Introduction: Analysis of dioxins and furans requires highest selectivity and sensitivity in GC-MS. Combined with increased sample size preparation techniques the required lowest detection limits can be achieved routinely for most matrices, such as feed and food. However, extreme small sample sizes as in bio-monitoring of contaminants in infant dried blood spots with sample volumes as small as 20-100 uL represent a unique challenge. Current routine analysis techniques do not achieve the required instrument sensitivity. However, large archives of dried blood spot samples exist in hospitals globally. These samples - routinely collected from children at birth in many countries - present an invaluable resource for epidemiological studies of population background exposure to dioxins and other contaminants and are consequently of highest toxicological interest. In this study a novel GC signal enhancement tool was investigated for lowest level Dioxin analysis in human serum samples: time controlled cryogenic zone compression (t-CZC) coupled to high resolution GC-MS. CZC in combination with high resolution GC-MS was first described by Patterson et al. [1]. In CZC analytes eluting from the first column dimension are trapped completely in one event maximizing the signal enhancement effect as known from GCxGC. Patterson et al. achieved this effect by using single short columns attached to a cryogenic GCxGC modulator combined with long modulation times. Their method was refined here into timed controlled CZC, which basically consists in time controlled switching of a single cryogenic modulator jet. In this way CZC is simplified and flexibility is strongly increased, e.g. allowing the use of standard GC columns. Results and discussion: CZC relevant parameters were investigated and optimized in order to achieve maximum sensitivity and targeted refocusing of selected analytes within a GC analysis run. In all experiments, for standards and for real sample extracts, the CZC signal enhancement effect could be seen unambiguously with peak heights increasing inversely in function of the peak width, e.g. 2378-TCDD in standard analysis with peaks of 9-10 sec baseline peak width vers. 600-700 ms and thus more than 10 fold increased peak height in CZC. A number of real serum samples with different target analyte concentrations was analyzed and compared to standard analysis conditions. Down to 500 ag/ul 2378-TCDD could be detected in standards under optimized conditions. Although further optimisation is required; combining time controlled CZC with the sensitive and selective detection of high resolution mass spectrometry seems to be a promising approach to push absolute instrumental detection limits to the very low femtogram range and potentially further down into the attogram range for specific POPs including 2378-TCDD. Reference: 1. Patterson DG, Welch SM, Turner WE, Sjödin A, Focant JF; (2011) J. of Chromatography A, 1218, 3274-3281