

PERSONAL INFORMATION **Martina Weise**

WORK EXPERIENCE

- July 2016- Present **Head, Licensing Division 2**
Federal Institute for Drugs and Medical Devices (BfArM) (Germany)
The position includes scientific and personnel responsibility for three multidisciplinary units, one unit on special toxicology and an administration unit.
- October 2011-June 2016 **Head, Unit on Diabetes/Cardiovascular Disorders**
Federal Institute for Drugs and Medical Devices (BfArM) (Germany)
The position included scientific and personnel responsibility for a multidisciplinary team consisting of quality, non-clinical and clinical assessors, and secretaries.
- July 2005-September 2011 **Head, Unit on Endocrinology/Gynecology**
Federal Institute for Drugs and Medical Devices (BfArM) (Germany)
The position included scientific and personnel responsibility for a multidisciplinary team consisting of quality, non-clinical and clinical assessors, and secretaries.
- October 2001-June 2005 **Head, Unit on Endocrinology/Diabetes**
Federal Institute for Drugs and Medical Devices (BfArM) (Germany)
The position included scientific and personnel responsibility for a clinical assessor team and secretaries.
- July 1997-September 2001 **Clinical Fellow**
Developmental Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health (United States)
Fellowship in paediatric endocrinology including inpatient and outpatient care, mainly in children but also adults. Clinical, animal and laboratory research on epiphyseal, bone and adrenal disorders. 1998 Permanent ECFMG certification (USA).
- January 1997-June 1997 **Adjunct Scientist**
Developmental Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health (United States)
Animal and laboratory research on epiphyseal and bone disorders
- February 1988-July 1989 **Clinical Fellow**
Department of Paediatrics, Johann Wolfgang Goethe-University, Frankfurt am Main (Germany)
Outpatient care in children with endocrinological disorders. Clinical research.

EDUCATION AND TRAINING

- August 1989-June 1995 **Board Certificate in Paediatrics**
Department of Paediatrics, Johann Wolfgang Goethe-University, Frankfurt am Main (Germany)
Training in all subspecialties of Paediatrics according to curriculum. Board Certification in Paediatrics in June 1995. Doctoral thesis with doctor's degree in 1992.
- April 1980-December 1986 **Medical doctor (MD)**
Johann Wolfgang Goethe-University, Frankfurt am Main (Germany)
Medical training including one year of internship.

ADDITIONAL INFORMATION

- Expertise** Paediatrics, Endocrinology, Diabetology, Biosimilars, Clinical and Laboratory Research in Endocrinology
- Publications** 1. Groll A, Meiser A, Weise M, Rettwitz-Volk W, v.Loewenich V, Gussetis ES, Kornhuber B. Interleukin-6 as early mediator in neonatal sepsis. *Pediatr Infect Dis J* 1992; 11: 496-8

2. Groll A, Wildfeuer A, Weise M, Gussetis ES, Schwabe D, Gerein V, Kornhuber B. Pharmacokinetics of fluconazole in a pediatric subgroup. In: Adam D, Lode H, Rubinstein E (eds.). *Recent Advances in Chemotherapy*. Futuramed Publishers, Munich 1992: 526-527E
3. Weise M, James D, Leitner CH, Hartmann KKP, Boehles HJ, Attanasio A and the German Lilly UTS Study Group. Glucose metabolism in Ullrich Turner-Syndrome: Long term effects of therapy with Human Growth Hormone. *Horm Res* 1993; 39: 36-41
4. Weise M, James D, Hartmann KH, Reinhardt D, Leitner CH, Boehles HJ, Attanasio A and the German Lilly UTS Study Group. Dose-dependent effect of growth hormone therapy on glucose metabolism in subjects with Turner Syndrome. *Horm Res* 1993; 39(Suppl 2): 25-9
5. Groll A, Nowak-Goettl U, Wildfeuer A, Weise M, Schwabe D, Gerein V, Kornhuber B. Fluconazole treatment of oropharyngeal candidosis in pediatric cancer patients with severe mucositis following antineoplastic chemotherapy. *Mycoses* 1993; 35 (Suppl 1): 35-40
6. Weise M, Abad V, Considine RV, Nieman LK, Rother KI. Leptin secretion in Cushing's syndrome: Preservation of diurnal rhythm and absent response to Corticotropin-Releasing Hormone. *J Clin Endocrinol Metab* 1999; 84(6):2075-9.
7. Merke DP, Chrousos GP, Eisenhofer G, Weise M, Keil MF, Rogol AD, Van Wyk JJ, Bornstein SR. Adrenomedullary dysplasia and hypofunction in patients with classic 21-hydroxylase deficiency. *New Engl J Med* 2000; 343(19):1362-8.
8. Weise M, De-Levi S, Barnes KM, Gafni RI, Abad V, Baron J. Effects of estrogen on growth plate senescence and epiphyseal fusion. *Proc Natl Acad Sci USA* 2001; 98(12):6871-6.
9. Gafni RI, Weise M, Robrecht DT, Meyers JL, Barnes KM, De-Levi S, Baron J. Catch-up growth is associated with delayed senescence of the growth plate in rabbits. *Pediatr Res*. 2001; 50(5):618-23.
10. Abad, V., Meyers, J.L., Weise, M., Gafni, R.I., Barnes, K.M., Nilsson, O., Bacher, J.D., Baron, J. The role of the resting zone in growth plate chondrogenesis. *Endocrinology* 2002, 143(5):1851-7.
11. Gafni RI, McCarthy EF, Hatcher T, Meyers JL, Inoue N, Reddy C, Weise M, Barnes KM, Abad V, Baron J. Recovery from osteoporosis through skeletal growth: early bone mass acquisition has little effect on adult bone density. *FASEB J*. 2002, 16(7):736-8.
12. Weise M, Merke DP, Pacak K, Walther MM, Eisenhofer G. Utility of plasma free metanephrines for detecting childhood pheochromocytoma. *J Clin Endocrinol Metab* 2002, 87(5):1955-60.
13. Charmandari E, Weise M, Bornstein SR, Eisenhofer G, Keil MF, Chrousos GP, Merke DP. Children with classic congenital adrenal hyperplasia have elevated serum leptin concentrations and insulin resistance: potential clinical implications. *J Clin Endocrinol Metab* 2002, 87(5):2114-20.
14. Weise M, Eisenhofer G, Merke DP. Pubertal and gender-related changes in the sympathoadrenal system in healthy children. *J Clin Endocrinol Metab* 2002, 87(11):5038-43).
15. Pacak K, Weise M, Eisenhofer G, Brouwers FM, Koch CA. Disorders of the adrenal medulla: Catecholamine-Producing Tumors in Childhood. In *Pediatric Endocrinology*, 4th ed, New York: Marcel Dekker; ed F Lifshitz, 2003.
16. Weise M, Flor A, Barnes KM, Cutler Jr. GP, Baron J. Determinants of growth during GnRH analog therapy for precocious puberty. *J Clin Endocrinol Metab* 2004, 89(1):103-7.
17. Weise M, Mehlinger SL, Drinkard B, Charmandari E, Hiroi M, Eisenhofer G, Yanovski J, Chrousos GP, Merke DP. Patients with classic congenital adrenal hyperplasia have decreased catecholamine reserve and defective glucose elevation in response to high intensity exercise. *J Clin Endocrinol Metab* 2004, 89(2):591-7.
18. Weise M, Drinkard B, Mehlinger SL, Rawson E, Charmandari E, Hiroi M, Eisenhofer G, Chrousos GP, Merke D. Stress dose of hydrocortisone is not beneficial in patients with classic congenital adrenal hyperplasia undergoing short-term high-intensity exercise. *J Clin Endocrinol Metab* 2004, 89(8):3679-84. (Editorial pp. 3677-78).
19. Liza Green-Golan, Catherine Yates, Bart Drinkard, Carol VanRyzin, Graeme Eisenhofer, Martina Weise, Deborah P. Merke. Patients with Classic Congenital Adrenal Hyperplasia Have Decreased Epinephrine Reserve and Defective Glycemic Control During Prolonged Moderate-Intensity Exercise. *J Clin Endocrinol Metab* 2007, 92: 3019-3024.
20. Kathleen Coyle, Kristina I.Rother, Martina Weise, Alaa Ahmed, Frederick W. Miller, Lisa G. Rider. Metabolic Abnormalities and Cardiovascular Risk Factors in Children with Myositis. *J Pediatr* 2009, 155(6): 882-7.
21. Martina Weise, Christian K Schneider. Biosimilars in the EU: the interplay of regulators, treating physicians and pharmacists. *Hospital Pharmacy Europe* 2009, 43: 31-35.
22. Somya Verma, Liza Green-Golan, Carol VanRyzin, Bart Drinkard, MSPT, Martina Weise, Graeme Eisenhofer, Deborah Merke. Adrenomedullary Function in Patients with Nonclassic Congenital Adrenal Hyperplasia. *Horm Metab Res* 2010, 42(8):607-612.
23. Buttel IC, Chamberlain P, Chowers Y, Ehmann F, Greinacher A, Jefferis R, Kramer D, Kropshofer H, Lloyd P, Lubiniecki A, Krause R, Mire-Sluis A, Platts-Mills T, Ragheb JA, Reipert BM, Schellekens H, Seitz R, Stas P, Subramanyam M, Thorpe R, Trouvin JH, Weise M, Windisch J, Schneider CK. Taking immunogenicity assessment of therapeutic proteins to the next level. *Biologicals* 2011, 39(2):100-9.
24. Harald G. Enzmann, Martina Weise. Current European Regulatory Perspectives on Insulin Analogues. *Diabetol Metab Syndr* 2011, 3:14.
25. Martina Weise, Marie-Christine Bielsky, Karen De Smet, Falk Ehmann, Niklas Ekman, Narayanan Gopalan, Hans-Karl Heim, Esa Heinonen, Kowid Ho, Robin Thorpe, Camille Vleminckx, Meenu Wadhwa, and Christian K Schneider. Biosimilars - Why terminology matters. *Nature Biotechnol* 2011, 29(8):690-3.
26. Schneider CK, Borg JJ, Ehmann F, Ekman N, Heinonen E, Ho K, Hoefnagel MH, van der Plas RM, Ruiz S, van der Stappen AJ, Thorpe R, Tiitso K, Tsiftoglou AS, Vleminckx C, Waxenecker G, Welin M, Weise M, Trouvin JH; Working Party on Similar Biological (Biosimilar) Medicinal Products (BMWP); Biologicals Working Party (BWP) of the Committee for Medicinal Products for Human Use

(CHMP). In support of the European Union biosimilar framework. *Nature Biotechnol* 2012, 30:745-8.

27. Martina Weise, Marie-Christine Bielsky, Karen De Smet, Falk Ehmann, Niklas Ekman, Thijs J Giezen, Iordanis Gravanis, Hans-Karl Heim, Esa Heinonen, Kowid Ho, Alexandre Moreau, Gopalan Narayanan, Nanna A Kruse, Gabriele Reichmann, Robin Thorpe, Leon van Aerts, Camille Vleminckx, Meenu Wadhwa, and Christian K Schneider. Biosimilars: what clinicians should know. *Blood* 2012, 120(26):5111-7.

28. Schneider CK, Vleminckx C, Gravanis I, Ehmann F, Trouvin JH, Weise M, Thirstrup S. Setting the stage for biosimilar monoclonal antibodies. *Nat Biotechnol.* 2012, 30(12):1179-85.

29. Nilsson O*, Weise M*, Landman EB, Meyers JL, Barnes KM, Baron J. Evidence that estrogen hastens epiphyseal fusion and cessation of longitudinal bone growth by irreversibly depleting the number of resting zone progenitor cells in female rabbits. *Endocrinology* 2014, 155(8):2892-9. *shared first authorship.

30. Weise M, Kurki P, Wolff-Holz E, Bielsky MC, Schneider CK. Biosimilars: the science of extrapolation. *Blood* 2014, 20(22):3191-6.

31. Manuel Haas, Viktor Vlcek, Pavel Balabanov, Tomas Salmonson, Serge Bakchine, Greg Markey, Martina Weise, Gabriele Schlosser-Weber, Henning Brohmann, Concepcion Prieto Yerro, Macarena Rodriguez Mendizabal, Violeta Stoyanova-Beninska, Hans L. Hillege. European Medicines Agency review of ataluren for the treatment of ambulant patients aged 5 years and older with Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene. *Neuromuscular Disorders* 2015, 25(1):5-13.

32. Schneider CK, Weise M. Regulatory aspects of biosimilars: Myths and facts. *Z Rheumatol* 2015, 74(8):695-700.

33. Lemery SJ, Esteva FJ, Weise M. Biosimilars: Here and Now. *AM Soc Clin Oncol Educ Book* 2016, 35:e151-7

34. Weise M, Wolff-Holz E. Opportunities and challenges of extrapolation for biosimilars. *Z Gastroenterol* 2016 Nov;54(11):1211-1216.

35. Anton R, Haas M, Arlett P, Weise M, Balabanov P, Mazzaglia G, Prieto L, Keller-Stanislawski B, Raine J. Drug-induced progressive multifocal leukoencephalopathy in multiple sclerosis: European regulators' perspective. *Clin Pharmacol Ther* 2017, 102(2):283-289.

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37. Weise M. From bioequivalence to biosimilars: How much to regulators dare? *Z Evid Fortbild Qual Gesundheitswes.* 2019, 140:58-62

38. Wolff-Holz E, Tiitso K, Vleminckx C, Weise M. Evolution of the EU Biosimilar Framework: Past and Future. *BioDrugs* 2019; 33(6):621-634.

39. Pinheiro LC, Giezen TJ, Wolff-Holz E, Weise M, Laslop A, Hidalgo-Simon A.

Identifiability of Biologicals: An Analysis Using EudraVigilance, the European Union's Database of Reports of Suspected Adverse Drug Reactions. *Clin Pharmacol Ther* 2021, 110:1311-1317

40. Kurki P, Kang H-N, Ekman N, Knezevic I, Weise M, Wolff-Holz E. Regulatory Evaluation of Biosimilars: Refinement of Principles Based on the Scientific Evidence and Clinical Experience. *BioDrugs* 2022, 36:359-371

41. Guillen E, Ekman N, Barry S, Weise M, Wolff-Holz E. A Data Driven Approach to Support Tailored Clinical Programs for Biosimilar Monoclonal Antibodies. *Clin Pharmacol Ther* 2023, 113:108-123

Projects Introduction to the Principles and Practice of Clinical Research. WG Magnuson Clinical Center, National Institutes of Health, USA (Oct 1998 - March 1999, prerequisite for participation in clinical trials at NIH)

Clinical trials (completed)

Growth-hormone treatment in children with Ullrich Turner Syndrome (UTS), a German multicenter, randomized, placebo-controlled study.

Catecholamine Reserve and Exercise Tolerance in Subjects with Congenital Adrenal Hyperplasia and in Healthy Controls (USA).

A Double-Blind, Randomized, Placebo-Controlled Trial of the Effect of Biosynthetic Growth Hormone and/or Ethinyl Estradiol on Adult Height in Patients with Turner Syndrome (USA).

Different endocrine studies in healthy children and in children with congenital adrenal hyperplasia, Cushing's syndrome, pheochromocytoma or myositis (USA).

Regulatory Guidelines

Involvement in the drafting and revision of various CHMP guidelines especially in the field of Diabetes and Biosimilars and of WHO guidelines on Biotherapeutic products prepared by Recombinant DNA Technology and on Similar Biotherapeutic Products.

Memberships German member of the CHMP

Member of the Working Party on Similar Biological Medicinal Products (BMWP) of the CHMP

Expert to the WHO regarding biosimilars since 2007

Member of the Endocrine Society (USA)

Member of the European Association for the Study of Diabetes (EASD)

Other Relevant Information