

3. BACKGROUND OF THE DPP 3-1
3.1 Discontinuation of the Troglitazone Pharmacological Intervention..... 3-1

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See the DPP Protocol Section 3 for the background of the DPP including the prevalence of type 2 diabetes and IGT, morbidity and mortality, risk factors for type 2 diabetes and IGT, progression of IGT to type 2 diabetes, etiology, IGT and macrovascular disease, interventions that may decrease progression from IGT to type 2 diabetes and the rationale for the study.

3.1 Discontinuation of the Troglitazone Pharmacological Intervention

Randomization to the troglitazone pharmacological intervention was suspended on May 27, 1998, and discontinued by the NIDDK on June 3, 1998. The NIDDK, with input from the DPP Data Monitoring Board, decided to discontinue use of troglitazone in the DPP based on the following: Associated with troglitazone use in the DPP, there is an increased risk of liver toxicity resulting in serum ALT levels greater than or equal to 8 times the upper limit of normal. In the DPP, there has been one case of hepatic failure requiring liver transplantation. Within the context of this research trial, safety monitoring, even if intensified, is not likely to eliminate the risk. It is also too early in the trial to estimate reliably and compare the absolute risk or benefit of continuing troglitazone in this study population. We are not willing to continue to study a drug for the purpose and benefit of preventing progression from impaired glucose tolerance to diabetes when the drug has demonstrated liver toxicity with hepatic failure.

Participants randomized to troglitazone prior to May 27, 1998, were unmasked to their intervention assignment and monitored to ensure that no liver toxicity developed after discontinuing the troglitazone medication. Pharmacological participants randomized to metformin or double-placebo, discontinued their troglitazone-placebo, continue their coded metformin medication and remained masked to their pharmacological assignment (metformin or metformin-placebo).

This protocol describes the continued follow-up of the cohort of participants randomized to the troglitazone intervention of the DPP.