



## Curriculum Vitae

### Personal information **Marcel Maliepaard**

#### Work experience

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1. Employer: CBG
  - Start date: 092013
  - End date: 092016
  - Position: Alternate CMDh member
  - Activities:
  - Country: Netherlands
2. Employer: CBG
  - Start date: 082005
  - End date:
  - Position: Senior Clinical Assessor (PK\_PD)
  - Activities: Focus on pharmacokinetic interactions, pharmacogenetics, pharmacodynamics, bioequivalence. Member of the EMA Pharmacogenomics Working Party (PGWP) Co\_promotor of a PhD project on generic substitution, in collaboration with Maastricht University (Professor C. Neef) and Radboud University Nijmegen Medical Centre (Professor D. Burger).
  - Country: Netherlands
3. Employer: CBG
  - Start date: 022001
  - End date: 072005
  - Position: Clinical Assessor (PK\_PD)
  - Activities: Focus on pharmacokinetic interactions, pharmacogenetics, pharmacodynamics, bioequivalence.
  - Country: Netherlands
4. Employer: Netherlands Cancer Institute
  - Start date: 1996
  - End date: 012001
  - Position: Post\_doctoral Fellow
  - Activities: Main scientific topics at this position: interaction between platinum cytostatics and topoisomerase I inhibitors, the molecular mechanism of resistance against topoisomerase I inhibitors, improvement of the oral bioavailability of cytostatic agents in the clinic. For this purpose expression and modulation of multidrug resistance genes was investigated.
  - Country: Netherlands
5. Employer: Daniel den Hoed Clinic (Rotterdam Cancer Centre)
  - Start date: 1995
  - End date: 1996
  - Position: Post\_doctoral Fellow
  - Activities: Main scientific topics as above, position was continued at the Netherlands Cancer Institute.
  - Country: Netherlands

#### Education and training

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1. Subject: Nijmegen University Medical Centre
  - Start date: 2008
  - End date: 2010
  - Qualification: Degree in Clinical Pharmacology
  - Organisation:
  - Country: Netherlands
2. Subject: Utrecht University
  - Start date: 1990
  - End date: 1994
  - Qualification: PhD in Medicinal Chemistry
  - Organisation:
  - Country: Netherlands
3. Subject: Utrecht University
  - Start date: 1984
  - End date: 1990
  - Qualification: Masters degree in Biochemistry
  - Organisation:
  - Country: Netherlands

#### Additional information

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##### Publications

Audrey M. M. Hermans, Marc Maliepaard, Wouter P. C. Boon and Anna M. G. Pasmooij. Impact of the new European Union In Vitro Diagnostics Regulation on the practice of hospital diagnostic laboratories. *Expert Rev Mol Diagn* 2022. DOI: 10.1080/14737159.2022.2087508 Marc Maliepaard, Wieneke Carree, Marcel T.J.van Bussel. Dose selection and tolerability of anticancer agents evaluated by the European Medicines Agency in the period 2015\_2020. *ESMO Open* 2021; 6(6) doi.org/10.1016/j.esmoop.2021.100301 Pieter J.Glerum, Mert Hayta, David M.Burger, Cees Neef, Marcel L.Bouvy and Marc Maliepaard. Reasons for patients' generic drug switching at the pharmacy counter: a pilot study. *GaBI Journal* 2021 Vol. 10 Issue 3 Pages 119\_122. DOI: 10.5639/gabij.2021.1003.014 Pieter J. Glerum, · Kees Neef, · David M. Burger, · Yang Yu, · Marc Maliepaard. Pharmacokinetics and Generic Drug Switching: A Regulator's View. *Clin Pharmacokinet.* 2020;59(9):1065\_1069. doi: 10.1007/s40262\_020\_00909\_8. Pieter J.

Glerum, Marc Maliepaard, Vincent de Valk, David M. Burger and Kees Neef. Drug switching in the Netherlands: a cohort study of 20 active substances. *BMC Health Serv Res.* 2020;20(1):650. doi: 10.1186/s12913-020-05494-x.

Marc Maliepaard, Timi Toiviainen, Marieke L. De Bruin and Didier Meulendijks. Pharmacogenetic-Pharmacokinetic Interactions in Drug Marketing Authorization Applications via the European Medicines Agency between 2014 and 2017. *Clin Pharmacol Ther.* 2020;108(2):338-349. doi: 10.1002/cpt.1834. Epub 2020 Apr 23 Pieter J. Glerum, Marc Maliepaard, Vincent de Valk, Joep H.G. Scholl, Florence P.A.M. van Hunsel, Eugène P. van Puijtenbroek, David M. Burger and Kees Neef. Quantification of Adverse Drug Reactions Related to Drug Switches in The Netherlands. *Clin Transl Sci.* 2020;13(3):599-607. doi: 10.1111/cts.12746. Epub 2020 Feb 12. Yu Y, Maliepaard M. Comment on "Levothyrox(R) New and Old Formulations: Are they Switchable for Millions of Patients?" *Clin Pharmacokinetic.* 2020;59(2):281-282. doi: 10.1007/s40262-019-00850-5. Maliepaard M, Taams AC, Sung C, Poh J, Yu Y. Ethnicity\_Specific Drug Safety Data in European Medicines Agency Registration Dossiers, European Public Assessment Reports, and European and Singapore Drug Labels: Lost in Translation? *Pharmaceut Med.* 2019;33(5):407-416. doi: 10.1007/s40290-019-00302-2. Koziolok M, Alcaro S, Augustijns P, Basit AW, Grimm M, Hens B, Hoad CL, Jedamzik P, Madla CM, Maliepaard M, Marciani L, Maruca A, Parrott N, Pavek P, Porter CJH, Reppas C, van Riet-Nales D, Rubbens J, Statelova M, Trevaskis NL, Valentova K, Vertzoni M, Cepo DV, Corsetti M. The mechanisms of pharmacokinetic food\_drug interactions \_ a perspective from the UNGAP group. *Eur J Pharm Sci.* 2019;134:31-59. doi: 10.1016/j.ejps.2019.04.003. Yu Y, Maliepaard M. Interchangeability of Generics\_Experiences and Outlook Toward Pharmacokinetics Variability and Generic\_Generic Substitution. *Clin Pharmacol Ther.* 2019;105(2):292-294. doi: 10.1002/cpt.1250. Epub 2018 Nov 20. Glerum PJ, Yu Y, Yamada WM, Neely MN, Maliepaard M, Burger DM, Neef C. Interchangeability of Generic Drugs: A Nonparametric Pharmacokinetic Model of Gabapentin Generic Drugs. *Clin Pharmacol Ther.* 2018 Nov;104(5):966-973. doi: 10.1002/cpt.1023. Epub 2018 Feb 13. Gwaza, L, Gordon, J, Potthast, H, Maliepaard, M, Welink, J, Leufkens, H, Stahl, M, Garcia\_Arieta, A. Assessment of the interchangeability between generics. *GaBi Journal* 2016;5(2): 55-59. Yu, Y, Maliepaard, M. Voor\_ en nadelen generiek middel en spécialité gelijk. CBG heranalyseert negen bio\_equivalentie\_studies met zeven werkzame stoffen." *Pharmaceutisch Weekblad* 2016;151(26): 2. Yu, Y, Teerenstra, S, Neef, C, Burger, D, Maliepaard, M. A comparison of the intrasubject variation in drug exposure between generic and brand\_name drugs: a retrospective analysis of replicate design trials. *Br J Clin Pharmacol.* 2016 Apr;81(4):667-78. doi: 10.1111/bcp.12828. Mifsud, J. Maliepaard, M. Pharmacokinetics and Pharmacogenetics: Bringing the Magic Bullet Closer to Reality. In: *Preventive and Predictive Genetics: Towards Personalised Medicine*, vol 9. Eds Grech, G. Grossman, I. 2015:91-107 Yu Y, Teerenstra S, Neef C, Burger D, Maliepaard M. Investigation into the interchangeability of generic formulations using immunosuppressants and a broad selection of medicines. Yu Y, Teerenstra S, Neef C, Burger D, Maliepaard M. *Eur J Clin Pharmacol.* 2015 Aug;71(8):979-90. doi: 10.1007/s00228-015-1878-z. Epub 2015 Jun 12. Ehmann F, Caneva L, Prasad K, Paulmichl M, Maliepaard M, Llerena A, Ingelman\_Sundberg M, Papaluca\_Amati M. Pharmacogenomic information in drug labels: European Medicines Agency perspective. *Pharmacogenomics* 2013;15(3):201-10. doi: 10.1038/tpj.2014.86. Epub 2015 Feb 24. Yu Y, Teerenstra S, Vanmolktot F, Neef C, Burger D, Maliepaard M. Interchangeability of gabapentin generic formulations in the Netherlands: a comparative bioavailability study. *Clin Pharmacol Ther.* 2013 Oct;94(4):519-24. doi: 10.1038/clpt.2013.108. Epub 2013 May 24. Maliepaard M, Leufkens HGM, Yang Yu. Equivalence of generic medicines in general and immunosuppressants in particular - a regulatory opinion on switching of cyclosporin, tacrolimus and mycophenolate mofetil. *Generics and Biosimilars Initiative Journal (GaBi Journal)* 2013;2:1. Epub ahead of print. DOI: 10.5639/gabij.2013.0202.019 Maliepaard M, Nofziger C, Papaluca M, Zineh I, Uyama Y, Prasad K, Grimstein C, Pacanowski M, Ehmann F, Dossena S, Paulmichl M. Pharmacogenetics in the evaluation of new drugs: a multiregional regulatory perspective. *Nature Reviews Drug Discovery* 2013; 12:103-115. doi: 10.1038/nrd3931. Staab A, Rook E, Maliepaard M, Aarons L, Benson C. Modeling and Simulation in Clinical Pharmacology and Dose Finding. *CPT: Pharmacometrics & Systems Pharmacology* 2013; 2:e29 Paulmichl M, Maliepaard M, Papaluca M, Grimstein C. Regulatory considerations in Pharmacogenomics at EMA and US\_FDA. In: J. S. Bertino, A. Kashuba, J. D. Ma, U. Fuhr and C. L. Devane (Eds): *Pharmacogenomics: an introduction and clinical perspective*. New York. McGraw\_Hill. 2012. 37-46 Brandt ML, Abadie E, Daly A, Dere W, Ethgen D, Goel N, Gouze JN, Ingelman\_Sundberg M, Kaufman JM, Laslop Laurie AD, Maliepaard M, McHale D, Meyer, J, Mitlak B, Paulmichl M, Pirmohamed M, Reginster JY, Rizzoli R, Tsouderos Y, Vonderscher J, Flamion B. Challenges Faced in the Integration of Pharmacogenetics/Genomics into Drug Development. *Journal of Pharmacogenomics & Pharmacoproteomics* 2012; 3 Maliepaard M, van Gelder T. Stelling: generieke immuunsuppressiva zijn veilig en zouden uit kostenoverwegingen moeten worden voorgeschreven. *Nederlands Tijdschrift voor Nefrologie* 2102; 2:20-22. Maliepaard M, Banishki N, Gispen\_de Wied CC, Teerenstra S. Elferink AJ. Interchangeability of generic anti\_epileptic drugs: a quantitative analysis of topiramate and gabapentin. *European Journal Clinical Pharmacology* 2011; 67:1007-1016. Maliepaard M, Hekster YA, Kappelle A, van Puijtenbroek EP, Elferink AJ, Welink J, Gispen\_de Wieden CC, Lekkerkerker JFF. Requirements for generic anti\_epileptic medicines: a regulatory perspective. *Journal of Neurology* 2009;256:1966-1971. Versantvoort CHM, Maliepaard M, Lekkerkerker JFF. Generics: what is the role of registration Authorities. *The Netherlands Journal of Medicine* 2008; 66:62-66. Maliepaard M, Hekster YA, Kappelle A, van Puijtenbroek EP, Elferink AJ, Welink J, Gispen\_de Wieden CC, Lekkerkerker JFF. Eisen van het College ter Beoordeling van Geneesmiddelen aan generieke anti\_epileptica. *Tijdschrift voor Neurologie en Neurochirurgie* 2008;109:34-40 Maliepaard M, Lekkerkerker F. Geen reden tot onderscheid. Een Babylonische spraakverwarring. *Pharmaceutisch Weekblad* 2006; 20: 667. Maliepaard M, Lekkerkerker F. Een Babylonische spraakverwarring. CBG over het verschil tussen generieke uitwisseling en generieke substitutie. *Lekkerkerker Weekblad* 2006; 15: 516-517. Maliepaard M, Lekkerkerker F. Rapportage farmacokinetische interacties toegenomen. *Pharmaceutisch Weekblad* 2006; 41: 1296-1297. Cummings J, Zelcer N, Allen JD, Yao D, Boyd G, Maliepaard M, Friedberg TH, Smyth JF, Jodrell DI. Glucuronidation as a mechanism of intrinsic drug resistance in colon cancer cells: contribution of drug transport proteins. *Biochemical Pharmacology* 2004;67: 31-39. Crul M, Schoemaker NE, Pluim D, Maliepaard M, Underberg RW, Schot M, Sparidans RW, Baas P, Beijnen JH, Van Zandwijk N, Schellens JH. Randomized phase I clinical and pharmacologic study of weekly versus twice\_weekly dose\_intensive cisplatin and gemcitabine in patients with advanced non\_small cell lung cancer. *Clinical Cancer Research* 2003;9: 3526-3533. Schellens JH, Planting AS, van Zandwijk N, Ma J, Maliepaard M, van der Burg ME, de Boer\_Dennert M, Brouwer E, van der Gaast A, van den Bent MJ, Verweij J. Adaptive inpatient dose escalation of cisplatin in combination with low\_dose vp16 in patients with nonsmall cell lung cancer. *British Journal of Cancer* 2003;88:814-821. Diestra JE, Scheffer GL, Catala I, Maliepaard M, Schellens JH, Scheper RJ, Germa\_Lluch JR, Izquierdo MA. Frequent expression of the multi\_drug resistance\_associated protein BCRP/MXR/ABCP/ABCG2 in human tumours detected by the BXP\_21 monoclonal antibody in paraffin\_embedded material. *Journal of Pathology* 2002;198: 213-219. van Hattum AH, Hoogsteen IJ, Schluper HM, Maliepaard M, Scheffer GL, Scheper J, Kohlhaagen G, Pommier Y, Pinedo HM, Boven E. Induction of breast cancer resistance protein by the camptothecin derivative X\_8951f is associated with minor reduction of antitumour activity. *British Journal of Cancer* 2002;87: 665-672. Faneyte IF, Kristel PM, Maliepaard M, Scheffer GL, Scheper RJ, Schellens JH, van de Vijver MJ. 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Maliepaard M, Scheffer GL, Faneyte IF, van Gastelen MA, Pijnenborg AC, Schinkel AH, van De Vijver MJ, Scheper RJ, Schellens JH. Subcellular localization and distribution of the breast cancer resistance protein transporter in normal human tissues. *Cancer Research*, 2001, 61, 3458-3464. Erlichman C, Boerner SA, Hallgren CG, Spiekler R, Wang XY, James CD, Scheffer GL, Maliepaard M, Ross DD, Bibe KC, Kaufmann SH. The HER tyrosine kinase inhibitor CI1033 enhances cytotoxicity of 7\_ethyl\_10\_hydroxycamptothecin and topotecan by inhibiting breast cancer resistance protein\_mediated drug efflux. *Cancer Research* 2001;61:739-748. Maliepaard M, van Gastelen MA, Tohgo A, Hausheer FH, van Waardenburg RC, de Jong LA, Pluim D, Beijnen JH, Schellens JH. Circumvention of breast cancer resistance protein (BCRP)\_mediated resistance to camptothecins in vitro using non\_substrate drugs or the BCRP inhibitor GF120918. *Clinical Cancer Research* 2001, 7, 935-941. Schellens JH, Maliepaard M, Scheper RJ, Scheffer GL, Jonker JW, Smit JW, Beijnen JH, Schinkel AH. Transport of topoisomerase I inhibitors by the breast cancer resistance protein. Potential clinical implications. *Annals of the New York Academy of Sciences* 2000; 922:188-194. J.W. Jonker, J.W. Smit, R.F. Brinkhuis, M. Maliepaard,

J.H. Beijnen, J.H.M. Schellens, and A.H. Schinkel. Role of Breast Cancer Resistance Protein in the bioavailability and fetal penetration of topotecan. *Journal of the National Cancer Institute*, 2000, 92, 1651\_1656. G.L. Scheffer, M. Maliepaard, A.C.L.M. Pijnenborg, M.A. van Gastelen, M.C. de Jong, A.B. Schroeijers, D.M. van der Kolk, P. van der Valk, J.D. Allen, D.D. Ross, W.S. Dalton, J.H.M. Schellens, and R.J. Scheper. Breast Cancer Resistance Protein is localized at the plasma membrane in mitoxantrone and topotecan resistant cell lines. *Cancer Research*, 2000, 60, 2589\_2593. M. Maliepaard, M.A. van Gastelen, L.A. de Jong, D. Pluim, R.C.A.M. van Waardenburg, M.C. Ruevekamp\_Helmers, B.G.J. Floot, and J.H.M. Schellens. Overexpression of the BCRP/MXR/ABCP gene in a topotecan\_selected ovarian tumor cell line. *Cancer Research*, 1999, 59, 4559\_4563. D. Pluim, M. Maliepaard, R.C.A.M. van Waardenburg, J.H. Beijnen, and J.H.M. Schellens. 32P\_postlabeling assay for the quantification of the major platinum\_DNA adducts. *Analytical Biochemistry*, 1999, 275, 30\_38. M. de Graaff, M. Maliepaard, D. Pluim, B.J.G. Floot, I.C.E. Slaper\_Cortenbach, and J.H.M. Schellens. In vitro antagonistic cytotoxic interactions between platinum drugs and taxanes on bone marrow progenitor cell CFU\_GM. *Anticancer Drugs* 10, 1999, 213\_218. J. Ma, M. Maliepaard, K. Nooter, W.J. Loos, H.J. Kolker, J. Verweij, G. Stoter, and J.H.M. Schellens. Reduced cellular accumulation of topotecan: a novel mechanism of resistance in a human ovarian cancer cell line. *British Journal of Cancer* 77, 1998, 1645\_1652. J. Ma, M. Maliepaard, K. Nooter, A.W.M. Boersma, J. Verweij, G. Stoter, and J.H.M. Schellens. Synergistic cytotoxicity of cisplatin and topotecan or SN\_38 in a panel of 8 solid tumour cell lines in vitro. *Cancer Chemotherapy and Pharmacology* 41, 1998, 307\_316. J. Ma, M. Maliepaard, H.J. Kolker, J. Verweij, and J.H.M. Schellens. Abrogated energy\_dependent uptake of cisplatin in a cisplatin\_resistant subline of the human ovarian cancer cell line IGROV\_1. *Cancer Chemotherapy and Pharmacology* 41, 1998, 186\_192. J.H.M. Schellens, W.W. ten Bokkel\_Huinink, R. Dubbelman, M. Maliepaard, S. Rodenhuis, and J.H. Beijnen. *Klinische Farmacologie: kinetiek en dynamiek in onderzoek en opleiding*. *Pharmaceutisch Weekblad* 133, 1998, 151\_153. J.H.M. Schellens, M. Maliepaard, A.S.T. Planting, M. de Boer\_Dennert, E.H. Cox, A. de Vos, J. ter Steeg, G. Stoter, J. Verweij. Population pharmacokinetics and limited sampling model (LSM) of cisplatin *Proceedings of ASCO* 1997, 16, 206. M. Crul, J.H.M. Schellens, J.H. Beijnen, and M. Maliepaard. Cisplatin resistance and DNA repair. *Cancer Treatment Reviews* 23, 1997, 341\_366. M.J.P. Welters, M. Maliepaard, A.J. Jacobs\_Bergmans, R.A. Baan, J.H.M. Schellens, J. Ma, W.J.F. van der Vijgh, B.J.M. Braakhuis, and A.M.J. Fichtinger\_Schepman. Improved 32P\_postlabelling assay for the quantification of the major platinum\_DNA adducts. *Carcinogenesis* 18, 1997, 1767\_1774. M. Maliepaard, N.J. de Mol, M. Tomasz, D. Gargiulo, L.H.M. Janssen, J.P.M. van Duynhoven, E.J.J. van Velzen, W. Verboom, and D.N. Reinhoudt. Mitosene\_DNA adducts. Characterization of two major DNA mono\_adducts formed by 1,10\_bisacetoxymitosene upon reductive activation. *Biochemistry* 36, 1997, 1767\_1774. M. Maliepaard. Mitosenes and related antitumor drugs: rational design of cytostatic agents. Austin, Texas, USA: R.G. Landes Company, 1996. J.H.M. Schellens, J. Ma, A.S.T. Planting, M. Maliepaard, M. de Boer\_Dennert, M.E.L. van der Burg, M. Hartevelde, G. Stoter, J. Verweij. Adaptive intrapatient dose\_escalation of cisplatin. *Proceedings of ASCO* 1996, 15, 178. M. Maliepaard, S.E. Groot, N.J. de Mol, L.H.M. Janssen, M. Freriks, W. Verboom, D.N. Reinhoudt, M. Stephens, and I.J. Stratford. Chirality of a 1,10\_bisacetoxymitosene compound. Impact on reductive activation, DNA interstrand cross\_linking, and antitumor activity. *Anti\_Cancer Drug Design* 11, 1996, 403\_413. M. Maliepaard, A. Wolfs, S.E. Groot, N.J. de Mol, and L.H.M. Janssen. Indoloquinone EO9: DNA interstrand cross\_linking upon reduction by DT\_diaphorase or xanthine oxidase. *British Journal of Cancer* 71, 1995, 836\_839. M. Maliepaard, N.J. de Mol, L.H.M. Janssen, A.R. Goeptar, J.M. te Koppele, N.P.E. Vermeulen, W. Verboom, and D.N. Reinhoudt. Reduction of antitumor mitosenes in non\_aqueous and aqueous environment. An electron spin resonance and cyclic voltammetry study. *Free Radical Research* 22, 1995, 109\_121. M. Maliepaard, C.A.M.C. Sitters, N.J. de Mol, L.H.M. Janssen, I.J. Stratford, M. Stephens, W. Verboom, and D.N. Reinhoudt. Potential antitumor mitosenes: Relationship between in vitro DNA interstrand cross\_link formation and DNA damage in *Escherichia coli* K\_12 strains. *Biochemical Pharmacology* 48, 1994, 1371\_1377. M. Maliepaard, N.J. de Mol, L.H.M. Janssen, J.C. Hoogvliet, W. van der Neut, W. Verboom, and D.N. Reinhoudt. Reductive activation of potential antitumor mitosene compounds. *Journal of Medicinal Chemistry* 36, 1993, 2091\_2097. F.A. de Wolf, M. Maliepaard, F. van Dorsten, I. Berghuis, K. Nicolay, and B. de Kruijff. Comparable interaction of doxorubicin with various acidic phospholipids results in changes of lipid order and dynamics. *Biochimica et Biophysica Acta* 1096, 1991, 67\_80.

#### Projects

Co\_promotor of two PhD projects on generic substitution (regulatory science), in collaboration with Maastricht University (Professor C. Neef) and Radboud University Nijmegen Medical Centre (Professor D. Burger)

#### Memberships

#### Other Relevant Information