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Survey on Use of alternative methods

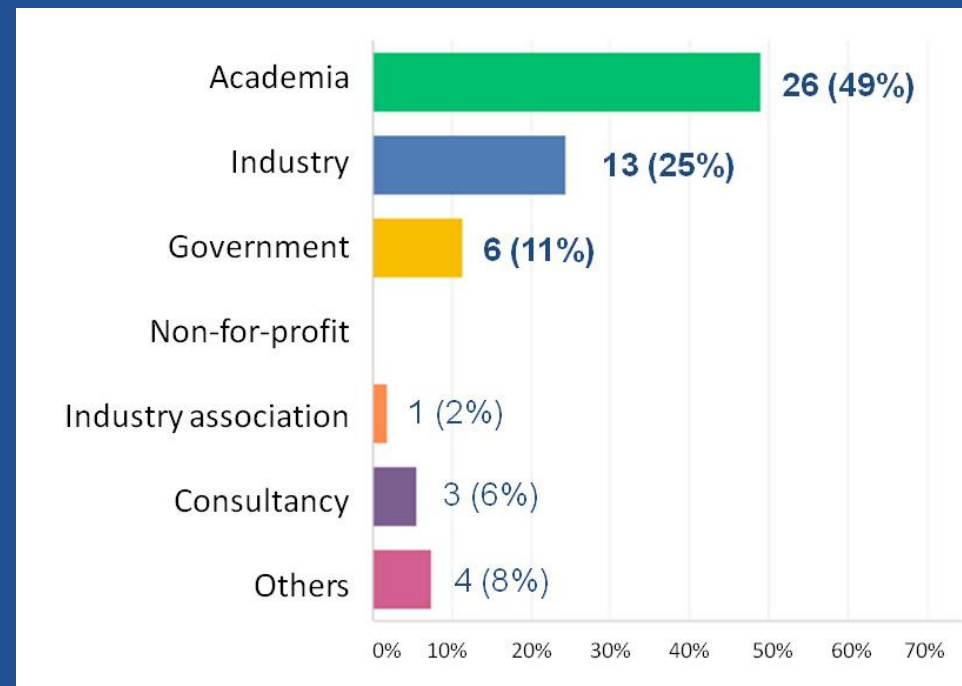
- Survey from 19 July to 10 August 2017 among ESTIV members
- 10 questions to understand current uses & possible bottlenecks R&D and regulatory levels
- Q1: In which sector do you currently work?
(53/53 answers)

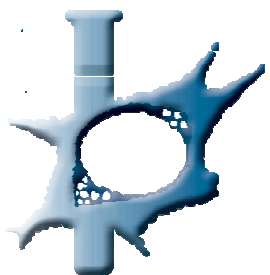
49% academia

36% industry

15% government

Others: Public research institute; European Agency; Clinical Research; CRO





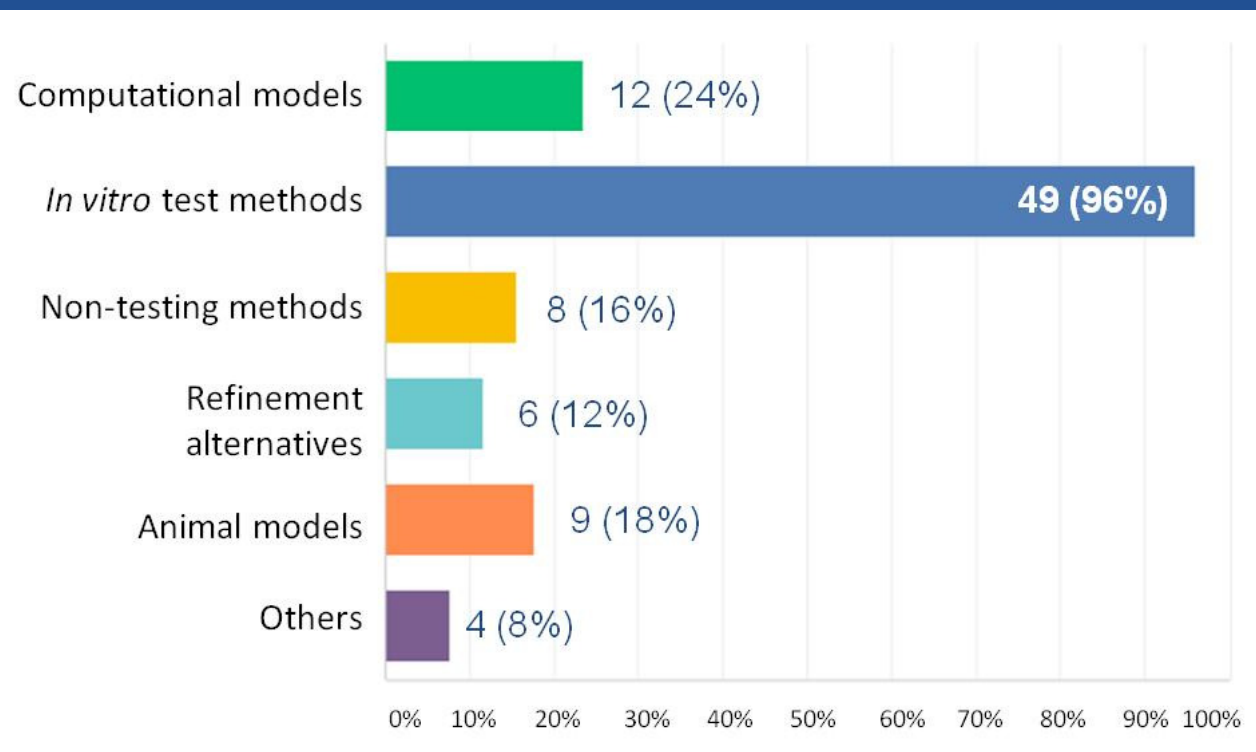
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Q2: Which type of test methods do you mainly make use of?
(51/53 answers)

In vitro
>
Computational
>
Animal
>
Non-testing
>
Refinement





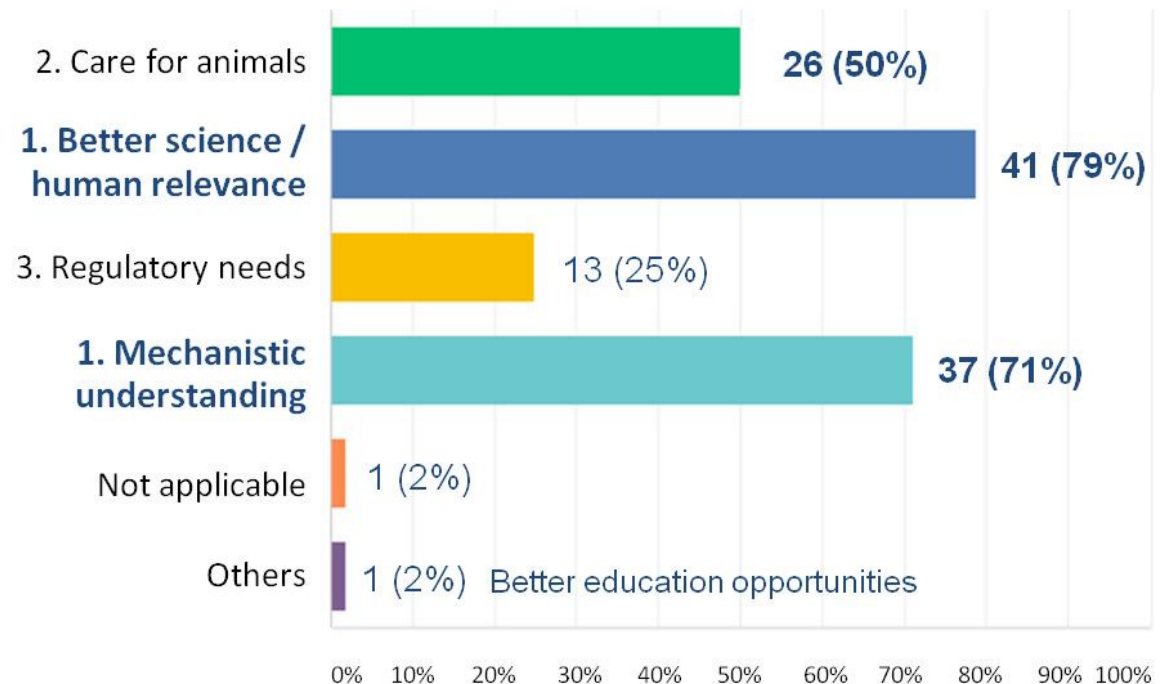
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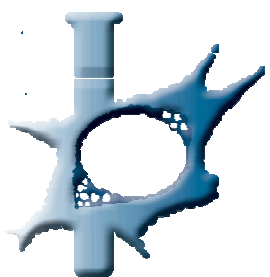
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Q3: Why did you start working with/on alternative methods?
(52/53 answers)

Human /mechanistic
relevance
>
Ethics
>
Regulatory needs





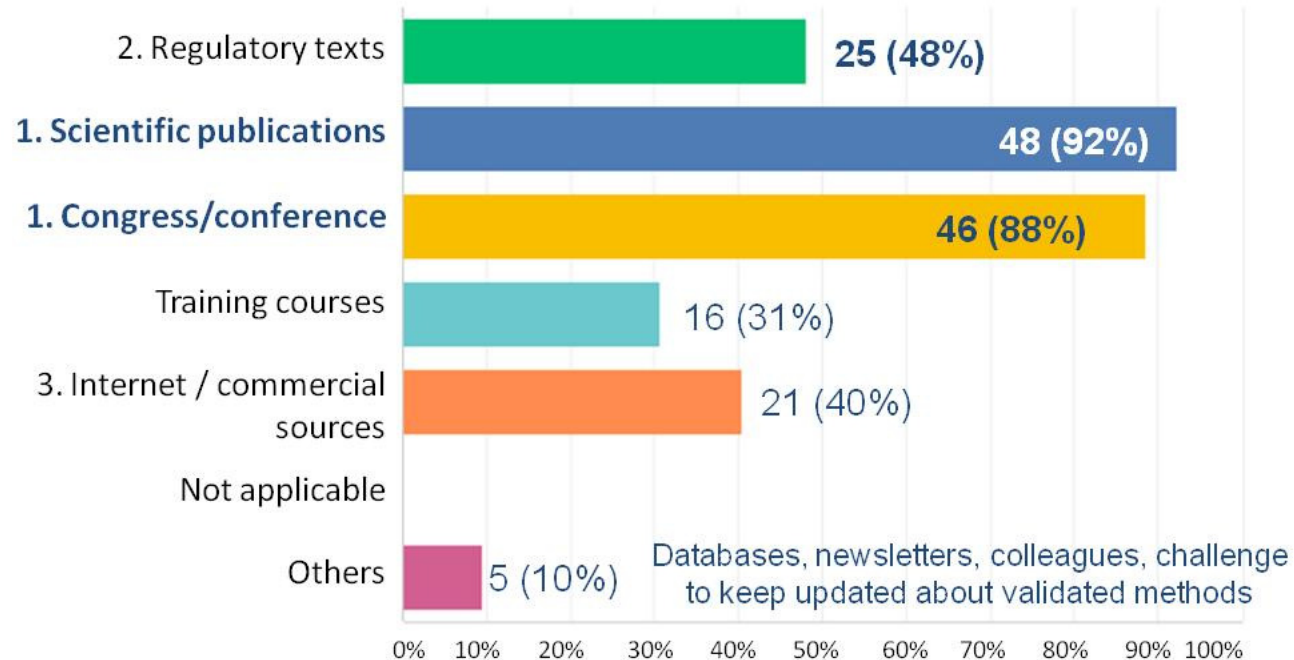
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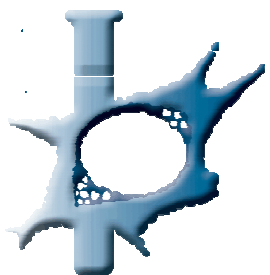
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Q4: How do you retrieve information on alternative methods?
(52/53 answers)

Scientific publications
& congresses
>
Regulatory texts
>
Internet & commercial
sources



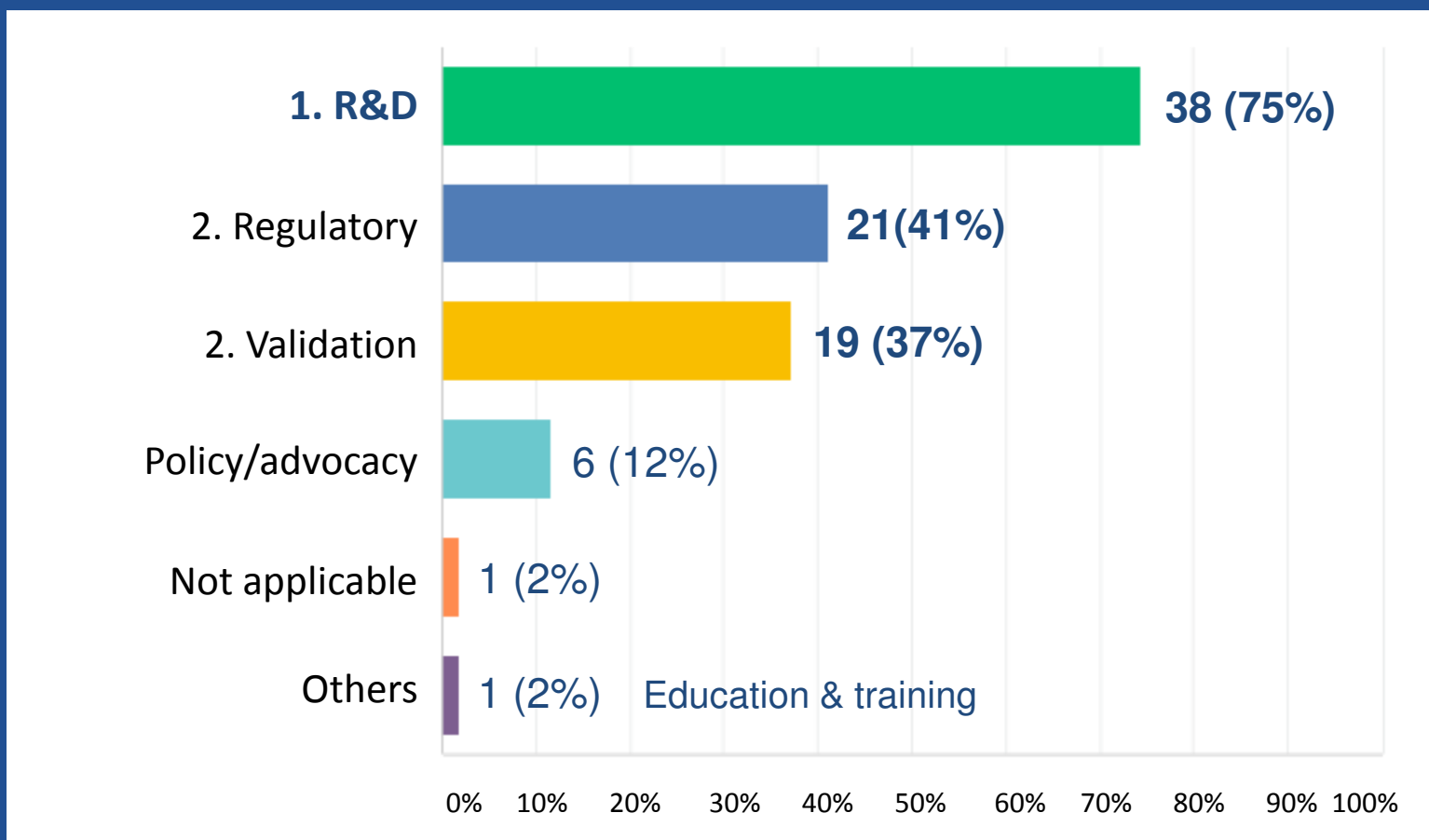


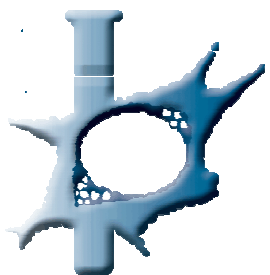
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Q5: For which purposes do you make use of alternative methods? (51/53 answers)



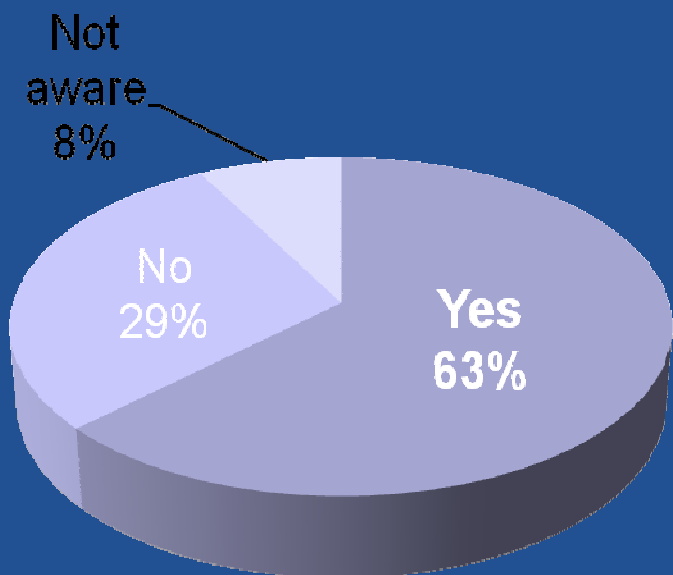


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Q6: Do regulatory requests on use of alternative methods have an impact on your activities? (51/53 answers)



If yes, how did it affect?	N.
Implementation of alternative test methods <i>Official TG, cosmetic ingredients, prioritization, direct implication</i>	6
Development of alternative methods <i>Regulatory purposes & education</i>	3
Investment on alternative methods <i>Grant investment, cost justification</i>	2
Quality control and performance standards	1
Being aware of latest regulatory developments	1

Q7: Do you believe use of alternative methods in R&D could be improved?



n = 50

What are the main obstacles you perceive today? (n=28) n.

- | | |
|---|-----------|
| 1. Conservative approach / animal studies considered gold standard (e.g. regulatory authorities, scientists, journal reviewers) | 12 |
| 2. Methods availability & physiological functions that cannot be studied with alternative methods (e.g. multi-organ, immune-based) | 6 |
| 2. Lack of funding & personnel | 6 |
| 3. Limited understanding of the potential of (combined) alternative methods | 5 |
| - Some alternative tests can be more costly and more time consuming than traditional testing (only regulatory requirements can lead to changes) | 3 |
| - Need for better accuracy (e.g. skin sensitization) | 2 |
| - Reproducibility & GIVMP | 2 |
| - Determining at WHAT dose a compound becomes toxic, internal doses of contaminants, effects related to experimental rather than nominal doses | 2 |
| - Long regulatory processes | 1 |
| - Better guidance and awareness on the possibilities to move from R&D to validation | 1 |
| - Use & development should be driven by science and not by legislation | 1 |
| - Misunderstanding on need to validate in preclinical studies | 1 |
| - Some methods not adapted to screening in early stages of R&D | 1 |
| - Testing of complex mixtures | 1 |

Q8: Do you believe use of alternative methods for regulatory purposes could be improved?



n = 49

What are the main obstacles you perceive today? (n=26) n.

1. Lack of acceptance / harmonization / willingness to change / familiarity (from e.g. regulators, toxicologists)	11
2. Long validation & legal implementation processes (perhaps piece-meal validation from a framework would be of benefit)	5
3. Well defined applicability domains, even if restricted (e.g. mixtures)	4
4. Complexity & costs of using multiple tests / testing strategies	3
- Use and development should be driven by science (not by legislation). Increased acceptance of non-guideline studies that are scientifically sound could increase use of alternatives for regulatory purposes	2
- Lack of incentives and information	2
- Lack of funding	2
- Need more predictive models	2
- Define most relevant situation: human vs animal	1
- Risk management	1
- Lack of standardized data interpretation procedures (e.g. ESC)	1
- Lack of reproducibility	1
- Development of suitable protocols from basic research	1

Q9: Which areas do you believe alternative methods could be further implemented? (n=43)

	Overall n	Regulatory purposes ranking	R&D purposes ranking
Carcinogenicity	55	#2 (26)	#1 (29)
Reproductive & developmental toxicity	53	#1 (28)	#4 (25)
Pharmacokinetics	52	#3 (24)	#2 (28)
Systemic toxicity	49	#4 (23)	#3 (26)
Disease modelling	44	#8 (16)	#2 (28)
Skin sensitization	41	#3 (24)	#11 (17)
Genotoxicity	40	#5 (20)	#8 (20)
Investigative toxicology	40	#9 (15)	#4 (25)
Immunogenicity	39	#6 (18)	#7 (21)
Biodistribution & pharmacodynamics	36	#7 (17)	#9 (19)
Tissue engineering	35	#10 (12)	#5 (23)
Phototoxicity	34	#6 (18)	#12 (16)
Vaccines quality control	34	#7 (17)	#11 (17)
Cell technology	31	#13 (9)	#6 (22)
Topical toxicity	30	#6 (18)	#14 (12)
Regenerative medicine	28	#13 (9)	#9 (19)
Biomedicine	27	#12 (10)	#11 (17)
Biotechnology	27	#13 (9)	#10 (18)
Local tolerance	24	#11 (11)	#13 (13)

Others: Education & training, ecotoxicology, hepatotoxicity, reprotox



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Q10: How could the use of alternative methods be further promoted? (49/53 answers)

Funding
>
Legislation &
cross-sector
communication

>
Professional training

Others: Dissemination in other fields, early education, industry collaboration, webinars, regulatory acceptance, one central website

