

DILIN Causality Categories and Definitions
(Supplemental Table 1)

Category	Numerical Scale	Summary	Timing	Competing causes	Drug and Signature
Definite	>95% likely	The relationship between the drug and liver injury is essentially certain. The evidence that the drug caused the injury is "beyond a reasonable doubt."	The timing of onset and recovery are highly compatible with drug induced liver injury.	No other potentially competing drug is being (or has been) received and all other possible diagnoses are unequivocally excluded.	Liver injury is highly typical for the particular drug in question, which is well known to cause hepatotoxicity (a "signature" is thus typically present). In the event that the drug is new and there is no previous record of toxicity, all other elements of the association must be certain.
Highly likely	75 to 95% likely	The link between the drug and liver injury is very strong, but may not be absolutely certain. The evidence for the drug causing the injury is "clear and convincing" but may not be definite.	The timing of onset and recovery are highly compatible with drug induced liver injury, although subtle variations in timing may be present.	Other potential diagnoses have been ruled out and other known hepatotoxins are unlikely to cause the liver injury.	The drug in question has been known to cause liver injury but the signature may be somewhat atypical for this agent; or it has been less certainly linked to liver injury in the past. In the event that the drug is new and there is no previous record of toxicity, other elements of the association must be certain.

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Probable	50 to 75% likely	Liver injury is compatible with the drug but the clinical picture may not be entirely typical. The “preponderance of the evidence” supports the link between the drug and the liver injury.	The timing of onset and recovery are compatible with drug induced liver injury, but variations may be present.	Other potential diagnoses have been largely ruled out and other known hepatotoxins are unlikely to cause the liver injury.	The agent has been linked to liver injury in the past, although this association may be weak. A signature, if present, may be atypical for this agent.
Possible	25 to 50% likely	Liver injury is possibly due to the drug, but the clinical picture may not be typical or convincing. Because there is less than “preponderance of evidence,” attribution of the liver injury is weak but cannot be excluded.	The temporal association between liver injury and receipt of the drug is often weak.	Other potential diagnoses have not necessarily been eliminated from the differential diagnosis. Other known hepatotoxins may have possibly caused the liver injury.	The agent may have been only equivocally linked to liver injury and the pattern may not be typical.

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Unlikely	<25% likely	Liver injury is not compatible with the drug. The bulk of the evidence is against an association between the drug and liver injury.	Although there may be a temporal association between the liver injury and receipt of the drug, the relationship is atypical.	Other potential diagnoses have not been excluded, and in fact are more likely to be responsible for the liver injury than the drug in question. Other known hepatotoxins may have possibly caused the liver injury.	The agent has been only weakly linked to liver injury and/or the pattern is highly atypical.
<p>Footnote: Causes are assessed for causality and categorized as definite, highly likely, probable, possible or unlikely or insufficient information for categorization. It should be emphasized that insufficient information precludes adequate categorization when there are significant facts missing in the history or laboratory results that do not permit accurate assessment of causality, even though the evidence for drug injury might have been definite, highly likely, probable or possible.</p>					