

Appendix to Zofran MDL PSC's Presentation to FDA Regarding Japanese Animal Studies
- Responsive to GSK's 2019 Citizen Petition

<u>Tab –</u>	
P1.	1985 – WPT85084 – Preliminary Rat Oral R10564
P2.	1988 - WBP88037 - Placental transfer in pregnant NZW rabbit oral
P3.	1988 - WBP88038 - Placental transfer in pregnant Dutch rabbit I.V.
P4.	1988 - WBP88039 - Placental transfer in pregnant rat oral
P5.	1991- FDA Medical Officer Review, including Pharmacology Review
P6.	1993 - ICH S5R2 Guidelines on Detection of Toxicity to Reproduction for Medicinal Products
P7.	1993.12.23 - GSK Ltr. to FDA re Japanese Studies
P8.	2002 - GSK Internal Document Excerpt re Bradycardia and Malformations
P9.	2008 - EMA Guideline on Risk Assessment of Medicinal Products on Human Reproduction
P10.	2008.11.11 - GSK GLC Label Recommendation – Zofran and hERG
P11.	2011 - FDA Guidance on Reproductive and Developmental Toxicities
P12.	2012 - C. Danielsson et al, K- Channel Block as a Common Teratogenic Mechanism
P13.	2014.10.29 - FDA Request for Full Details Cover Letter – ZFN00352064
P14.	2014.10.29 - FDA Request for Full Details - ZFN00352065
P15.	2015.03.03 - GSK Response re Full Details - ZOFNDAB0154694
P16.	2015.03.27 - S5 R3 Final Concept Paper – Detection of Toxicity to Reproduction
P17.	2015.04.21 - GSK internal comments on Zofran animal studies v10
P18.	2016.05.16 - FDA Correspondence with Novartis re Zofran Labeling
P19.	2017 - ICH S5R3 Detection of Toxicity to Reproduction for Human Pharmaceuticals
P20.	2017.06.28 - Deposition of Derek Newall, Ph.D. Excerpts
P21.	2017.08.03 - Deposition of Dinesh Stanislaus, Ph.D. Excerpts
P22.	2018.03.28 - Deposition of Patrick Weir, Ph.D. Excerpts
P23.	2018.07.05 - Bengt Danielsson, MD Ph.D. Expert Report
P24.	2018.08.24 - Danielsson, Webster and Ritchie - J. Reproductive Toxicology
P25.	2018.08.26 - Brian Harvey, MD Declaration and Expert Report
P26.	2018.08.27 - Bengt Danielsson, MD, Ph.D. Rebuttal Expert Report
P27.	2018.10.12 - Deposition of Bengt Danielsson, MD, Ph.D.
P28.	2018.10.29 - Deposition of Raymond York, Ph.D. - Excerpts
P29.	2019.07.11 - EMA (PRAC) Updated Signal Assessment – Ondansetron “Studies in animals have shown reproductive toxicity”
P30.	2020 - ICH S5R3 Guideline on Detection of Reproductive Toxicity

Additional Documents Referenced in Zofran MDL PSC's March 30, 2020 Presentation to FDA – (Documents Already Submitted to FDA in Appendix to GSK Citizen Petition)

Citizen Petition Appendix Tab	Document Title
18.	NTX/90/006: Reproduction Study on GR38032F (SN-307) in rats by oral administration during the period of organogenesis (Study No. 100422) (ZOFNDAA0002496).
19.	NTX/91/001: Reproduction Study on GR38032F (SN-307) in rats by intravenous administration during the period of organogenesis (Study No. 100424) (ZFN00077547).
20.	NTX/90/009: Reproduction Study (Seg II) on GR38032F (SN-307) in rabbits by oral route. (Study No. 100441) (ZFN00077391).
21.	NTX/95/009: Reproduction Study on GR38032F (SN307) in Rats by Intravenous Administration Prior to and during the Early Stage of Pregnancy (TRL Study No. 100425). (ZFN00077788-951)
22.	NTX/88/004: GR38032F (SN-307): Preliminary study for the reproduction study in rats by oral administration during the period of fetal organogenesis (Seg. II) (Study No. 100421). (ZFN00076968-029)
23.	NTX/88/005: GR38032F (SN-307): Preliminary study for the reproduction study in rats by intravenous administration during the period of fetal organogenesis (Seg. II) (Study No. 100423). (ZFN00077030-90)
24.	NTX/89/001: GR38032F: Preliminary study for the reproduction study in rabbits by oral administration during the period of fetal organogenesis (I) (Study No. T-881001). (ZFN00077091-113)
25.	NTX/89/002: GR38032F (SN-307): Preliminary study for the reproduction study in rabbits by oral administration during the period of fetal organogenesis (II). (Study No. T-881002). (ZFN00077114-145)
26.	Danielsson B, Webster WS, Ritchie HE. Ondansetron and teratogenicity in rats: evidence for a mechanism mediated via embryonic hERG blockade. Reprod Toxicol 2018;81:237-245.
35.	WPT/84/150: GR38032B: Effect of oral administration on pregnant AHA rats and their progeny (Study No. R10590). (ZOFNDAA0010051)
36.	WPT/86/021: GR38032F: Effects of intravenous administration on pregnant AHA rats and their progeny. (Study No. R10937) (ZOFNDAA0009774)
37.	WPT/85/031: GR38032B: Effects of oral administration on pregnant New Zealand white rabbits and their progeny. (Study No. L10649) (ZOFNDAA0010471)
38.	WPT/85/145: GR38032F: Effects of intravenous administration on pregnant Dutch rabbits and their progeny. (Study No. L10873) (ZOFNDAA0010274)