

## Causality Assessment of a Drug in a Case of Acute Liver Injury. CIOMS\* Scale

	HEPATO CELLULAR TYPE		CHOLESTATIC OR MIXED TYPE		ASSESSMENT
TIME TO ONSET					
Incompatible	Reaction occurred before starting the drug or more than 15 days after stopping the drug (except for slowly metabolized drugs)		Reaction occurred before starting the drug or more than 30 days after stopping the drug (except for slowly metabolized drugs)		
Unknown	When Information is not available to calculate time to onset, then the case is				insufficiently Documented
	Initial treatment	Subsequent treatment	Initial treatment	Subsequent treatment	SCORE
-From the beginning of the drug Suggestive Compatible	5-90 days <5 or >90 days	1-15 days >15 days	5-90 days <5 or > 90 days	1-90 days > 90 days	+2 +1
-From cessation of the drug Compatible	<= 15 days	<= 15 days	<= 30 days	<= 30 days	+1
COURSE	Difference between the peak of ALT (SGPT) and upper limits of normal values		Difference between the peak of A.P. (or TB) and upper limits of normal values		
Alter cessation of the drug Highly suggestive Suggestive Compatible Inconclusive	Decrease $\geq$ 50% within 8 days Decrease $\geq$ 50% within 30 days Not applicable No information or decrease $\geq$ 50%, after the 30th day		Not applicable Decrease $\geq$ 50% within 180 days Decrease < 50% within 180 days Persistence or Increase or no Information		+3 +2 +1 0
Against the role of the drug	Decrease $\leq$ 50%, after the 30th days or recurrent increase		No situation. Not applicable		-2
If the drug is continued Inconclusive	All situations		All situations		0
RISK FACTORS	Ethanol		Ethanol or pregnancy		
Presence Absence					+1 0
Age of the patient $\geq$ 55 years Age of the patient < 55 years					+1 0
CONCOMITANT DRUG(S)					
None or no information or concomitant drug with incompatible time to onset Concomitant drug with compatible or suggestive time to onset Concomitant drug known as hepatotoxin and with compatible or suggestive time to onset Concomitant drug with evidence for its role in this case (positive rechallenge or validated test)					0 -1 -2 -3
SEARCH FOR NON DRUG CAUSES					
Group I (6 causes) Recent viral infection with HAV (IgM anti HAV) or HBV (IgM anti HBV) or HCV (anti HCV and non A- non B hepatitis); Biliary obstruction (ultrasonography); Alcoholism (AST/ALT $\geq$ 2); Acute recent hypotension history (particularly if heart disease)			All causes - group I and II - reasonably ruled out		+2
Group II Complications of underlying disease; Clinical and/or biological Context suggesting CMV, EBV or Herpes virus infection			The 6 causes of group I ruled out		+1
			4 or 5 causes of group I ruled out		0
			Less than 4 causes of group I ruled out		-2
			Non drug cause highly probable		-3
PREVIOUS INFORMATION ON HEPATOTOXICITY OF THE DRUG					
Reaction labelled in the product characteristics Reaction published but unlabelled Reaction unknown					+2 +1 0
RESPONSE TO READMINISTRATION					
Positive Compatible	Doubling of ALT with the drug alone Doubling of ALT with the drugs already given at the time of the 1st reaction		Doubling of AP (or TB) with the drug alone Doubling of AP (or TB) with the drug already given at the time of the 1st reaction		+3 +1
Negative	Increase of ALT but less than N in the same conditions as for the first administration		Increase of AP (or TB) but less than N in the same conditions as for the first administration		-2
Not done or not interpretable	Other situations		Other situations		0
Total (add the encircled figures)					

The total score may be classified in 5 degrees: SCORE  $\leq$  0 excluded; 1-2 unlikely; 3-5 possible; 6-8 probable; above 8 highly probable.  
\* Council for the International Organization of Medical Sciences.