



## Curriculum Vitae

### Personal information **Christine Siezen**

#### Work experience

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1. Employer: Medicines Evaluation Board
  - Start date: 062011
  - End date: present
  - Position: Senior Pre\_clinical assessor
  - Activities: General pharmaco\_toxicological assessments Reproduction toxicity Carcinogenicity Centralized procedures SmPC assessments Oligonucleotide therapeutics
  - Country: Netherlands
2. Employer: National Institute of Public Health and Environment
  - Start date: 012007
  - End date: 062011
  - Position: Pre\_clinical assessor
  - Activities: General pharmaco\_toxicological assessments Reproduction toxicity Carcinogenicity Centralized procedures SmPC assessments
  - Country: Netherlands
3. Employer: National Institute of Public Health and Environment
  - Start date: 072005
  - End date: 122006
  - Position: Post\_doctoral scientist
  - Activities: Molecular genetics / epidemiology research
  - Country: Netherlands
4. Employer: Erasmus University Rotterdam
  - Start date: 092000
  - End date: 032005
  - Position: PhD student
  - Activities: Molecular genetics / epidemiology research
  - Country: Netherlands

#### Education and training

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1. Subject: Erasmus University Rotterdam
  - Start date: 092000
  - End date: 032005
  - Qualification: PhD
  - Organisation: Molecular genetics / epidemiology research Animal studies
  - Country: Netherlands
2. Subject: Wolverhampton University
  - Start date: 091995
  - End date: 052000
  - Qualification: BSc Biomedical Sciences
  - Organisation: Molecular genetics Microbiology Immunology Biochemistry Pharmacology
  - Country: United Kingdom

#### Additional information

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##### Publications

- Stock C, Duijndam B, Siezen CLE, Pasmooij AMG. Reduced Genotoxicity Testing Is Possible for Noncoding Oligonucleotide-Based Therapeutics Containing Well-Characterized Modifications: A European Regulatory Perspective. *Nucleic Acid Therapeutics*. 2026;0(0). doi:10.1177/21593337261429852
- Hannas BR, Bender SM, Blasi E, Bowman CJ, Cavagnaro JA, Chen CL, Coder PS, Duijndam B, Hoberman A, Kim TW, Leconte I, Maki K, Matsumoto M, Mikashima F, Misner DL, Mueller L, Powles-Glover N, Rayhon S, Saffarini C, Siezen C, Sisler J, Wange RL, White T, Templin MV. Developmental and Reproductive Toxicity Testing Strategies for Oligonucleotides: A Workshop Proceedings. *Nucleic Acid Ther*. 2025 Jun;35(3):93-113
- van der Laan JW, Andersson M, Beken S, Bonelli M, Brendler-Schwaab S, Kane R, Pasanen M, Ponzano S, Paur J, Siezen C, Soleng A, Whomsley R. EMA commentary on the ICH guideline for testing for carcinogenicity of pharmaceuticals. *Br J Clin Pharmacol*. 2023 Jun 2
- Aartsma-Rus A, van Roon-Mom W, Lauffer M, Siezen C, Duijndam B, Coenen-de Roo T, Schüle R, Synofzik M, Graessner H. Development of tailored splice-switching oligonucleotides for progressive brain disorders in Europe: development, regulation, and implementation considerations. *RNA*. 2023 Apr;29(4):446-454
- Ghalandari N, Dolhain RJEM, Hazes JMW, Siezen CLE, van der Laan JW, Crijns HJM, van Puijnenbroek EP, van der Woude CJ. The pre\_ and post\_ authorisation data published by the European medicines agency on the use of biologics during pregnancy and lactation. *Br J Clin Pharmacol*. 2020 Oct 21
- Ter Braak B, Siezen CL, Lee JS, Rao P, Voorhoeve C, Ruppig E, van der Laan JW, van de Water B. Insulin\_like growth factor 1 receptor activation promotes mammary gland tumor development by increasing glycolysis and promoting biomass production. *Breast Cancer Res*. 2017 Feb 7;19(1):14
- Theunissen PT, Beken S, Beyer BK, Breslin WJ, Cappon GD, Chen CL, Chmielewski G, De Schaepprijver L, Enright B, Foreman JE, Harrouk W, Hew KW, Hoberman AM, Hui JY, Knudsen TB, Laffan SB, Makris SL, Martin M, Mc Nerney

ME, Siezen CL, Stanislaus DJ, Stewart J, Thompson KE, Tornesi B, Van der Laan JW, Weinbauer GF, Wood S, Piersma AH. Comparison of rat and rabbit embryo\_fetal developmental toxicity data for 379 pharmaceuticals: on the nature and severity of developmental effects. *Crit Rev Toxicol*. 2016 Nov;46(10):900\_910

Theunissen PT, Beken S, Beyer B, Breslin WJ, Cappon GD, Chen CL, Chmielewski G, de Schaeppdrijver L, Enright B, Foreman JE, Harrouk W, Hew KW, Hoberman AM, Y Hui J, Knudsen TB, Laffan SB, Makris SL, Martin M, McNerney ME, Siezen CL, Stanislaus DJ, Stewart J, Thompson KE, Tornesi B, Van der Laan JW, Weinbauer GF, Wood S, Piersma AH. Comparing rat and rabbit embryo\_fetal developmental toxicity data for 379 pharmaceuticals: on systemic dose and developmental effects. *Crit Rev Toxicol*. 2016 Oct 21:1\_13

Bronsveld HK, ter Braak B, Karlstad Ø, Vestergaard P, Starup\_Linde J, Bazelier MT, De Bruin ML, de Boer A, Siezen CL, van de Water B, van der Laan JW, Schmidt MK. Treatment with insulin (analogues) and breast cancer risk in diabetics; a systematic review and meta\_analysis of in vitro, animal and human evidence. *Breast Cancer Res*. 2015 Aug 5;17:100

ter Braak B, Wink S, Koedoot E, Pont C, Siezen C, van der Laan JW, van de Water B. Alternative signaling network activation through different insulin receptor family members caused by pro\_mitogenic antidiabetic insulin analogues in human mammary epithelial cells. *Breast Cancer Res*. 2015 Jul 19;17:97

ter Braak B, Siezen C, Speksnijder EN, Koedoot E, van Steeg H, Salvatori DC, van de Water B, van der Laan JW. Mammary gland tumor promotion by chronic administration of IGF1 and the insulin analogue AspB10 in the p53R270H/+WAPCre mouse model. *Breast Cancer Res*. 17:14\_27, 2015

ter Braak B, Siezen CL, Kannegieter N, Koedoot E, van de Water B, van der Laan JW. Classifying the adverse mitogenic mode of action of insulin analogues using a novel mechanism\_based genetically engineered human breast cancer cell panel. *Arch Toxicol*. 88:953\_66, 2014

Knopperts AP, Nielsen M, Niessen RC, Tops CM, Jorritsma B, Varkevisser J, Wijnen J, Siezen CL, Heine\_Bröring RC, van Kranen HJ, Vos YJ, Westers H, Kampman E, Sijmons RH, Hes FJ. Contribution of bi\_allelic germline MUTYH mutations to early\_onset and familial colorectal cancer and to low number of adenomatous polyps: case\_series and literature review. *Fam Cancer*, 12:43\_50, 2013

Schuurhof A., Bont L., Siezen C.L.E., Hodemaekers H., van Houwelingen H.C., Kimman T.G., Hoebee B., Kimpfen J.L.L. and Jansen R. IL\_9 SNP in infants with respiratory syncytial virus infection: an opposite gender\_specific effect. *Pediatric pulmonology*, 45:608\_13, 2010.

van den Berg S.W., Dolle M.E.T., Imholz S., van der A D.L., van 't Slot R., Wijmenga C., Verschuren W.M.M., Strien C., Siezen C.L.E., Hoebee B., Feskens E.J.M., and Boer J.M.A. Genetic variation in regulatory pathways of fatty acid and glucose metabolism are associated with obesity\_phenotypes: a population based cohort study. *International Journal of Obesity*, 33:1143\_52, 2009.

Siezen C.L.E., Bont L., Hodemaekers H.M., Ermers M.J., Doornbos G., van 't Slot R., Wijmenga C., van Houwelingen H.C., Kimpfen J.L.L., Kimman T.G., Hoebee B., and Janssen R. Genetic susceptibility to RSV bronchiolitis in preterm children is associated with airway remodeling genes and innate immune genes. *Pediatr Infect Dis J*, 28:333\_5, 2009.

van Kranen H.J., and Siezen C.L.E. Arachidonic acid pathway. In Schwab M. (Ed.), *Encyclopedia of Cancer* 2nd edition, Berlin Heidelberg New York: Springer\_Verlag, 230\_235, 2008.

Pot G.K., van Heijningen E.M.B, Geelen A., Siezen C.L.E., van Kranen H.J., and Kampman E. Opposing associations of serum n\_3 and n\_6 polyunsaturated fatty acids with colorectal adenoma risk: an endoscopy\_based case\_control study. *International Journal of Cancer*, 123:1974\_7, 2008.

Doorduyn Y., van Pelt W., Siezen C.L.E., van der Horst F., van Duynhoven Y.T.H.P., Hoebee B., and Janssen R. Novel insight in the association between salmonellosis or campylobacteriosis and chronic illness, and the role of host genetics in susceptibility to these diseases. *Epidemiology and Infection*, 136:1225\_34, 2008.

Banus H.A., Bottema R.W.B., Siezen C.L.E., Vandebriel R.J., Reimerink J., Mommers M., Koppelman G.H., Hoebee B., Thijs C., Postma D.S., Kimman T.G., and Stelma F.F. A Toll\_like receptor 4 polymorphism is associated with the response to whole\_cell pertussis vaccination in children. *Clinical and Vaccine Immunology*, 14:1377\_1380, 2007.

Siezen C.L.E., Janssen R., Bont L., Hodemaekers H.M., Ermers M.J., Doornbos G., van 't Slot R., Wijmenga C., Goeman J.J., Kimpfen J.L.L., van Houwelingen H.C., Kimman T.G., and Hoebee H. Genetic susceptibility to RSV bronchiolitis is predominantly associated with innate immune genes. *Journal of Infectious Disease*, 196:826\_834, 2007.

Siezen C.L.E., Bueno\_de\_Mesquita H.B., Peeters P.H.M., Kram N.R., van Doeselaar M. and van Kranen H.J. Polymorphisms in arachidonic acid pathway genes, fish consumption and the risk of colorectal cancer. *International Journal of Cancer*, 119:297\_303, 2006.

Siezen C.L.E., Tjhuis M.J., Kram N.R., van Soest E.M., de Jong D.J., Fodde R., van Kranen H.J., and Kampman E. Protective effect of nonsteroidal anti\_inflammatory drugs on colorectal tumors is modified by a polymorphism in peroxisome proliferated\_activated receptor δ. *Pharmacogenetics*, 16:43\_50, 2006.

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Busstra M.C., Siezen C.L.E., Grubben M.J.A.L., van Kranen H.J., Nagengast F.M., and van 't Veer P. Tissue levels of fish fatty acids and risk of colorectal adenomas: a case\_control study (Netherlands). *Cancer Causes Control*, 14: 269\_276, 2003.

## Projects

Carcinogenicity of growth factors, research funded by the National Institute of Public Health and Environment, and Medicines Evaluation Board. Co\_promoter for PhD defence of B. ter Braak, 18\_06\_2015 Mechanistic differentiation of nongenotoxic carcinogenic pharmaceuticals and their human relevance, research funded by the Medicines Evaluation Board

Non-clinical development of oligonucleotide therapeutics. Supervision of Master student project of I. el Miloudi, september 2023. Evaluation of non-clinical safety data package as submitted by companies in scientific advice procedures or marketing authorization applications.

## Memberships

Additional expert at the EMA Non-Clinical Working Party

Member of Operational Expert Group (OEG) for Weight of Evidence approach evaluations for carcinogenicity (ICH S1B) at EMA

Regulatory chair of Implementation Working Group (IWG) of ICH S1B addendum

EU representative and topic lead for guideline on on-clinical development of oligonucleotide therapeutics (ICH S13)

Board Member of the National Society of Toxicology (NVT), toxicology of medicines division

## Other Relevant Information