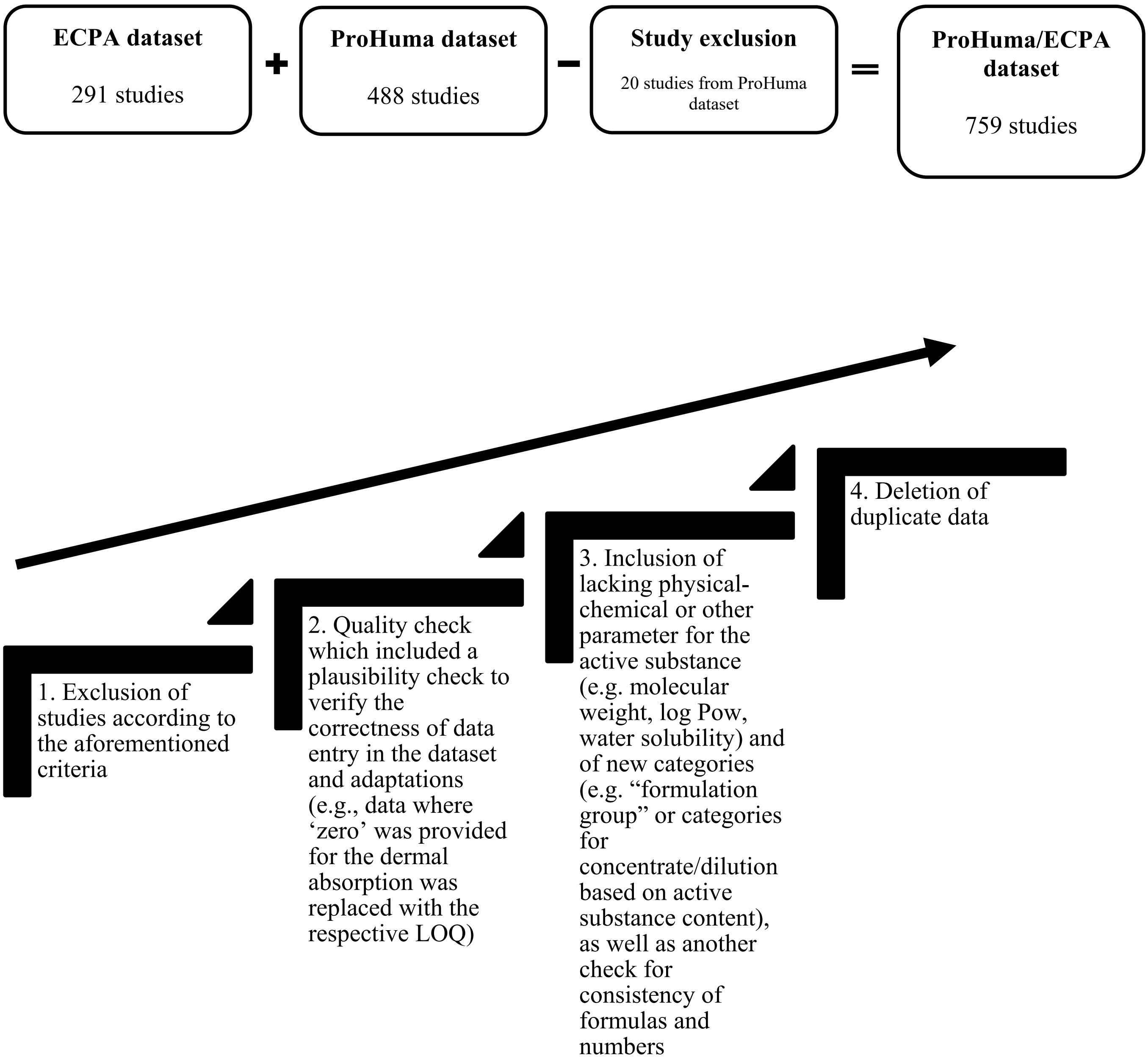
Supplementary Material

The following is the Supplementary data to this project.

Appendix A. Data collection (Top) and steps involved in the data processing (Bottom)



Note: This figure must be read from left to right (1-4).

Appendix B. Description of the method implemented by R function

Given a sample x = {x_1, x_2, …, x_n} of size n, the goal is to estimate the quantile q_alpha and the corresponding confidence interval. The function operates as follows:

1. **Calculate the empirical quantile**: For a given quantile level alpha, the empirical quantile is the value x_r such that P(q_alpha <= x_r) <= beta, where beta is the desired confidence level;
2. **Determine the rank r**: The rank r is chosen such that the probability of the quantile being less than or equal to the r-th order statistic is greater than or equal to beta.

The function 'ub.leftCI' as presented in Craig and Guillot, 2017 might return 'NA', as describe in Table B7 from EFSA, 2017 in situations where the sample size is too small, particularly when the confidence level beta is very high, and the required rank r exceeds the sample size. This can occur when the empirical distribution is highly skewed or when extreme quantiles (e.g., 99th percentile) are being estimated from small samples. To copy with such situation, it was also used an alternative approach of estimating the upper bound of a confidence interval using a bootstrap method (DiCiccio and Efron, 1996, Etzioni *et al.*, 2020, Justus *et al.*, 2024).

The bootstrap method offers an alternative approach to estimating confidence intervals, particularly when the assumptions of the 'ub.leftCI' function are not met or when the sample size is inadequate.

The bootstrap procedure involves the following steps:

1. **Resampling**: From the original sample x, generate a large number B of bootstrap samples x^*_b (for b = 1, 2, … , B) by resampling with replacement;
2. **Estimate the quantile for each sample**: For each bootstrap sample, compute the desired quantile q_alpha.
3. **Construct the confidence interval**: The confidence interval is constructed by taking the empirical quantiles from the distribution of the bootstrap estimates {q*_{alpha,1}, q*_{alpha,2}, … , q{alpha,B}}.

In the present analysis, it was implemented a non-parametric bootstrap method with 100,000 resamples, drawing samples with replacement from the observed dataset. For each resample, it was computed the 95th percentile (q95) and other relevant quantiles. The bootstrap confidence intervals were then obtained using the percentile method, where the 2.5th and 97.5th percentiles of the bootstrap distribution served as the bounds for the 95% confidence interval.

Appendix C. Effect of formulation type

Table 1: Overview of dermal absorption's percentiles (%) by formulation types for concentrates and dilutions

Formulation type	Number of observations		95th percentile (95% upper confidence interval) – Bootstrap method	
	Concentrates	Dilutions	Concentrates	Dilutions
Organic solvent				
EC	1413	2146	12.30	41.85
EW	144	224	20.63	56.67
ME	74	135	6.48	52.89
OD	157	268	11.39	33.16
SE	362	545	6.67	47.69
Water-based/dispersed				
CS	72	102	7.33	56.37
FS	474	311	3.30	16.09
SC	1651	2566	3.67	39.54
SL	251	416	9.99	32.48
ZC	61	68	7.65	38.16
Solid				
SG	60	66	5.18	71.67
WG	816	1338	3.06	36.96
WP	73	106	6.98	41.29

Appendix D. Procedure for extrapolation of dermal absorption data (reproduced from Aggarwal *et al*., 2015)

Step 1

- If there is no remarkable difference in available dermal absorption data for 2 or more spray dilutions, there is no need to test a new dilution. If there is a remarkable difference, follow Steps 2 and 3.

Step 2

- If the new dilution is ≤2-fold the lowest concentration tested, there is no need to adjust the untested new dilution.

Step 3

- If the new spray >2-fold more dilute than the lowest concentration tested, a pro-rated correction is applied up to a 5-fold difference or the 30% default dermal absorption is reached, whichever is lower.