ☐ Nonrenal hamartomas
B. 基因檢測 (請	

項目	填寫部分
附實驗室報告影本)	
C.影像報告(可選)	
1. 腦部影像學報告	□ 未做 □ 已做 (□正常 □異常，說明：_____ _____)
2. 心臟超音波報告	□ 未做 □ 已做 (□正常 □異常，說明：_____ _____)
3. 腹部超音波報告 (包含腎臟)	□ 未做 □ 已做 (□正常 □異常，說明：_____ _____)
4. 肺部高層次電腦斷層報告	□ 未做 □ 已做 (□正常 □異常，說明：_____ _____)
D.備註(病人為非典型之表現，不完全符合以上之診斷標準，但仍診斷為此疾病之理由	

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(審查資料表)

-脊髓肌肉萎縮症 [Spinal Muscular Atrophy, SMA] -



說明：1.患者 18 歲以前發病，符合全部 SMA 主要及次要臨床表徵，雖 *SMN1* gene 沒有缺失或點突變，亦可診斷為非 5q SNA，但這樣的個案需檢附完整的肌電圖及肌肉切片報告。

2.其它運動神經元疾病如：SMARD1（spinal muscular atrophy with respiratory distress 1），X-SMA, Distal SMA, Juvenile ALS（amyotrophic lateral sclerosis）等。

參考資料：1.Zerres K, Davies KE. Neuromusc Disord 1999;9:272-8；2.Wang CH, et al. J Child Neurol 2007;22:1027-49；3.D'Amico A, et al. Orphanet J Rare Dis 2011;6:71.

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(送審資料表)

-脊髓肌肉萎缩症 [Spinal Muscular Atrophy, SMA] -

1. 患者之檢查均需附上正式報告或影本
2. ※為必要填寫項目
3. ＃為選擇檢附項目

History※	Symptoms： ☐ Age at onset：_____months, or_____years ☐ Symmetric muscle weakness ☐ Floppy infant ☐ Swallowing or feeding difficulty ☐ Cough difficulty ☐ Hospitalization due to pulmonary atelectasis or pneumonia Best motor function：☐ walk unaided, ☐ stand unaided, ☐ sit unaided, ☐ lie on bed
Physical examinations※	☐ Fasciculation of tongue ☐ Tremor of hands ☐ Weakness in the leg is greater than in the arms ☐ Truncal weakness ☐ Generalized hypotonia ☐ Muscle atrophy ☐ Absence of tendon reflexes ☐ Sensation is preserved ☐ Normal cerebral and heart function
Molecular genetics of *SMN1* (survival motor neuron) gene※	☐ The homozygous deletion/ mutation of *SMN1* gene Diagnostic methods：☐ MLPA ☐ DHPLC ☐ CE ☐ Others_____
Electromyogram＃	☐ Neurogenic changes
Muscle biopsy＃	☐ Neurogenic changes
Clinical diagnosis※	☐ Type 1, ☐ Type 2, ☐ Type 3, ☐ Type 4 of spinal muscular atrophy
備註(病人為非典型之表現，不完全符合以上之診斷標準，但仍診斷為此疾病之理由)	

-肌萎縮側索硬化症 [Amyotrophic Lateral Sclerosis, ALS] -

* 基因檢測結果可能對疑似散發型個案家族造成心理創傷衝擊，建議送檢前透過遺傳咨詢審慎評估利弊得失。

* 持續追蹤是指：

1)臨床是否出現更多肌萎縮側索硬化症相關症狀，或

2)神經傳導/肌電圖出現更多異常，支持或排除肌萎縮側索硬化症的可能性；

3)影像學出現病灶：影像學的追蹤包括腦部及頭部脊髓磁振造影檢查

1. Amyotrophic Lateral Sclerosis Fact Sheet: http://www.ninds.nih.gov/disorders/amyotrophiclateralsclerosis/detail_ALS.
2. 網址：http://www.alsgene.org/； http://alsod.iop.kcl.ac.uk/；
3. J Formosan Med Ass 2013 http://dx.doi.org/10.1016/j.jfma.2013.01.008
4. Arch Neurol 2012;69:1410.
5. Am J Neuroradiol 2010;31:1769.
6. Amyotroph Lateral Scler 2011;12:238..

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(送審標準表)

-肌萎縮側索硬化症[Amyotrophic Lateral Sclerosis, ALS]-

項目	填寫部分
A.病歷資料(必要) (請附上本院及他院多次看診紀錄影本)	
1. 主訴及病史	
2. 神經學臨床檢查	
B.神經電生理檢查資料(必要) (請附上所有報告及原始紀錄影本)	
1. 神經傳導	
2. 肌電圖	
C.影像報告(必要) (請附上相關影像資料)	
1. 腦部 MRI	
2. 頸部脊髓 MRI	
D.基因檢測(選擇性) (請附上實驗室報告影本)	

罕見疾病個案通報審查標準(審查醫師填寫)
-粒線體疾病[Mitochondrial Disease]

* 持續追蹤是指：

1)臨床是否出現更多粒線體疾病症相關症狀，或

2)或臨床及基因檢測出現更多異常，支持或排除粒線體疾病的可能性；

3)影像學出現病灶：包含MRS之乳酸信號增加。

1.NEUROLOGY 2002;59:1406–1411

2. Eur J Pediatr1993;152:178–184.

3. http://www.mitomap.org/MITOMAP

4.Lerner Alan J. Diagnostic Criteria in Neurology, 2006, Humana Press Inc.

計算主要診斷及次要診斷符合項目之流程

主要診斷標準評估

1. 臨床診斷符合一項以上(含)之證據(附件一)
2. 肌肉組織切片 Gomori Trichrome 染色必須合乎 2%以上之 ragged red fibers 染色
3. 肌肉呼吸酵素活性下降必須符合附件二條件之一
4. 纖維母細胞 ATP 合成效率小於正常之 3 個標準差以下

次要標準評估

1. 臨床診斷符合該粒線體肌肉組織切片
2. 肌肉組織切片符合下列條件之一(附件三)
3. 肌肉呼吸酵素活性下降且符合下列條件之一(附件四)
4. 纖維母細胞 ATP 合成效率小於正常之 2-3 個標準差以下，或纖維母細胞無法再無糖(但有 galactose)之細胞培養液中生長
5. 基因診斷：發現可能與呼吸鏈異常之基因突變
6. 代謝異常之生物指標，如乳酸、丙酮酸或是 FGF21 等文獻報告之代謝異常指標

符合_____項主要診斷標準

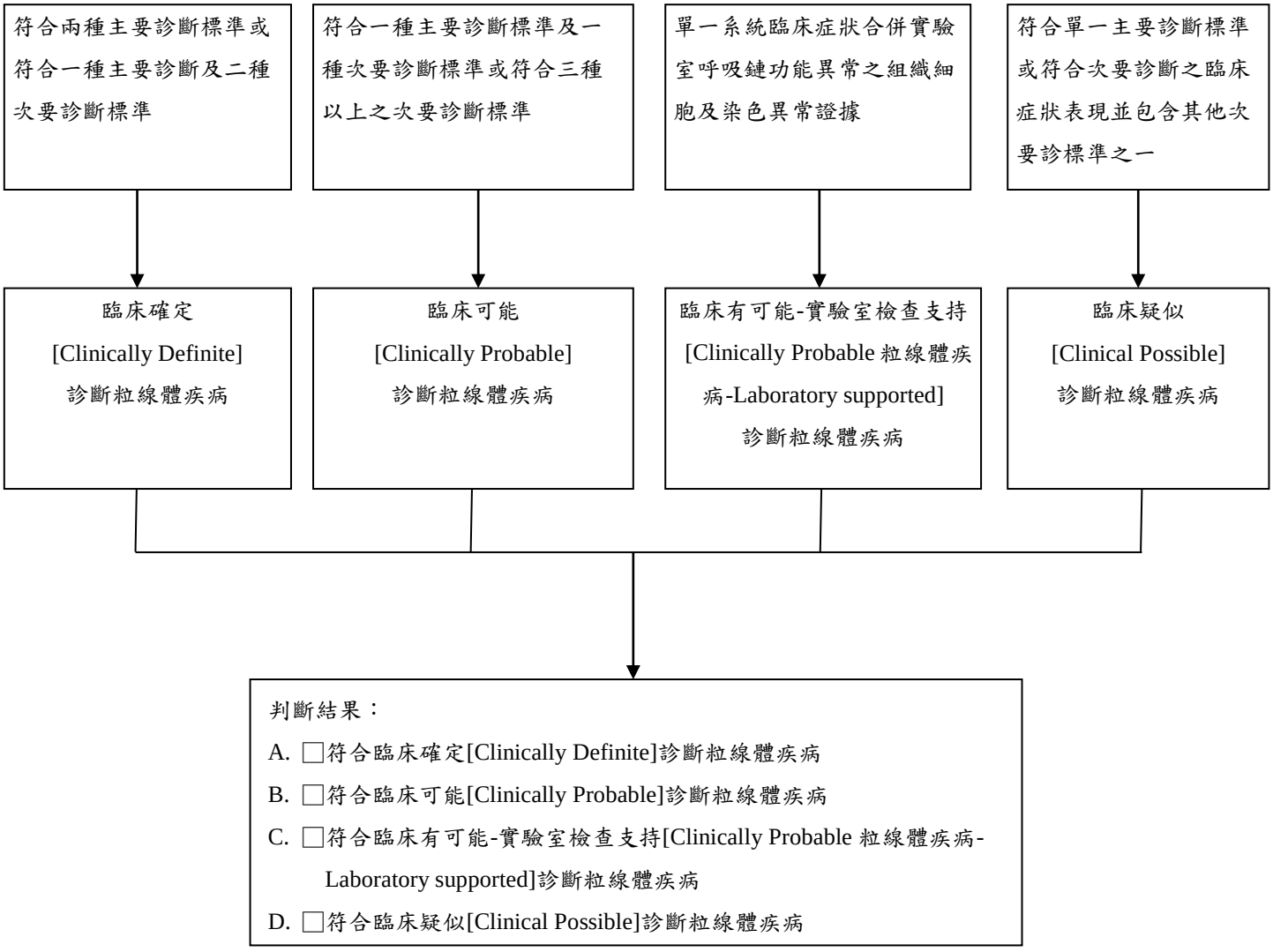
符合_____項次要診斷標準

符合何種基因突變：_____

罕見疾病個案通報審查標準(審查醫師填寫)

-粒線體疾病[Mitochondrial Disease]

判斷臨床診斷之等級



判斷結果：

A. □符合臨床確定[Clinically Definite]診斷粒線體疾病

B. □符合臨床可能[Clinically Probable]診斷粒線體疾病

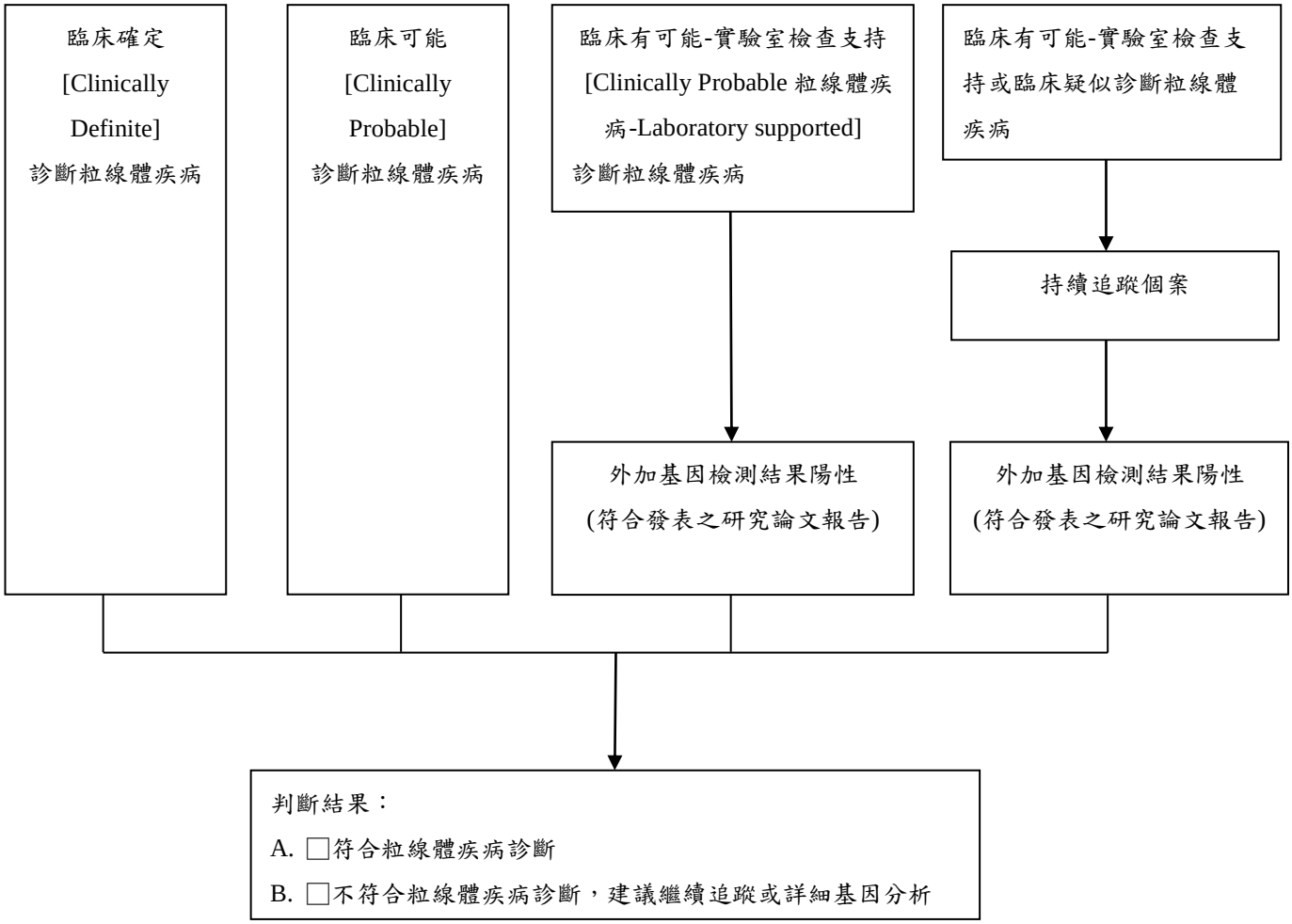
C. □符合臨床有可能-實驗室檢查支持[Clinically Probable 粒線體疾病-Laboratory supported]診斷粒線體疾病

D. □符合臨床疑似[Clinical Possible]診斷粒線體疾病

罕見疾病個案通報審查標準(審查醫師填寫)

-粒線體疾病[Mitochondrial Disease]

判斷符合罕見粒線體疾病



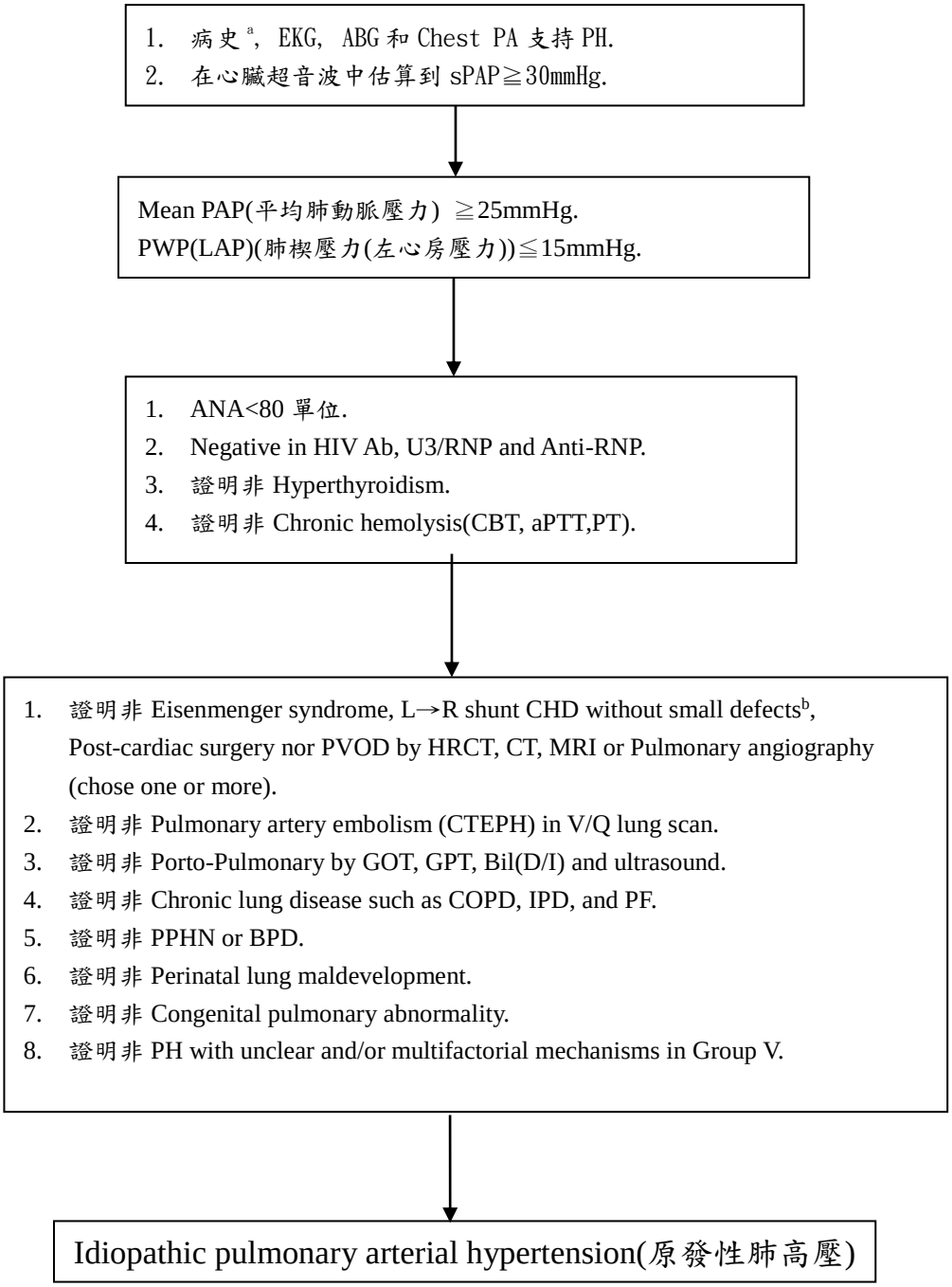
衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(送審標準表)

-粒線體疾病(Mitochondrial Disease)-

項目	填寫部分
A. 病歷資料	
1. 主訴及病史	
2. 身體及神經學診察(症候群性粒線體疾病者須呈現該症相關的特殊症狀或必要症狀及徵兆)	
B. 實驗檢查	
1. 一般生化檢查：其中需包括血氨、血糖、乳酸、丙酮酸等	
2 .文獻報告之代謝異常指標，包括尿液有機酸及/或血液胺基酸及/或葡萄糖生乳酸刺激試驗等	
C.影像報告	
1. MRI	
2. MRS	
3. 超音波(心臟超音波等)	
D. 肌肉細胞功能及病理切片	
1. 肌肉切片病理報告(組織染色及/或細胞電子顯微鏡檢查)	
2. 呼吸鏈酵素染色	
3. 呼吸功能測試	
E. 纖維母細胞呼吸功能測試	
F. 基因檢測(附實驗室報告)	
G. 其他檢查(包括電氣生理學檢查等)	
H. 備註(病人為非典型之表現，不完全符合以上之診斷標準，但仍診斷為此疾病之理由)	

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(審查標準表)

-原發性肺動脈高壓[Idiopathic pulmonary arterial hypertension]-



Abbreviation:

a:症狀包括 dyspnea, syncope, chest pain, peripheral edema, fatigue. b:small defects: VSD<1cm, ASD<2cm, PDA<0.2cm. HRCT: high resolution CT. PVOD:pulmonary venous obstructive disease. CTEPH: chronic thromboembolic pulmonary hypertension. COPD: chronic obstructive pulmonary disorder. IPD :idiopathic pulmonary disease .PF :pulmonary fibrosis. PPHN: Persistent pulmonary hypertension of newborn. Group V:; Group V in clinical classification of PH in 2013 (表一、肺高血壓分類).

衛生福利部國民健康署「罕見疾病個案通報審查標準機制」(送審標準表)

-原發性肺動脈高壓 [Idiopathic pulmonary arterial hypertension]-

1. 檢查均需附上正式報告或影本
2. 需附上相關影像資料
3. ※為續使用者必要檢附資料
4. #為如有必要選擇檢查項目
5. 其他說明如 'out of proportion' 肺高血壓

History	Symptoms：(Duration, Times or Frequency) ☐ Dyspnea ☐ Fatigue ☐ Syncope ☐ Chest Pain ☐ Peripheral edema
Physical examination	☐ Right ventricular heave ☐ Clubbing fingers ☐ Loud P2 ☐Hepatojugular reflux ☐ Peripheral edema ☐ Ascites ☐ High jugular venous pressure ☐ 心雜音 舒張期 Gr._____/ VI at____ 收縮期 Gr._____/ VI at____
Chest X-ray	☐ Enlarged pulmonary artery ☐ Enlarged right ventricle
ECG	☐ Right axis deviation ☐ Right ventricular hypertrophy ☐ Peaked P-wave ☐ Other: _____
Pulmonary function tests	☐ Standard spirometry_____ ☐ Diffusion capacity_____
※ **Transthoracic echocardiography**	Right heart dilatation：_____ 估算的 RVSP：_____mmHg,TR severity：_____,PR severity：_____
Laboratory data	☐ Complete blood count, aPTT, PT ☐ LFT: AST____, ALT_____, Bilirubin_____ total protein_____, Albumin_____, others_____ ☐ BUN____, Creatinine____, Na____ , K____ ☐ Arterial blood gas: paO2：_____ paCO2：_____ ☐ Thyroid function test：

	TSH：__ free-T4__ or [TSH：_____T4：____T3：___] ☐ HIV Ab：□ Positive □ Negative (－)
Lung V/Q perfusion scan	☐ Negative (－) ☐ Positive (＋): _____
#Chest CT (or MDCT)	☐ Negative (－) ☐ Positive (＋): _____
#Transesophageal echocardiography	Congenital heart disease: ☐ Negative (－) ☐ Positive (＋): _____
#Abdominal ultrasound	☐Negative (－) ☐ Positive (＋): _____
Autoimmune profile and rheumatology consult	☐ ANA：_____ ☐ Anti-Scl70：_____ ☐ Anti-RNP：_____ #☐ C3: _____C4: _____RF: _____
#Right Heart catheterization and vasoreactivity test	PAP(S/D/M)：___/___/ _mmHg RAP：_____/___/ ___mmHg PCWP：___/___/ _____mmHg C.O. ：_____L/min C.I. ：_____ L/min/m^2 TPG [Transpulmonary pressure gradient]：_____/ mmHg PVR：_____Wood units, or PVRI: _____ ☐ Vasodilator test： ☐ Negative (－) ☐ Positive (＋) : _____
備註(病人為非典型之表現，不完全符合以上之診斷標準，但仍診斷為此疾病之理由)	
其他說明	