



Therapeutic  
Drug Monitoring



SERUM PLASMA

# Acetaminophen (ACTM)

## Simplified Reagent Handling

### Clinical Significance

Acetaminophen, a commonly used analgesic drug, is rapidly absorbed, with peak concentration observed 2 hours after ingestion. Acetaminophen overdose may cause severe hepatic toxicity or death. Initial clinical findings in acetaminophen toxicity are relatively mild and nonspecific, and not predictive of possible hepatic necrosis. The measurement of serum acetaminophen concentration is paramount for proper assessment of the overdose and for making appropriate therapeutic decisions in emergency situations.<sup>1</sup>

Acetaminophen half-life is approximately 4 hours.<sup>2</sup> Acetaminophen is metabolized primarily by glucuronic acid conjugation and a minor oxidative pathway, cytochrome P450. The toxic, oxidative metabolite, N-acetyl-iminoquinone, is detoxified by conjugation with limited amounts of hepatic glutathione and subsequent renal excretion. Glutathione is rapidly depleted in toxic ingestions, forcing N-acetyl-imidoquinone to bind covalently to hepatic macromolecules and causing hepatic necrosis.<sup>3</sup> Cytochrome P450 inducers such as ethanol increase the concentration of the toxic metabolite. N-acetylcysteine (NAC) provides an analogue of glutathione and can be used as a direct antidote for acetaminophen toxicity.<sup>3</sup>

Acetaminophen concentrations are determined to predict potential toxicity and to institute NAC therapy. In cases of suspected overdose, serum acetaminophen concentration should be determined four or more hours after ingestion. When the type of acetaminophen ingested is not known or includes an extended-release product, a second measurement should be obtained four to six hours after the first. It is possible to relate serum acetaminophen concentration and time following acute ingestion to the probability of hepatic necrosis (Figure 1).<sup>4</sup> If the time of ingestion is not known (within 2 hours), two or more blood samples taken at intervals may be used to estimate the acetaminophen elimination half-life. Half-life may be a better predictor of hepatotoxicity than interpretation based on a single serum concentration.<sup>5</sup>

### Therapeutic and Toxic Levels<sup>1,6</sup>

#### Therapeutic range:

10-30 mg/mL (66-199 μmol/L)

#### Toxic levels:

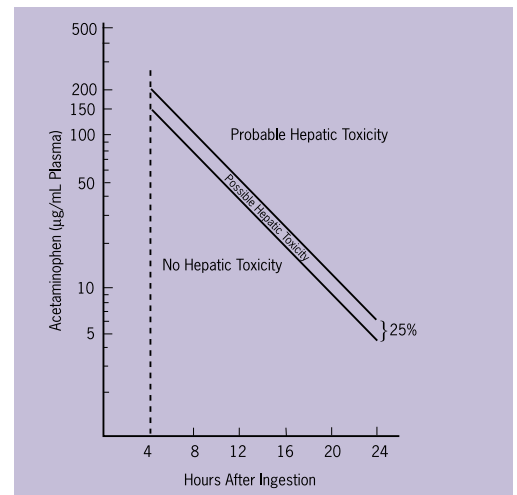
>150 μg/mL (993 μmol/L) at 4 hours  
>75 μg/mL (496 μmol/L) at 8 hours  
>40 μg/mL (265 μmol/L) at 12 hours

### Methodology

SYNCHRON® Acetaminophen Reagent is used to measure acetaminophen concentration by a particle enhanced turbidimetric inhibition immunoassay method. Particle-bound drug (PBD) binds to the acetaminophen specific antibody (Ab) resulting in the formation of insoluble aggregates causing light scatter. Non-particle-bound acetaminophen in the patient sample competes with the PBD for the antibody binding sites, inhibiting the formation of insoluble aggregates. The rate and amount of particle aggregation is inversely proportional to the concentration of acetaminophen in the sample.

The SYNCHRON system automatically proportions the appropriate sample and reagent volumes into the cuvette at 37°C. The system monitors the aggregate formation by measuring the change in absorbance at 340 nm. This change in absorbance is inversely proportional to the concentration of acetaminophen in the sample and is used by the SYNCHRON system to calculate and express the acetaminophen concentration based on a multi-point calibration curve.

**Figure 1.** Serum acetaminophen vs. potential hepatotoxicity after single dose of acetaminophen.<sup>4</sup>



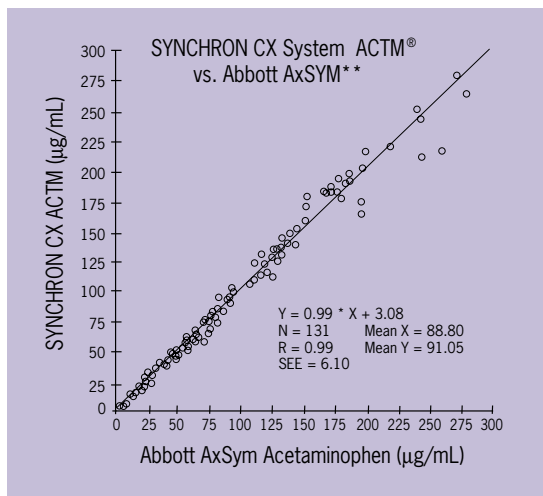
### Reaction Scheme

Acetaminophen (sample) + PBD + Ab → PBD–Ab (aggregates) + Acetaminophen (sample)–Ab



## Performance Characteristics

### Correlation\*



### Within-Run Precision\*

Typical precision was evaluated by assaying 3 levels of serum control according to the NCCLS Guideline EP5-A.<sup>7</sup>

Control Level	N	Mean (µg/dL)	SD	%CV
1	80	19	0.8	4.0
2	80	71	1.2	1.8
3	80	139	3.2	2.3

### Total Imprecision\*

Control Level	N	Mean (µg/dL)	SD	%CV
1	80	19	1.2	6.4
2	80	71	2.2	3.0
3	80	139	4.5	3.2

### Characteristics

Sample Type/Size	Serum/Plasma, 5 µL
Analytical Range	10 to 300 µg/mL (conventional units) 66 to 1986 µmol/L (S.I. units)
On-instrument Stability	42 days
Calibration Stability	14 days
Within-lot Calibration	60 days

### Ordering Information

SYNCHRON Acetaminophen (ACTM)	
Reagent, 1 x 100	472169
Drug Calibrator 2	469630
SYNCHRON Control, Multi-Level 6 x 20 mL	657365
Vigil TDM Control Level 1, 3 x 3 mL	472461
Vigil TDM Control Level 2, 3 x 3 mL	472467
Vigil TDM Control Level 3, 3 x 3 mL	472472

### References

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- Pappas AA, Taylor EH, Ackerman B, Toxicology and Drugs of Abuse, in Howanitz J, Howanitz P (ed), Laboratory Medicine: Test Selection and Interpretation, New York: Churchill Livingstone, 1991:382-3.
- Rumack BH, Peterson RC, Koch FF, Amara IA, Acetaminophen Overdose: 662 Cases with Evaluation of Oral Acetylcysteine Treatment, Arch Intern Med 1981;141:380.
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- Prescott LF, Roscoe P, Wright N, Brown SS, Plasma-paracetamol Half-life and Hepatic Necrosis in Patients with Paracetamol Overdose, Lancet 1971; 1:519-22.
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- National Committee for Clinical Laboratory Standards, Evaluation of Precision Performance of Clinical Chemistry Devices, Approved Guideline, Volume 19, No. 2, NCCLS Publication EP5-A. Villanova, PA (1999).

\*The precision and correlation studies were obtained during limited evaluation and are not intended to represent performance specifications for this reagent.

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