### Additional File 3. Summary of *ex vivo* and *in vitro* studies showing the effect of PCCs on NOAC-induced coagulation (January 2013–February 2017)

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| Study citation | NOAC | PCC | Laboratory parameters tested | Reversal of NOAC effects with PCC |
| *ex vivo* studies using samples from NOAC-treated patients  |
| Khoo *et al*. 2013 | Dabigatran | aPCC (FEIBA®) | TGA parameters: peak TG, lag time, ETP | (+) |
| Herrmann *et al*. 2014 | Dabigatran | 3F‑PCC (Prothrombinex®) or aPCC (FEIBA®) | aPTT and TCTPTCAT parameters: lag time, ETP and peak | (+) with both PCCs(+) with aPCC only(+) with both PCCs |
| Rivaroxaban | PT aPTT TCT CAT parameters: lag time, ETP and peak | (+) with both PCCs(+) with aPCC only(+) with 3F-PCC only(+) with both PCCs |
| Schenk *et al*. 2016 | Rivaroxaban | 4F-PCC (Beriplex®) or aPCC (FEIBA®) | TEM parameters: CTTGA parameters: * ETP
* Peak
* Lag time
 | (+) with both PCCs, aPCC > 4F-PCC (reagent dependent)(+) with both PCCs, aPCC > 4F-PCC(+) with both PCCs, 4F-PCC > aPCC(+) with both PCCs, aPCC > 4F-PCC |
| Schultz *et al*. 2017 | Rivaroxaban | 4F-PCC (Cofact®) or aPCC (FEIBA®) | TGA parameters: lag time, peak, velocity index, ETPTEM parameters: CT, CFT, MCF, maximum velocity, AUC | (+) with both PCCs, aPCC > 4F-PCC (no significant effect on lag time with PCC)(+) with both PCCs, aPCC > 4F-PCC (no effect on MCF, maximum velocity and AUC) |
| *ex vivo* study using samples from NOAC-dosed healthy volunteers |
| Arellano-Rodrigo *et al*. 2015 | Dabigatran | 4F‑PCC (Beriplex®) or aPCC (FEIBA®) | PT aPTT TGA parameters: lag time, ETP, peak, time to peakTEM parameters: CT, CFT and MCF  | Partial with both PCCs(+) with aPCC only(+) with both PCCs(+) with aPCC only *(no effect on CFT)* |
| Rivaroxaban | PT aPTT TGA parameters: lag time, ETP, peak, time to peakTEM parameters: CT, CFT and MCF  | (+) with aPCC; partial with 4F-PCC(+) with aPCC only(+) with aPCC; lag time and ETP only with 4F-PCC(+) with both PCCs |
| *in vitro* studies using samples from healthy volunteers |
| Solbeck *et al*. 2014a | Dabigatran | 4F-PCC (Octaplex®) | TEG parameters  | (‒) |
| Solbeck *et al*. 2014b | Dabigatran | 4F-PCC (Octaplex®) | Sonoclot parameters | (‒) |
| Lindahl *et al*. 2015 | Dabigatran | 4F-PCC (Cofact®) or aPCC (FEIBA®) | CT Initial rate of clot growth | (+) with aPCC only(‒) |
| Perzborn *et al*. 2014 | Rivaroxaban | 4F-PCC (Beriplex®) or aPCC (FEIBA®) | PT CT TGA parameters:* ETP
* Lag time
* Peak
 | (+) with both PCCs, aPCC > 4F-PCCPartial with aPCC only(+) with both PCCs, aPCC > 4F-PCCPartial with both PCCs, aPCC > 4F-PCCPartial with aPCC only |
| Escolar *et al*. 2015 | Rivaroxaban | 4F-PCC (Beriplex®) or aPCC (FEIBA®) | TGA parameters TEM parameters: CT, CFT and MCF  | (+) with both PCCs, aPCC > 4F-PCC(+) with both PCCs, aPCC > 4F-PCC |
| Körber *et al*. 2014 | Rivaroxaban | 4F-PCC (Octaplex®) | CT, aPTT, PT ratio, PT | (‒) |
| Körber *et al*. 2016 | Rivaroxaban | 4F-PCC (Octaplex®) or aPCC (FEIBA®) | CTaPTTPT ratioPT | (+) (significant effect dose-dependent with 4F-PCC)(+)(+) with aPCC only (+) with aPCC only |
| Dinkelaar *et al*. 2013 | Rivaroxaban | 4F-PCC (Cofact®) | ETP, peakPT, lag time | (+) (in whole blood CAT)(‒) |
| Nagakari *et al*. 2017 | Rivaroxaban, edoxaban or apixaban | 4F-PCC (PPSB-HT®) or aPCC | PT | (+) |
| Iba *et al*. 2016 | Edoxaban | 4F-PCC (PPSB-HT®) or aPCC | PT | (+)  |
| Halim *et al*. 2014 | Edoxaban | aPCC (FEIBA®) | PT and aPTT | (+) |
| Escolar *et al*. 2013 | Apixaban | 4F-PCC (Beriplex®) or aPCC (FEIBA®) | TGA parameters: * Lag phase, peak (phospholipid reagent)
* Time to peak, peak (TF and phospholipid reagent)

TEM parameters: CT, CFT, MCF  | (+) with both PCCs(+) with aPCC only(+) with aPCC; significant effect only observed for MCF with 4F-PCC |
| Martin *et al*. 2015 | Apixaban | 4F-PCC (Kanokad®) or aPCC (FEIBA®) | TGA parameters * ETP
* Lag time
* Peak height

PT aPTT Fibrin polymerisation kinetics TEM parameters  | (+) with both PCCs, aPCC > 4F-PCC(+) with 4F-PCC, overcorrection with aPCC(+) with aPCC only(+) with both PCCs(+) with both PCCsPartial with aPCC only(+) with aPCC onlyPartial with aPCC only *(no effect on MCF)* |
| Dinkelaar *et al*. 2014 | Apixaban | 4F-PCC (Cofact®) | PT ETP TEG parametersaPTT, peak, lag time | (+)(+)Partial for pooled plasma (no effect on whole blood TEG parameters)(‒) |
| Dabigatran | PT ETP Peak TG Whole blood TEG parameters aPTT, lag time  | Partial(+)(+)(+) dependent on reagent used for whole blood *(no effect on pooled plasma TEG parameters)*(‒) |

(‒), negative result; (+), positive result.

3F-PCC, three-factor prothrombin complex concentrate; 4F-PCC, four-factor prothrombin complex concentrate; aPCC, activated prothrombin complex concentrate; aPTT, activated partial thromboplastin time; AUC, area under the curve; CAT, calibrated automated thrombogram; CFT, clot formation time; CT, clotting time; ETP, endogenous thrombin potential; MCF, maximum clot firmness; PT, prothrombin time; TCT, thrombin clotting time; TEG, thromboelastography; TF, tissue factor; TG, thrombin generation; TGA, thrombin generation assay; TT, thrombin time; TEM, thromboelastometry.