

SENTINEL SURVEILLANCE FOR HERBAL AND DIETARY SUPPLEMENT INDUCED LIVER INJURY IN THE US: A NEW INITIATIVE BY THE DILIN

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INTRODUCTION

The Drug-Induced Liver Injury Network (DILIN) has collected cases of liver injury due to herbal and dietary supplements (HDS) since its inception in 2004. A rise in the number of cases and the resultant risk for HDS induced liver injury (HILI) comprises the rationale for a national surveillance system to identify potentially injurious HDS early and thus allow for more expedient epidemiological investigations and regulatory actions.

AIM

Our aim is to report the early results of sentinel surveillance for HDS-induced liver injury (HILI) that includes chemical analysis of suspect HDS and coordination with the Human Foods Program (HFP) of the Food and Drug Administration (FDA) for early signal detection and outbreak management.

METHOD

- A surveillance system was developed as shown in the figure.
- De-identified information was assembled from cases enrolled as described¹ at 6 DILIN sites
- Available products were analyzed at the National Center for Natural Products Research using liquid chromatography-mass spec to verify label ingredients and detect adulterants
- All information was recorded onto a case report form, and investigators (DH, AS, VN) provide a DILIN expert opinion causality score (1= definite to 5= unlikely).
- A target turn-around time (TAT) of 30 days was established from enrollment to submission of all information to the FDA

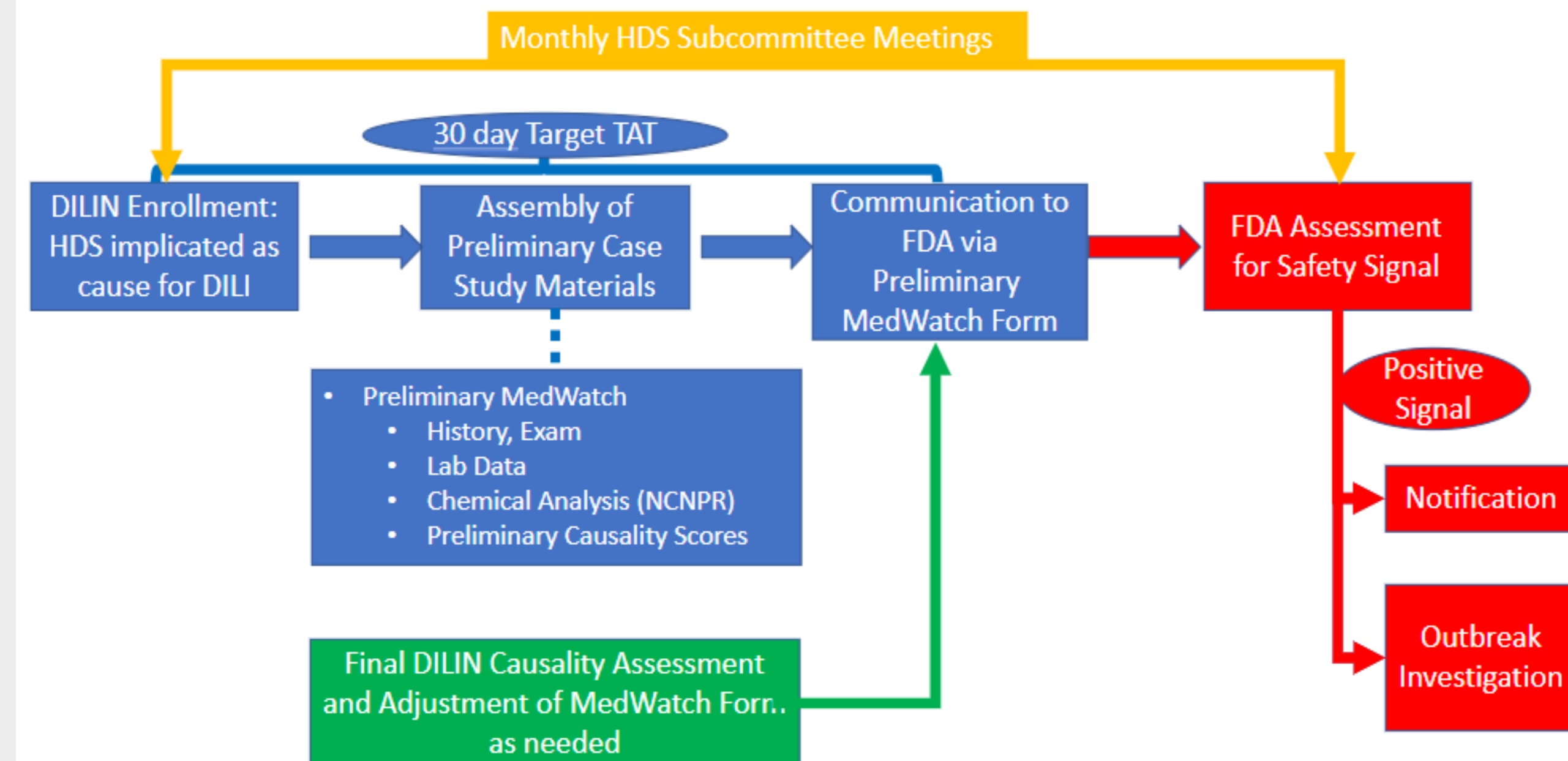


Figure legend: The surveillance pathway (blue) has a 30 day TAT target from enrollment to communication of a preliminary MedWatch to the FDA. The preliminary MedWatch Form reflecting initial causality assessment is confirmed by DILIN at 6 months (green) and adjusted as needed. The FDA determines a safety signal and appropriate regulatory follow up (red). The DILIN HDS Subcommittee oversees surveillance and interfaces with the FDA (gold).

RESULTS 1

- Between 1/1/25 and 9/1/25 15 suspected HILI cases were enrolled and adjudicated as part of this sentinel surveillance process
- Median age was 48 years, 67% were female, 68% White, 20% Black.
- 7 (47%) had jaundice, and 12 (80%) were hospitalized.
- Median ALT at onset was 638 U/L (range 63-4820), AST 657 U/L (41-4373), Alk Phos 221 U/L (120-792), and bilirubin 5.5 mg/dL (0.4-22.1).
- Initial causality assessment determined 7 (47%) of cases were convincing DILI (either Definite, Highly Likely, or Probable DILI).
- 25 products were implicated as a cause for HILI; 18 were collected for analysis.
- Labeled ingredients were verified in all 18 products; no adulterants or contaminants were detected.
- As shown in the table, cases were reported to the FDA (MedWatch) with a Turn Around Time (TAT) between 3 and 96 days.
 - Median 22.5 days
 - Mean 28.7 days

RESULTS 2

Case	Implicated HDS Product Name	Initial Casualty Score	TAT (Days)
1	Super Youth Multi-Collagen Peptides	Unlikely	38
2	Organic Turmeric Curcumin with Black Pepper	Highly Likely	36
3	Curcumin Phytosome, Collagen peptides	Possible	37
4	Premium CLA 3-6-9	Possible	17
5	GOLD STANDARD WHEY EXTREME MILK CHOCOLATE	Possible	22
6	GI Microb-X, GI Revive	Highly Likely	21
7	DOSE, ISatori L- Carnitine LS3 3000 ,Turmeric Curcumin, Fenugreek, DHEA, Nitric Oxide	Highly Likely	23
8	Turmeric/Ginger/ACV, Oil of Oregano Black Seed Oil	Highly Likely	17
9	Force FactorTest X180 Boost	Possible	3
10	Turmeric curcumin plus organic ginger and bioperine	Possible	14
11	Turmeric (from You Theory), VMG + (From DoTerra)	Highly Likely	5
12	Turmeric Powder by Sunrise Pure	Possible	34
13	Turmeric (from You Theory)	Definite	30
14	Bronze Chews, Ancef IV	Possible	15
15	Hydroxycut Hardcore Elite	Highly Likely	96

Abbreviations used: TAT, Turn Around Time; DHEA, dehydroepiandrosterone; MSM, methylsulfonylmethane.

CONCLUSION

- Sentinel surveillance for HILI via a prospective, multicenter research network like DILIN is feasible, achieving an acceptable TAT from a regulatory standpoint.
- Surveillance tended to detect serious liver injury, insofar as most patients had jaundice and were hospitalized.
- Surveillance will support early identification of serious HILI safety signals that can trigger outbreak investigations and facilitate expedient regulatory action to enhance early warning and consumer safety.

REFERENCES

Drug safety 2009;32:55-68.

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