It is difficult to evaluate nanomaterials potential toxicity and to make science-based societal choices. To better assess potential hepatotoxicity issues, human liver HepG2 cells were exposed to four TiO_2 and two CeO_2 nanomaterials at 30 ug ml^{-1} for three days with dry mean primary particle sizes ranging from 8 to 142 nm. Two nanomaterials were also run at 3 ug ml^{-1}. A metabolomics study was then performed using three mass spectroscopy dependent platforms (LC and GC). Five of the six nanomaterials strongly reduced glutathione concentration. The two strongest effects were from exposures to a TiO_2 (59 nm) and a CeO_2 (8 nm), both from NanoAmor. The decreases in the GSH system were observed in (a) GSH precursors (glutamate and cysteine), (b) GSH itself and (c) GSH metabolites (the gamma-glutamyl condensation products with glutamate, glutamine, alanine, valine and also 5-oxoproline and cysteine–GSH). The glutathione decreases were the largest decreases seen among the 265 biochemical metabolites determined and is consistent with nanomaterials acting *via* an oxidative stress mode of action. CeO_2, but not TiO_2, increased asymmetric dimethylarginine concentration and thus possible decreases in iNOS activity and NO concentration could result. One CeO_2 (8 nm from NanoAmor) increased concentrations of many lipids, particularly fatty acids. Similar statistically significant elevations were seen in several other classes of lipids (lysolipid, monoacylglycerol, diacylglycerol and sphingolipid) but not in all classes of lipids (glycerolipid, carnitine and fatty acid dicarboxylate). None of the other 5 nanomaterials had this lipid effect. Thus, metabolomic analysis of nanomaterial treated HepG2 cells revealed several previously unknown biochemical effects.