

reanalysis of the IOWA study results. As described in more detail later in this section, this new study indicates that the infectivity of *Cryptosporidium* oocysts varies over a wide range. The UCP oocysts appeared less infective than those of the IOWA study while the TAMU oocysts were much more infective. Although the occurrence of these isolates among environmental oocysts is unknown, a meta-analysis of these data conducted by EPA suggests the overall infectivity of *Cryptosporidium* may be significantly greater than was estimated for the IESWTR (USEPA 2003a).

This section begins with a description of the infectivity data considered for the IESWTR. This is followed by a presentation of additional data that have been evaluated for the proposed LT2ESWTR and a characterization of the significance of these new data.

#### 1. *Cryptosporidium* Infectivity Data Evaluated for IESWTR

Data from the IOWA study (DuPont *et al.* 1995) were evaluated for the IESWTR. In that study, 29 individuals were given single doses ranging from 30 oocysts to 1 million oocysts. This oocyst isolate was originally obtained from a naturally infected calf. Seven persons received doses above 500, and all were infected. Eleven of the twenty two individuals receiving doses of 500 or fewer were classified as infected based on oocysts detected in stool samples.

The IOWA study data were analyzed using an exponential dose-response model established by Haas *et al.* (1996) for *Cryptosporidium*:

$$\text{Probability \{Infection / Dose\}} = 1 - e^{-\text{Dose}/k}$$

Based on the maximum likelihood estimate of  $k$  (238), the probability of infection from ingesting a single oocyst ( $1/k$ ) is approximately 0.4% (4 persons infected for every 1,000 who each ingest one oocyst). Based on the same estimate, the dose at which 50% of persons

become infected (known as the median infectious dose or ID<sub>50</sub>) is 165.

#### 2. New Data on *Cryptosporidium* Infectivity

A study of two additional *Cryptosporidium* isolates was conducted at the University of Texas-Houston Health Science Center (Okhuysen *et al.* 1999). One of the isolates (UCP) was originally collected from naturally infected calves. The other isolate (TAMU) was originally collected from a veterinary student who became infected during necropsy on an infected foal.

The TAMU and UCP studies were conducted with 14 and 17 subjects, respectively. Because thousands of oocysts per gram of stool can go undetected, researchers elected to use both stool test results and symptoms as markers of infection (only stool test results had been used for the IOWA study). Under this definition, two additional IOWA subjects were regarded as having been infected. As shown in Table III-1, all but two of the TAMU subjects were presumed infected and all but six of the UCP subjects were presumed infected following ingestion of the indicated oocyst doses.

TABLE III-1.—*Cryptosporidium Parvum* INFECTIVITY IN HEALTHY ADULT VOLUNTEERS

Isolate and dose (# of oocysts)	Number of subjects <sup>1</sup>	Number infected <sup>1</sup>
IOWA:		
30 .....	5	2
100 .....	8	4
300 .....	3	2
500 .....	6	5
1,000 .....	2	2
10,000 .....	3	3
100,000 .....	1	1
1,000,000 .....	1	1
TAMU:		
10 .....	3	2
30 .....	3	2
100 .....	3	3

TABLE III-1.—*Cryptosporidium Parvum* INFECTIVITY IN HEALTHY ADULT VOLUNTEERS—Continued

Isolate and dose (# of oocysts)	Number of subjects <sup>1</sup>	Number infected <sup>1</sup>
UCP:		
500 .....	5	5
1,000 .....	5	3
5,000 .....	3	2
10,000 .....	5	2
10,000 .....	4	4

<sup>1</sup> The two right columns list the number of subjects belonging to each category.

EPA conducted a meta-analysis of these results in which the three isolates were considered as a random sample (of size three) from a larger population of environmental oocysts (Messner *et al.* 2001). This meta analysis was reviewed by the Science Advisory Board (SAB). In written comments from a December 2001 meeting of the Drinking Water Committee, SAB members recommended the following: (1) two assumed infectivity distributions (of parameter  $r = 1/k$  as logit normal and logit-t) should be used in order to characterize uncertainty and (2) EPA should consider excluding the UCP data set because it seems to be an outlier (see Section VII.K). In response, EPA has used the two recommended distributions for infectivity and has conducted the meta-analysis both with and without the UCP data due to uncertainty about whether it is appropriate to exclude these data.

Table III-2 presents meta-analysis estimates of the probability of infection given one oocyst ingested. Results are shown for the four different analysis conditions (log normal and log-t distributions; with and without UCP data) as well as a combined result derived by sampling equally from each distribution. A more complete description of the infectivity analysis is provided in Economic Analysis for the LT2ESWTR (USEPA 2003a).

TABLE III-2.—RISK OF INFECTION, GIVEN ONE OOCYST INGESTED

Basis for analysis		Probability of infection, one oocyst ingested	
Studies used	Distributional model	Mean	80% Credible interval
IOWA, TAMU, and UCP .....	Normal .....	0.07	0.007–0.19
IOWA, TAMU, and UCP .....	Student's t (3df) <sup>1</sup> .....	0.09	0.015–0.20
IOWA and TAMU .....	Normal .....	0.09	0.011–0.23
IOWA and TAMU .....	Student's t (3df) <sup>1</sup> .....	0.10	0.014–0.25
Equal Mix of the Four Above .....	.....	0.09	0.011–0.22

<sup>1</sup> Student's t distribution with 3 degrees of freedom (3df).