SUPPLEMENTAL DATA

"Increases in levels of epoxyeicosatrienoic and dihydroxyeicosatrienoic acids (EETs and DHETs) in liver and heart *in vivo* by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and in hepatic EET:DHET ratios by cotreatment with TCDD and the soluble epoxide hydrolase inhibitor AUDA"

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Drug Metabolism and Disposition

Supplemental Figure Legends

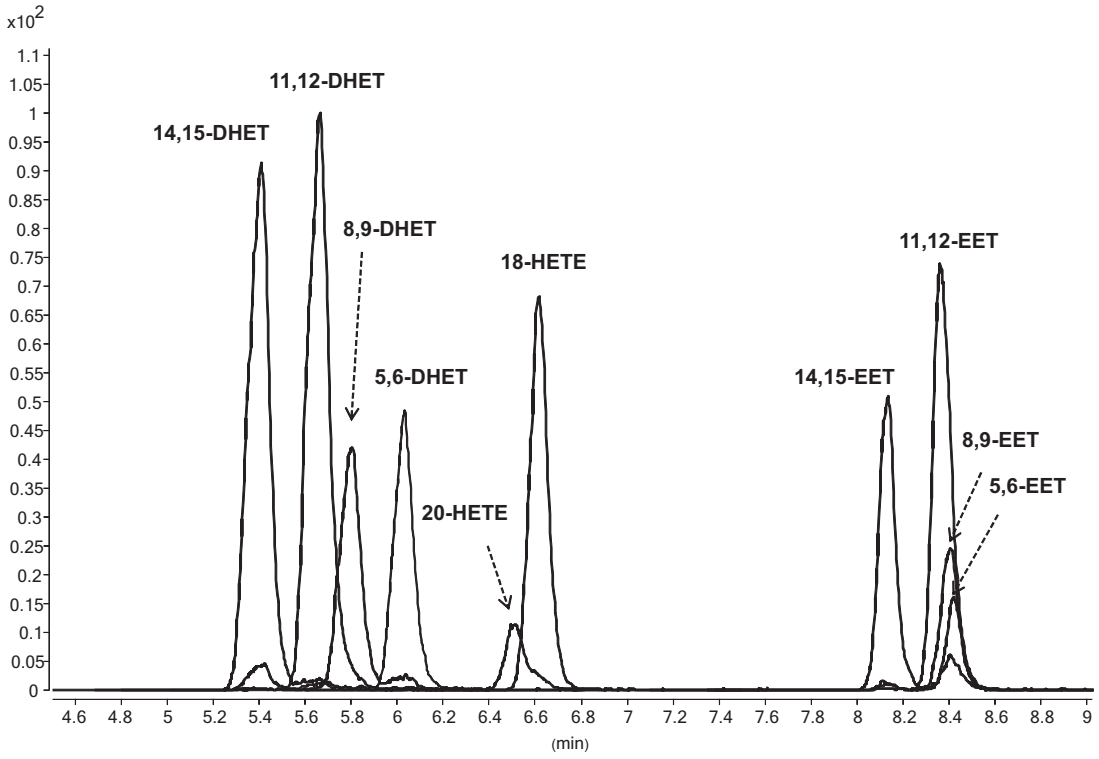
Supplemental Figure1. A. LC–MS/MS analysis of a mixture of standards for DHETs (*m/z* =337; 640 ng/ml); EETs (*m/z* 319; 1,600 ng/ml) and HETEs (*m/z* =319; 640 ng/ml). A mixture containing ten standards was separated using an Agilent SB-Aq 2.1X100 mm 1.8uM C18 column, as described in Material and Methods. The mass spectrometer was operated in the dynamic MRM mode. MRM transitions from parent to product ions were as follows: from *m/z* 337 to *m/z* 207 (14,15-DHET), to 167 (11,12-DHET), to 127 (8,9-DHET), and to 145 (5,6-DHET); from *m/z* 319 to *m/z* 245 (20-HETE), to 261 (18-HETE), to 219 (14,15-EET), to 167 (11,12-EET), to 69 (8,9-EET), and to 191 (5,6-EET). The small peaks at 5.4 and 6.1 min accompanied the MRM transition for 8,9-DHET and the peak at 8.4 min, the MRM transition for 14,15-EET, and were considered non-specific. **B.** and **C.** Representative MRM chromatograms showing detection of EETs, DHETs and HETEs in samples from control (dotted lines) and

TCDD treated CE (solid lines) from liver (**B**) and heart (**C)**. Arrows point to the specific target compounds when multiple peaks were obtained. For C, 8,9- and 14,15-EETs were not reliably identifiable (S/N<3). The peak for 11,12-EET could be identified but was not quantifiable (S/N<10). For **A.-C.** the y-axis shows ion abundance.

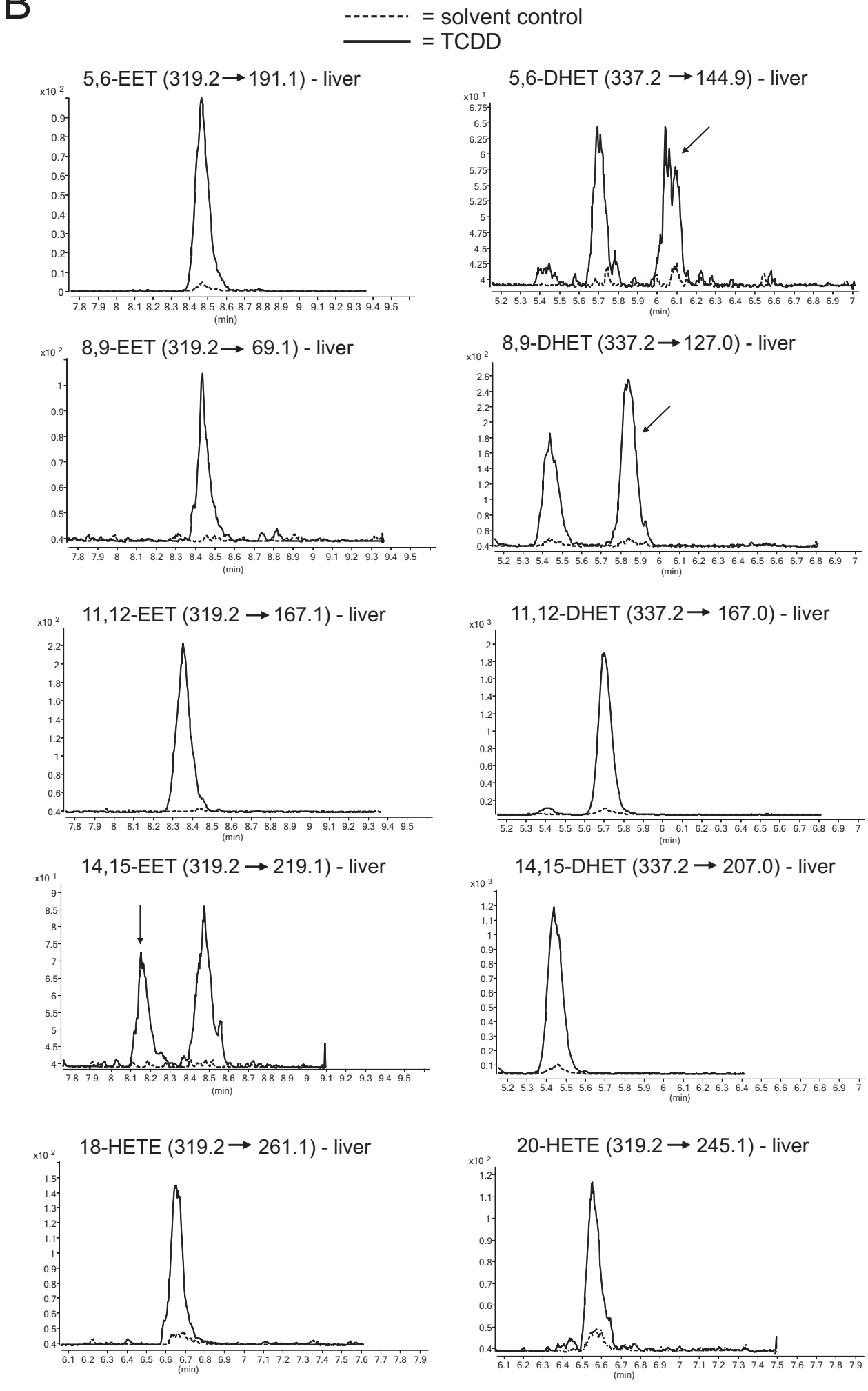
Supplemental Figure 2. *Upper panel*: Scatter plot showing peak areas for 11,12-EET_{d11} from MRM chromatograms (MRM transition from *m/z* 330 to *m/z* 167) in replicate standards (left panel) containing 11,12-EET_{d11} (10 ng/50 µl) (n=12) or liver samples (right panels) spiked with the same amount of 11,12-EET_{d11} and followed by acetonitrile extraction (n=10 individual livers). Means ± SE are also shown. *Lower panels:* Representative MRM chromatograms for 11,12-EET_{d11} in standard (left) and spiked liver samples (right). Peak areas are shown above the peaks.

Supplemental Figure 1

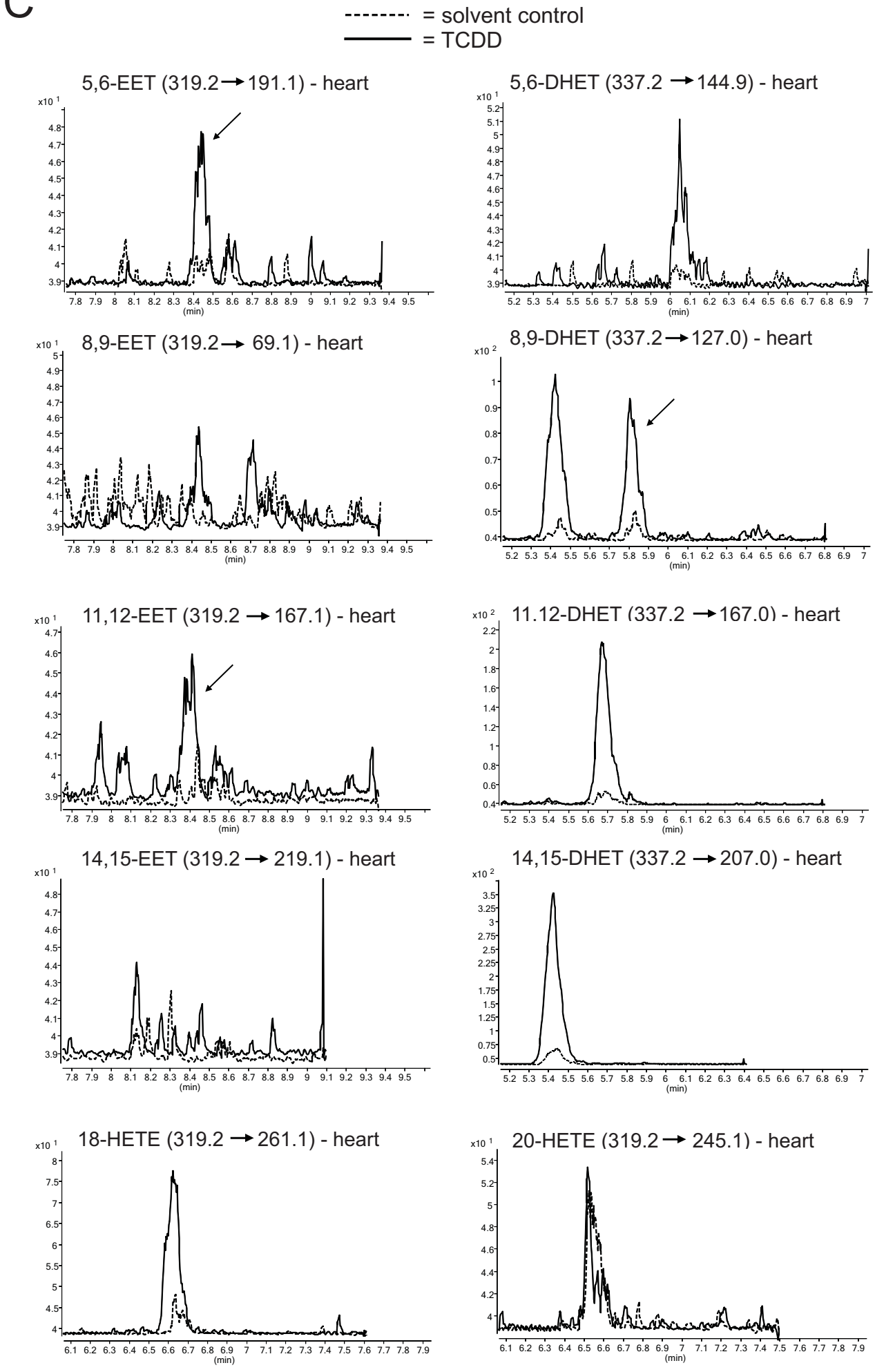
A



B


= solvent control
= TCDD
5,6-EET (319.2→191.1) - liver
5,6-DHET (337.2 →144.9) - liver
8,9-EET (319.2→ 69.1) - liver
8,9-DHET (337.2→127.0) - liver
11,12-EET (319.2 → 167.1) - liver
11,12-DHET (337.2→ 167.0) - liver
14,15-EET (319.2 → 219.1) - liver
14,15-DHET (337.2 → 207.0) - liver
18-HETE (319.2→ 261.1) - liver
20-HETE (319.2 → 245.1) - liver
(min)

C


= solvent control
= TCDD
5,6-EET (319.2→191.1) - heart
5,6-DHET (337.2 →144.9) - heart
8,9-EET (319.2→ 69.1) - heart
8,9-DHET (337.2→127.0) - heart
11,12-EET (319.2 → 167.1) - heart
11.12-DHET (337.2 →167.0) - heart
14,15-EET (319.2 → 219.1) - heart
14,15-DHET (337.2 →207.0) - heart
18-HETE (319.2 → 261.1) - heart
20-HETE (319.2→ 245.1) - heart
(min)

Supplemental Figure 2