



CURRICULUM VITAE

Name : Gispen-de Wied
First name : Christine Charlotte
Degree(s) : MD, PhD
Date of birth : 02-11-1954
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Concise Introduction

Christine Gispen-de Wied (1954) received her MD degree at the University of Groningen (1981). Subsequently she worked as Resident in the Psychiatric Hospital Wolfheze (NL). Thereafter, she joined the field of clinical research at the Department of Psychiatry, University Medical Center Utrecht, UMCU. She received her PhD in 1991 at Utrecht University, based on her thesis, entitled 'The Hypothalamo Pituitary Adrenal Axis in Depression'. She was registered as Pharmacologist in 2005.

In 2002 she started working for the Medicines Evaluation Board, successively as clinical assessor, Head of the CNS Department, and, since 2008, as Head of the Scientific Program and National Scientific Advice. She was a member of the Scientific Advice Working Party, SAWP, at the European Medicines Agency, EMA, until 2012, and is a member of the CNS Working Party since 2010. The focus of her present work lies in the promotion of regulatory science and research within the agency and beyond, through collaboration with external parties.

Christine Gispen-de Wied is member and fellow of the European College of Neuropsychopharmacology, ECNP, and member of the Consultation Committee since 2008. In this position, she is responsible for the regulatory contribution to the scientific dialogue between academia, regulatory authorities and industry at the merit of CNS drug development and innovation.

Christine Gispen-de Wied is teaching the interdisciplinary course 'Human Stress Research' at the University College Roosevelt in Middelburg since 2008, and the University College in Utrecht since 2011. She teaches the translation of clinical scientific research into innovative drug development strategies in psychiatry. She also returned to the UMCU in 2011 to join the teaching staff.

Christine Gispen-de Wied has more than 60 publications in various scientific research fields, and is currently advocating the field of drug regulatory science.

Education

1974-1981 Medical Study, University of Groningen

Career

- 1982-1983 Intern Psychiatric Hospital Wolfheze, Wolfheze
- 1983-1991 PhD Division of Psychiatry, University Medical Centre Utrecht (UMCU)
- 1991 Thesis: 'The Hypothalamo Pituitary Adrenal Axis in Depression'
Supervision: Prof Dr J.M. van Ree and Prof Dr J.H.H. Thijssen
- 1992-1994 Assistant Professor, Division of Psychiatry, UMCU
Assignment: 'Neuroendocrine Aspects of Psychiatric Diseases'
- 1994-1998 Assistant Professor, Division of Psychiatry, UMCU
Assignment: 'Research Coordinate Schizophrenia Project' and supervising research in the field of 'Neuroendocrinology and Psychiatric Diseases'
- 1998-2004 Senior Scientist, Division of Psychiatry, UMCU
Assignment: Research in the field of 'Endocrinology of Stress and Adaptation in Psychiatric Diseases'
- 2002-2007 Clinical Assessor CNS, Medicines Evaluation Board (MEB), The Hague
- 2003-2004 Alternate member Scientific Advice Working Party (SAWP), European Medicines Agency (EMA), London
- 2004-2008 Free-lance fellow medical training program (CRU-99), UMCU
- 2004-2012 Member Scientific Advice Working Party (SAWP), EMA, London
- 2005- Registered as Pharmacologist
- 2005-2007 Clinical coordinate CNS department MEB
- 2006-2012 Fellow and MEB coordinate Drug Regulatory Science Master Track, Utrecht University (UU), Pharmaceutical Sciences
- 2007-2008 Head of CNS Department, MEB, The Hague
- 2008- Scientific Program manager MEB with the assignment of Academic Networking and Research, Training and Education of clinical assessors
- 2008- Fellow Roosevelt Academy, Utrecht University, Middelburg
- 2011- Fellow University College Utrecht and Amsterdam University College (2013)
- 2011- Senior Staff Teaching and Education, Division Brain (Psychiatry), University Medical Centre Utrecht (UMCU)
- 2012- Certified as SKO (Senior Kwalificatie Onderwijs/Senior Teaching Qualifications), Utrecht University

Memberships Societies

- European College of Neuropsychopharmacology, ECNP (1990-)
- Soroptimist International, Club de Bilt-Bilthoven (1998-)
- Dutch Pharmacological Society (2004-)
- ECNP Consultation Committee (2008-)
- International Society of Psychoneuroendocrinology, ISPNE (-2002)
- Rudolf Magnus School of Neuroscience (-2004)/Brain Centre Rudolf Magnus (2011-)

Skills and experiences

Managerial:

- Coordination of research groups at university and government.
- Research data management
- Head of department
- Scientific program management

Scientific, Educational:

- Lectures at national and international level
- Supervision of students, PhD's and Post-docs
- Organization of teaching programs at bachelor and master level:
Master Program Drug Innovation, Utrecht University (-2012)

Interdisciplinary 3rd year bachelor science course at Roosevelt Academy, University College Utrecht and Amsterdam (-2013): *'Human Stress Research: the Psychobiology of health and Disease'*,

Advisory Boards/Program Committee's:

EPHOR (Expertisecentrum Pharmacotherapie bij Ouderen)

FIGON Dutch Medicines Days

Editorial activities:

Review for scientific journals

Guest editor special issue European Neuropsychopharmacology: Use of Placebo in Psychiatry (2011)

Guest editor special issue European Neuropsychopharmacology: Regulatory Science: Focus on CNS (2013-)

Theses Defences:

Impaired stress processing in autistic-like disorders and schizophrenia. L Jansen (1999).

Promotores: Prof. dr. H van Engeland, Prof. dr. RS Kahn

Co-promotor: Dr. **CC Gispen-de Wied**

Effects of Atypical Antipsychotics in Schizophrenia. F Scheepers (2000).

Promotor: Prof. dr. RS Kahn

Co-promotor: Dr. **CC Gispen-de Wied**

Attention and Neurotransmission; towards a human pharmacological model for schizophrenia. B Oranje (2001).

Promotores: Prof. dr. RS Kahn, Prof. dr. MN Verbaten

Co-promotor: Dr **CC Gispen-de Wied**

Neonatal Amygdala Lesions and Stress Responsivity in Rats; Relevance to Schizophrenia. J Terpstra (2004).

Promotores: Prof. dr. VM Wiegant, Prof. dr. JM van Ree

Co-promotor: Dr. **CC Gispen-de Wied**

Antipsychotics and the prevalence of Diabetes Mellitus in Schizophrenia. D Cohen (2006).

Promotores: Prof. dr. DE Grobbee, Prof. dr. R Stolk

Co-promotor: Dr. **CC Gispen-de Wied**

Marketing Authorization of New Medicines in the EU: towards evidence-based improvement. Michelle Putzeist (2013).

Promotores: Prof. dr. HW Leufkens, Prof. dr. AW Hoes

Co-promotores: Dr. A Mantel-Teeuwen, Dr. **CC Gispen-de Wied**

The scientific value of non-clinical animal studies in drug development. Peter van Meer (2013).

Promotores: Prof. dr. Prof. Dr. Huub Schellekens, Prof. dr. Ellen Moors, Prof. Beatriz Silva-Lima

Co-promotor: Dr. **CC Gispen-de Wied**

List of Publications (68):

1. Kooijman M, van Meer PJ, **Gispén-de Wied CC**, Moors EH, Hekkert MP, Schellekens H (2013). The risk based approach to ATMP development – Generally accepted by regulators but infrequently used by companies. *Regul Toxicol* Aug 7
2. Van Meer PJ, Kooijman M, Brinks V, **Gispén-de Wied CC**, Silva-Lima B, Moors EH, Schellekens H (2013). Immunogenicity of mAbs in non-human primates during safety assessment. *MAbs* 5(5)
3. **Gispén-de Wied CC**, Leufkens HG (2013). From molecule to market access: Drug regulatory science as an up-coming discipline. *Eur J Pharmacol* Jul 24
4. Putzeist M, Mantel-Teeuwisse AK, Llinares J, **Gispén-de Wied CC**, Hoes AW, Leufkens HG (2013). EU marketing authorization review of orphan and non-orphan drugs does not differ. *Drug Discov Today* Jul 5
5. Nutt D, **Gispén-de Wied CC**, Arango C, Keefe RS, Penadés R, Murphy DG, Robbins TW, Sahakian BJ (2013). Cognition in Schizophrenia: Summary Nice Consultation Meeting 2012. *Eur Neuropsychopharmacol* May 15
6. Putzeist M, Mantel-Teeuwisse AK, Aronsson B, Rowland M, **Gispén-de Wied CC**, Vamvakas S, Hoes AW, Leufkens HG, Eichler HG (2012). Factors influencing non-approval of new drugs in Europe. *Nat Rev Drug Discov*11(12):903-4
7. **Gispén-de Wied C**, de Andres-Trelles F. (2012). Editorial. Use of placebo in psychiatry. *Eur Neuropsychopharmacol*.;22(11):769
8. van Meer PJ, Kooijman M, **Gispén-de Wied CC**, Moors EH, Schellekens H. (2012). The ability of animal studies to detect serious post marketing adverse events is limited. *Regul Toxicol Pharmacol*. 64(3):345-9
9. Isaac M, Pani L, **Gispén-de Wied C**, Koch A. (2012). European licensing of maintenance treatment in schizophrenia. *Lancet*11;380(9841):562-3
10. **Gispén-de Wied C**, Stoyanova V, Yu Y, Isaac M, Pani L, de Andres-Trelles F (2012). The placebo arm in clinical studies for treatment of psychiatric disorders: a regulatory dilemma. *Eur Neuropsychopharmacol* 22(11):804-11
11. Crijns HJ, van Rein N, **Gispén-de Wied CC**, Straus SM, de Jong-van den Berg LT (2012). Prescriptive contraceptive use among isotretinoin users in the Netherlands in comparison with non-users: a drug utilisation study. *Pharmacoepidemiol Drug Saf*. 21(10):1060-6
12. Putzeist M, Heemstra HE, Garcia JL, Mantel-Teeuwisse AK, **Gispén-De Wied CC**, Hoes AW, Leufkens HG (2012). Determinants for successful marketing authorisation of orphan medicinal products in the EU. *Drug Discov Today*17(7-8):352-8
13. Crijns I, Straus S, Luteijn M, **Gispén-de Wied C**, Raine J, de Jong-van den Berg L (2012). Implementation of the harmonized EU isotretinoin Pregnancy Prevention Programme: a questionnaire survey among European regulatory agencies. *Drug Saf* 1;35(1):27-32
14. Van Venrooij JA, Fluitman SB, Lijmer JG, Kavelaars A, Heijnen CJ, Westenberg HG, Kahn RS,

- Gispén-de Wied CC** (2012). Impaired Neuroendocrine and Immune Response to Acute Stress in Medication-Naïve Patients With a First Episode of Psychosis. *Schizophr Bull* 38 (2): 272-9
15. Vellas B, Aisen PS, Sampaio C, Carrillo M, Scheltens P, Scherrer B, Frisoni GB, Weiner M, Schneider L, Gauthier S, **Gispén-de Wied CC**, Hendrix S, Feldman H, Cedarbaum J, Petersen R, Siemers E, Andrieu S, Prvulovic D, Touchon J, Hampel H (2011). Prevention trials in Alzheimer's disease: an EU-US task force report. *Prog Neurobiol.* 95(4):594-600
 16. Crijns HJ, Jentink J, Garne E, **Gispén-de Wied CC**, Straus SM, de Jong-van den Berg LT; EUROCAT Working Group (2011). The distribution of congenital anomalies within the VACTERL association among tumor necrosis factor antagonist-exposed pregnancies is similar to the general population. *J Rheumatol* 38(9):1871-4
 17. Maliepaard M, Banishki N, **Gispén-de Wied CC**, Teerenstra S, Elferink AJ (2011). Interchangeability of generic anti-epileptic drugs: a quantitative analysis of topiramate and gabapentin. *Eur J Clin Pharmacol* 67(10):1007-16
 18. Mattila T, Stoyanova V, Elferink A, **Gispén-de Wied C**, de Boer A, Wohlfarth T (2011). Insomnia medication: Do published studies reflect the complete picture of efficacy and safety. *Eur Neuropsychopharmacol* 21(7):500-7
 19. Putzeist M, Mantel-Teeuwisse AK, **Gispén-de Wied CC**, Hoes AW, Leufkens HG (2011). Regulatory scientific advice in drug development: does company size make a difference? *Eur J Clin Pharmacol* 67(2):157-64
 20. Crijns HJ, Straus SM, **Gispén-de Wied CH**, de Jong-van den Berg LT (2011). Compliance with Pregnancy Prevention Programs of Isotretinoin in Europe: a systematic review. *Br J Dermatology* 164(2): 238-44
 21. Stoyanova-Beninska VV, Wohlfarth T, Isaac M, Kalverdijk LJ, van den Berg H, **Gispén-de Wied C** (2011). The EU paediatric regulation Effects on psychopharmacology in Europe. *Eur Neuropsychopharmacology* 21 (8): 565-70
 22. De Wied M, **Gispén-de Wied C**, van Boxtel A (2010). Empathy dysfunction in children and adolescents with disruptive behavior disorders. *Eur J Pharmacol* 626 (1): 97-103.
 23. Maliepaard M, Hekster YA, Kapelle A, van Puijenbroek EP, Elferink AJ, Welink J, **Gispén-de Wied CC**, Lekkerkerker FJ (2009). Requirements for generic anti-epileptic medicines: a regulatory perspective. *J Neurol* 256 (12):1966-71
 24. Wohlfarth T, Kalverdijk L, Rademaker C, Schothorst P, Minderaa R, **Gispén-de Wied C** (2009). Psychopharmacology for children: from off label use to registration. *Eur Neuropsychopharmacol* 19 (8): 603-8.
 25. **Gispén-de Wied CC**, Kritsidima M, Elferink AJ (2009). The validity of biomarkers as surrogate endpoints in Alzheimer's disease by means of the Quantitative Surrogate Validation Level of Evidence Scheme (QSVLES). *J Nutr Health Aging* 13 (4): 376-87.
 26. Oranje B, **Gispén-de Wied CC**, Westenberg HG, Kemner C, Verbaten MN, Kahn RS (2009). Haloperidol counteracts the ketamine-induced disruption of processing negativity, but not that of the P300 amplitude. *Int J Neuropsychopharmacol* 12 (6): 823-32

27. Mulder H, Cohen D, Scheffer H, **Gispén-de Wied C**, Arends J, Wilmink FW, Franke B, Egberts AC. HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia: a replication study. *J Clin Psychopharmacol* 29 (1): 16-20.
28. Van Westrhenen R, **Gispén-de Wied CC**, Lekkerkerker JF (2008). Blunting of the cardiovascular effect of aspirin by ibuprofen: what is the evidence? *Clin Pharmacol Ther* 83 (6): 812
29. Jansen LM, **Gispén-de Wied CC**, Wiegant VM, Westenberg HG, Lahuis BE, van Engeland H. (2006). Autonomic and neuroendocrine responses to a psychosocial stressor in adults with autistic spectrum disorder. *J Autism Dev Disord*. 36(7):891-9.
30. Cohen D, Stolk RP, Grobbee DE, **Gispén-de Wied CC**. (2006).Hyperglycemia and diabetes in patients with schizophrenia or schizoaffective disorders. *Diabetes Care*. 29(4):786-91.
31. Oranje B, **Gispén-de Wied CC**, Westenberg HG, Kemner C, Verbaten MN, Kahn RS. 2006. No effects of l-dopa and bromocriptine on psychophysiological parameters of human selective attention. *Psychopharmacol*. 20(6):789-98.
32. Wohlfarth TD, van Zwieten BJ, Lekkerkerker FJ, **Gispén-de Wied CC**, Ruis JR, Elferink AJ, Storosum JG. 2006. Antidepressants use in children and adolescents and the risk of suicide. *Eur Neuropsychopharmacol*. 16(2):79-83.
33. Cohen D, Dekker JJ, Peen J, **Gispén-de Wied CC**. 2006. Prevalence of diabetes mellitus in chronic schizophrenic inpatients in relation to long-term antipsychotic treatment. *Eur Neuropsychopharmacol*. 16(3):187-94.
34. Cohen D, Batstra M, **Gispén-de Wied CC** (2005).Immunological characteristics of Diabetes Mellitus in schizophreniallitis in schizophrenia. *Diabetologia*, 48 (9): 1941-2.
35. Storosum JG, Fouwels A, **Gispén-de Wied CC**, Wohlfarth T, van Zwieten BJ, van den Brink W (2004). How real are patients in placebo-controlled studies of manic episode? *Eur Neuropsychopharmacol* 14(4): 319-323.
36. Jansen LMC, **Gispén-de Wied CC**, Wiegant VM, Westenberg HGM, Lahuis BE, van Engeland H (2004). Autonomic and neuroendocrine responses to psychosocial stress in adults with Autistic Spectrum Disorder. *J Autism and Developmental Disorders*, accepted.
37. Cohen D, Puite B, Dekker JJ, **Gispén-de Wied CC** (2003). Diabetes mellitus in 93 chronic schizophrenic inpatients. *Eur J Psychiatry* 17: 38-47
38. Terpstra J, **Gispén-de Wied CC**, Broekhoven MH, Frankhuijzen AC, Kahn RS, van Ree JM, Wiegant VM (2003). Attenuated stress responsiveness in an animal model for neurodevelopmental psychopathological disorders. *Eur Neuropsychopharmacol*. 13(4): 249-256.
39. Cohen D, **Gispén-de Wied CC** (2003). Schizophrenia and diabetes mellitus: not an improbable combination. *Ned Tijdschr Geneeskd*. 147(21): 993-996.
40. Jansen LMC, **Gispén-de Wied CC**, van der Gaag RJ, van Engeland H (2003). Differentiation between autism and multiple complex developmental disorder in response to psychosocial

stress. *Neuropsychopharmacology* 28(3): 582-590.

41. Oranje B, **Gispén-de Wied CC**, Verbaten MN, Kahn RS (2002). Modulating sensory gating in healthy volunteers: the effect of ketamine and haloperidol. *Biol Psychiatry* 52(9): 887-895.
42. Oranje B, Van Oel CJ, **Gispén-de Wied CC**, Verbaten MN, Kahn RS (2002). Effects of typical and atypical antipsychotics on the prepulse inhibition of the startle reflex in patients with schizophrenia. *J Clin Psychopharmacol* 22(4): 359-365.
43. Scheepers FE, **Gispén-de Wied CC**, Westenberg HGM, Kahn RS (2002). Effect of olanzapine on glutamate levels in cerebrospinal fluid of patients with schizophrenia. *J Clin Psychopharmacol* 22(3): 333-334.
44. **Gispén-de Wied CC**, Jansen LMC (2002). The stress-vulnerability hypothesis in psychotic disorders: focus on the stress response systems. *Curr Psychiatry Rep* 4(3): 166-70.
45. Scheepers FE, **Gispén-de Wied CC**, Kahn RS (2001). The effect of olanzapine treatment on m-chlorophenylpiperazine-induced hormone release in schizophrenia. *J Clin Psychopharmacol* 21(6): 575-582.
46. Scheepers FE, **Gispén-de Wied CC**, Hulshoff Pol HE, Kahn RS (2001). Effect of clozapine on caudate nucleus volume in relation to symptoms of schizophrenia. *Am J Psychiatry* 158 (4): 644-646.
47. Scheepers FE, **Gispén-de Wied CC**, Hulshoff Pol HE, van der Flier W, van der Linden JA, Kahn RS (2001). The effect of clozapine on caudate nucleus volume in schizophrenic patients previously treated with typical antipsychotics. *Neuropsychopharmacology* (1): 47-54.
48. Scheepers FE, **Gispén-de Wied CC**, Westenberg HGM, Kahn RS (2001). The effect of olanzapine treatment on monoamine metabolite concentrations in the cerebrospinal fluid of schizophrenic patients. *Neuropsychopharmacology* 25(4): 468-475.
49. **Gispén-de Wied CC** (2000). Stress in schizophrenia: an integrative view. *Eur J Pharmacol* 405 (1-3): 375-84.
50. Oranje B, Bijl S, Campagne A, **Gispén-de Wied CC** (2000). Commentary on plasma levels of homovanillic acid (phVA) under influence of mental stress. *Neuropsychopharmacology* 23(3): 345-346.
51. Jansen LMC, **Gispén-de Wied CC**, van der Gaag RJ, ten Hove F, Willemsen-Swinkels SW, Hartevelt E, van Engeland H (2000). Unresponsiveness to psychosocial stress in a subgroup of autistic-like children, multiple complex developmental disorder. *Psychoneuroendocrinology* 25(8): 753-764.
52. Hulshoff Pol HE, Hoek HW, Susser E, Brown AS, Dingemans A, Schnack HG, van Haren NE, Pereira Ramos LM, **Gispén-de Wied CC**, Kahn RS (2000). Prenatal exposure to famine and brain morphology in schizophrenia. *Am J Psychiatry* 157 (7): 1170-1172.
53. Jansen LMC, **Gispén-de Wied CC**, Kahn RS (2000). Selective impairments in the stress response in schizophrenic patients. *Psychopharmacology* 149(3): 319-325.
54. **Gispén-de Wied CC**, Jansen LM, Duyx JH, Thijsen JH, van Engeland H (2000). Pituitary-

adrenal function in adolescent psychiatric patients: impact of depressive symptoms. *J Affect Disord* 59(1): 71-76.

55. Selten JP, van der Graaf Y, van Duursen R, **Gispén-de Wied**, Kahn RS (1999). Psychotic illness after prenatal exposure to the 1953 Dutch Flood Disaster. *Schizophr Res.* 35(3): 243-245.
56. Jansen LMC, **Gispén-de Wied CC**, Jansen MA, van der Gaag RJ, Matthys W, van Engeland H (1999). Pituitary-adrenal reactivity in a child psychiatric population: salivary cortisol response to stressors. *Eur Neuropsychopharmacol.* 9(1-2): 67-75.
57. Jansen LMC, **Gispén-de Wied CC**, Gademan PJ, De Jonge RC, van der Linden JA, Kahn RS (1998). Blunted cortisol response to a psychosocial stressor in schizophrenia. *Schizophr Res.* 33(1-2): 87-94.
58. Van Berckel BN, Lipsch C, **Gispén-de Wied CC**, Wynne HJ, Blankenstein MA, van Ree JM, Kahn RS (1998). The partial NMDA agonist D-cycloserine stimulates LH secretion in healthy volunteers. *Psychopharmacology* 138(2): 190-197.
59. **Gispén-de Wied CC**, Jansen LMC, Wynne HJ, Matthys W, van der Gaag RJ, Thijssen JH, van Engeland H (1998). Differential effects of hydrocortisone and dexamethasone on cortisol suppression in a child psychiatric population. *Psychoneuroendocrinology* 23(3): 295-306.
60. Van Goozen SH, Matthys W, Cohen-Kettenis PT, **Gispén-de Wied CC**, Wiegant VM, Van Engeland H (1998). Salivary cortisol and cardiovascular activity during stress in oppositional-defiant disorder boys and normal controls. *Biol Psychiatry* 43 (7): 531-539.
61. Van Berckel BN, Lipsch C, Timp S, **Gispén-de Wied CC**, Wynne H, van Ree JM, Kahn RS (1997). Behavioral and neuroendocrine effects of the partial NMDA agonist D-cycloserine in healthy subjects. *Neuropsychopharmacology* 16(5): 317-324.
62. Thijssen JH, **Gispén-de Wied CC**, van Heeswijk GM, Veeman W (1996). Determination of dexamethasone in saliva. *Clin Chem* 42(8 Pt 1): 1238-1242.
63. **Gispén-de Wied CC**, Kok FW, Koppeschaar HP, Wynne HJ, Westenberg HGM, Thijssen JH, van Ree JM (1993). Stimulation of the pituitary-adrenal system with graded doses of CRH and low dose vasopressin infusion in depressed patients and healthy subjects: a pilot study. *Eur Neuropsychopharmacol* 3(4): 533-541.
64. **Gispén-de Wied CC**, D'Haenen H, Verhoeven WM, Wynne HJ, Westenberg HGM, Thijssen JH, van Ree JM (1993). Inhibition of the pituitary-adrenal axis with dexamethasone and cortisol in depressed patients and healthy subjects: a dose-response study. *Psychoneuroendocrinology* 18(3): 191-204.
65. **Gispén-de Wied CC**, Westenberg HGM, Koppeschaar HP, Thijssen JH, van Ree JM (1992). Stimulation of the pituitary-adrenal axis with a low dose [Arg8]-vasopressin in depressed patients and healthy subjects. *Eur Neuropsychopharmacol* 2(4): 411-419.
66. Brand AN, Jolles J, **Gispén-de Wied CC** (1992). Recall and recognition memory deficits in depression. *J Affect Disord* 25(1): 77-86.
67. Kahn RS, Westenberg HGM, Verhoeven WM, **Gispén-de Wied CC**, Kamerbeek WD (1987). Effect of a serotonin precursor and uptake inhibitor in anxiety disorders; a double-blind

comparison of 5-hydroxytryptophan, clomipramine and placebo. *Int Clin Psychopharmacol* 2(1): 33-45.

68. **Gispen-de Wied CC**, Westenberg HGM, Thijssen JH, van Ree JM (1987). The dexamethasone and cortisol suppression test in depression: beta-endorphin as a useful marker. *Psychoneuroendocrinology* 12(5):355-366.