The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) and European Chemical Industry Council Long-Range Research Initiative (Cefic LRI) Human Health and Exposure Sciences Scoping Meeting 2020

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The *European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC)* and the *European Chemical Industry Council Long-range Research Initiative (Cefic LRI)* convened the *Human Health and Exposure Sciences Scoping Meeting 2020* that took place on 30 and 31 January 2020 in Brussels, Belgium. Approximately 60 invited participants from Europe and North America representing ECETOC and Cefic member companies, academia, regulators, and consultancies attended the meeting; see meeting programme here for a list of participants.

Olivier de Matos (Secretary General, ECETOC, Belgium) and **Bruno Hubesch** (Cefic LRI, Belgium) opened the meeting, outlined its agenda and provided an overview of activities that were initiated and conducted since the 2019 Human Health and Exposure Sciences Scoping Meeting:

In 2019, nine ECETOC Task Forces (TFs) and one new Transformational Programme (TP) on human health and exposure sciences were active as well as seven TFs on environmental sciences, and a number of workshops (WSs) and expert group meetings (ExpGs) TFs were held. Overall, more than one hundred experts were involved, which is a sign of the trust and relevance of the ECETOC work. In 2020, planned outputs include nine Technical Reports (TRs), a range of publications and workshop reports.

Cefic LRI initiated four new human health and exposure sciences projects that were initiated in 2019 and are planned to begin in 2020 (Table 1).

Table 1: Cefic LRI – human health and exposure sciences projects planned to begin in 2020

Project	Budget	Lead researcher
B22: Tiered methods for quantifying exposure to complex substances ("TMEx-Complex") [a]	293k € over 2 years	J. Mark Parnis, Trent University (CA)
B23: Optimizing the benefit of REACH worker exposure assessments: ensuring meaningful health risk communication	255k € over 2 years	Wouter Fransman, TNO (NL)
C8: Metabolomics ring trial for chemical grouping (MATCHING) [b]	455k € over 2 years	Mark Viant, University of Birmingham (UK)
EMSG69: Incidence trends of selected endocrine-related diseases and conditions in Europe and North America, and the contribution of changes in human reproduction [c]	247k € over 2 years	Eva Negri, Università degli Studi di Milano (IT)

Footnote to Table 1 – corresponding Requests for Proposal (RfPs):

[a] Human exposure assessment framework for complex substances

[b] Assessing the repeatability of metabolomics within a regulatory context through a multi-laboratory ring-trial

[c] Are changes in human reproduction a major factor in explaining the increases in 14 diseases and health parameters thought to be related to the endocrine system?

For the remainder of Day 1, the meeting moderator **Dennis Landsbert-Noon** (Panda Communications, Belgium) lead through a series of elevator pitch presentations of proposals for new ECETOC and Cefic LRI activity. The elevator pitch presentations were 5-minute presentations

by the respective idea submitter or a designated colleague, each followed by a brief questions & answers (Q&A) session.

All proposed activities were further discussed on Day 2 in World Café sessions; see meeting programme here for process of the World Café sessions.

Below, **important points of discussion from the respective elevator pitch Q&A (Day 1) and World Café sessions (Day 2) are summarised together**. To complement this report, please refer to the slides from the elevator pitch presentations and the plenary slides summarising the outcomes of the World Café sessions available here.

Session 1: Hazard assessment and new approach methodologies (NAMs)

Mining the developmental toxicity biomarker genome in the zebrafish embryo test *[LRI]* Code HH 3

Aldert Piersma, RIVM (Netherlands)

The proposed genomic assessments shall not be restricted to the retinoic acid pathway. The investigation of this pathway, a central pathway for morphogenesis, is viewed as starting point aiming at identifying its specific impact on embryonic development, and shall be followed by investigations related to further pathways. Overall, the genome responsible for development (morphogenesis) is very conservative. Knowledge on the zebrafish genome will contribute to enhancing the understanding of the human and rat genomes, with comparisons to the human genome being the main incentive of the proposed project.

The 2016 ECETOC 'Omics WS confirmed the usefulness of 'omics for chemical risk assessment while highlighting the need to relate 'omics information to phenotypic alterations. It is an advantage of the zebrafish, whose embryonic development is completed within 5 days, that phenotypic investigations can be performed easily and more comprehensively than with any of the mammalian species that are commonly used for developmental toxicity testing.

Inflammation as the key player in the development of an integrated adverse outcome pathway (AOP) network for lung toxicity and disease *[LRI]* Code HH 5

Hedwig Braakhuis, RIVM (Netherlands)

As it is currently planned, the project shall focus on pulmonary inflammation (while explicitly excluding respiratory sensitisation). Pulmonary inflammation is relevant for particles and fibres, rather than other types of compounds that elicit intrinsic effects in the lung. Initially, it had been planned to include all pulmonary AOPs, but this goal was then considered too broad, and it was decided to focus first on inflammation. Ultimately, the AOP network shall cover all potential pulmonary AOPs.

It is hoped that the proposed project will also inform on the specific cellular effects induced by a specific substance. It is one of the major current challenges to enhance the understanding of how specific types of substances affect specific types of lung cells. Effects might not only be related to the type of substance, but more complexly also to the dose, the organisms' disposition, etc.

The AOP network shall be founded on 'high-quality' human data, and this is one of the reasons why it is planned to focus first on inflammation, an area where the availability of high-quality human data appears more likely.

Prediction of carcinogenic potential of agrochemicals using mechanistic information: exploration of quantitative approaches *[LRI]* Code HH 6

Mirjam Luijten, Hedwig Braakhuis and Harm Heusinkveld, RIVM (Netherlands); presented by Mirjam Luijten

The proposed project has been limited to agrochemicals because it shall build upon a previous activity conducted by the European Partnership for Alternative Approaches to Animal Testing (EPAA)[1] that focussed on the agrochemical sector. Due to the complexity of the topic, this focus was chosen since the 2-year rodent bioassay is legally mandated in this area. It is expected that the findings from the activity will also be relevant for other sectors.

Based upon the outcome of the EPAA work, the MoAs leading to approx. 100 tumours for which the underlying MoAs are not yet known, shall be identified. In this regard, it is recommendable to prioritise the list of tumours / MoAs to be addressed to ensure practicality of the proposed project.

In contrast to what was stated in the original proposal, it is now planned to also consider quantitative aspects of key event (KE) relationships. The proposed project shall focus on modes-of-action (MoAs) known to be relevant for humans. However, due the lack of reproducibility of the 2-year rodent bioassay, it will be challenging to perform species comparisons (rodents to humans) for quantitative correlations between KEs.

Improved interpretation of toxicological potential of chemical substances through mathematical modelling [LRI] Code HH 7

Mirjam Luijten, RIVM (Netherlands); Janine Ezendam, Tom Aldenberg, Jeroen Pennings, RIVM; David Kirkland, Kirkland Consulting (UK); David Lovell, University of London (UK); Stefan Pfuhler, Procter & Gamble (USA); presented by Mirjam Luijten

In building a comprehensive database, it is planned to use the data that are freely accessible on the ECHA dissemination portal as well as data from other inventories, as relevant. Since such data can derive from studies performed very recently, or several decades ago, it is pivotal to determine the version of the respective test guidelines (TGs) following which the studies were conducted.

It remains to be established how information from non-guideline-conform NAMs shall be integrated. When integrating all available evidence for a given substance, the mathematical modelling shall inform on the associated uncertainty, which is dependent upon the specific set of available data. This evaluation might also show that 'more data' does not imply 'better knowledge'.

The proposed project shall focus on the data-rich endpoints skin sensitisation and genotoxicity, for which a variety of NAMs are already available (both adopted as OECD TG and non-guideline-conform). Generally, the approach would also be applicable to endpoints that are not as data-rich (e.g. 90-day repeated-dose toxicity, developmental and reproductive toxicity), but for a meaningful application of the model, data from different study types should be available for the given endpoint.

The selection of appropriate 'gold standards' for statistical analyses (i.e. traditional animal data versus more relevant human data) requires further elaboration before onset of the project.

This proposed activity may have some overlap (or synergies) with proposed activity *HH 17: A new tool for risk assessment: The Quantitative Genetic Toxicology [LRI]* presented in Session 3 (*Risk assessment, management and perception*).

Use of the fish embryo model as a screening tool for early human toxicity assessment: exposure methodologies and applicability domains [LRI] Code HH 16

Jacques Aurélien Sergent, Solvay (Belgium) and Marc Léonard, L'Oréal (France)

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[1] https://ec.europa.eu/docsroom/documents/36296.

It remains to be determined if (and if so, how) this proposed activity might take advantage of findings from the LRI project ECO51 (*Strengthening weight-of-evidence for FET data to replace acute fish toxicity*), that is planned to begin in April 2020. Even though the two projects address different endpoints (early human toxicity versus acute fish toxicity), ECO51 might serve to substantiate the general usefulness of fish embryos for hazard assessments.

When aiming to use the fish embryo model as a screening tool for early human toxicity assessment, external exposure in fish needs to be related to internal exposure in humans. In this regard, the planned use of innovative micro-injection techniques for test material administration is expected to yield relevant quantitative information.

Expansion of a regulatory accepted in vitro testing battery for developmental neurotoxicity (DNT) evaluation [LRI] *Code HH 19*

Ellen Fritsche, IUF – Leibniz Research Institute for Environmental Medicine (Germany)

Since the AOPs leading to many neurodevelopmental diseases and disorders are still widely unknown, the proposed activity is not founded on a hypothesis-led approach. There are hardly any mechanistic data for the few substances for which data from the rodent DNT study are available. Further, there are only very few substances known to elicit DNT in humans. Due to the overall paucity of animal or human data, the approach is founded on biological knowledge, but not toxicological evidence, indicating that the selected cell types are relevant.

The *in vitro* battery shall cover a broad variety of KEs, for which reason a variety of different assays will need to be performed. Currently, all KEs are considered equally important; however, the *in vitro* battery includes high-quantity assays that allow addressing a number of KEs simultaneously. The proposed project shall serve to establish a database that might also be useful to rank the toxicological relevance of KEs.

Validation of the *in vitro* battery is likely to be challenging given the paucity of both animal and human data? It is planned to include those substances in the evaluation for which the most DNT data are available and to identify the most sensitive endpoint across all endpoints. In striving to bridge the gap between data from *in vitro* human cell assays and *in vivo* human data, it may be necessary to perform *in vitro* rodent cell assays and compare their outcomes to those from the few available rodent DNT studies.

Maximising the value of new toxicity screening models to better inform both ecological and health endpoints [ECETOC WS] *Code HH 21*

Sarah Hughes, Shell (USA); presented by Peter Boogaard, Shell Health (Netherlands)

While the goal of the proposed activity and the underlying concept are warranted, it will most likely be difficult to relate the findings from ecotoxicological assessments to human health endpoints. For example, the types of data driving ecotoxicological versus toxicological assessments are inherently different (e.g. effects on populations effects versus in individuals). Reproductive toxicity may be the endpoint interlinking the two. If findings from studies using invertebrates and fish (embryos) shall be used to inform on human toxicity endpoints, toxicokinetic considerations will be pivotal to ensure the meaningfulness of predictions.

The proposed activity should also consider activities of the SETAC One Health initiative (https://www.setac.org/page/scienceonehealth). Further, there may be an overlap between this proposed activity and HH 16 (*Use of the fish embryo model as a screening tool for early human toxicity assessment: exposure methodologies and applicability domains*?). Also, the present

proposed activity may serve to enhance the applicability of the model described in *HH 3 (Mining the developmental toxicity biomarker genome in the zebrafish embryo test).*

Session 2: Exposure assessment

Control of exposure to substances of very high concern (SVHCs) in a connected workplace *[LRI]*
Code HH 10

Jan Urbanus, Shell Health (Netherlands)

How shall the provisioning of portable biomonitoring devices be accomplished technically? – This will be part of the work plan. However, 'bringing the lab to the sample' as opposed to 'bringing the sample to the lab' is considered the appropriate way forward.

How shall the technical limitation be addressed that the available sensors are not very specific in detecting specific types of molecules? – The molecules can be recorded with the sensors at real-time, and then the information is forwarded to the 'backroom' for further investigation.

SVHCs derive from different chemical classes and can be organic, inorganic, volatile, etc. The assessment should focus on specific types of chemicals, also considering the opportunities of the current technology.

Building a common template for reporting the uncertainty in tiered exposure assessment *[ECETOC TF]* *Code HH 11*

Sarah Tozer, Procter and Gamble (UK); on behalf of the ECETOC Human Exposure TF

The TF is proposed as continuation of the 2016 ECETOC Human Health and Exposure Science Review Meeting. It shall begin by identifying the currently available concepts. Based thereupon, the common template shall be built. To motivate potential users to apply the planned template, the TF shall not only aim at building the template, but also at developing guidance for how it shall be used and, importantly, at providing case studies showing the added value of use of the template. Further, a workshop shall be organised to demonstrate use of the template.

The framework of the TF should also be used to enhance collaboration between human health and environmental toxicologists. Indeed, means to address uncertainty during risk assessment are also addressed in proposed activity ENV 8 (*Uncertainty of risk assessments: what is it, how do we tackle it?*) presented at the 2020 Environmental Sciences Scoping Meeting. Discussions related to that proposed activity highlighted that risk assessment approaches include both uncertainties and variance, but that the two are often not fully distinguished, albeit being different.

When building the common template for reporting the uncertainty in tiered exposure assessment, it should also be considered that exposure is never homogenous, and that it is even more inhomogeneous between sectors. Therefore, the purpose of the assessment needs to be specified.

Grouping of (multiple) chemicals for co-exposure assessment *[ECETOC TF/LRI]* *Code HH 12*

Tatsiana Dudzina, ExxonMobil (Belgium); on behalf of the ECETOC Human Exposure TF

Considering that the potency of a substance can affect exposure assessment, how shall it be considered during grouping? – Generally, the models shall be applied when information on the substances' hazard potential and potency is already available. Notably, however, dose addition is a general phenomenon and does not depend on the substances' MoAs. Substance hazard potential and potency shall be considered when prioritising substances for inclusion in the evaluation.

It is hoped to gain access to the human genome database. However, the analysis shall not be conducted on the level of the exposome, but on individual substances. When mining the data from

existing databases, multiple frameworks are available for quality assurance; further, different statistical analysis tools shall be used in parallel.

The challenge of exposure estimation of substances in plastic articles under REACH: use the food contact material experience to enable and improve exposure estimation methods *[LRI]* *Code HH 15*

Stefano Frattini and Andreas Ahrens, ECHA (Finland); presented by Stefano Frattini

The proposed activity focusses on plastic articles since it follows up from a project that addressed these articles. Nevertheless, other types of articles, e.g. textiles, toys or diapers, can be equally relevant. Generally, the proposed activity focusses on direct dermal contact, rather than exposure via the air, even though a substance's ability to be released may also affect in-door air quality. The German Federal Institute for Risk Assessment (BfR) possesses an abundance of information on dermal effects caused by toys. Also, PlasticsEurope might be in a position to assist in the provision of relevant data.

Since food contact materials are often multi-layered, partitioning in liquids might not be a suitable surrogate for dermal exposure. Indeed, preliminary investigations have shown that exposure estimates may differ depending on the route of exposure.

It was noted in the World Café sessions that this topic could perhaps be relevant for a WS or symposium.

Awareness of benefits of chemicals and acceptance of exposures *[LRI]* *Code HH 14*

Heli M. Hollnagel, Dow Europe GmbH (Switzerland)

Generally, the topic is very important, but the inherent challenges of succeeding in raising awareness of the benefits of chemicals and acceptance of exposures should not be underestimated. Experience gained in the crop protection product area showed that, while it was possible to reach out to the public in circumscribed panels, amplifying beyond the panel was a nearly unsurpassable hurdle. The vehicle used for amplification needs to be carefully sought out to ensure that the public will find it trustworthy, while also considering the complexity of the audience. Possibly, (sociological) research work is needed to identify the best suitable 'amplification tools', and Cefic LRI might not be the adequate framework for such research. The specific message(s) that should be conveyed also need to be determined further considering that opinions are not only formed by scientific evidence, but most importantly also by emotions.

High school education may be an appropriate point of access, e.g. to inform on the difference between hazard and risk, at best by including such topics in school curricula.

It was noted in the World Café sessions that this topic could perhaps be relevant for an ECETOC TF activity.

Session 3: Risk assessment, management and perception

Building a database of dose-response data as a basis for gaining generic information on dose-response behaviour *[ECETOC TP/LRI]* *Code HH 4*

Wout Slob, RIVM (Netherlands)

Useful databases that the proposed project might build upon are not available. To create a database of dose-response data, studies that include the relevant information need to be selected. Since data curation will be very intricate, it may be necessary to prioritise relevant studies. It is difficult to determine beforehand how many such studies will be required for the further evaluation.

Other than what was stated in the written proposed activity, MoAs shall be included in the evaluation, also to distinguish between genotoxic compounds (with non-thresholded MoAs) and non-genotoxic compounds (with thresholded MoAs) since the respective tools have recently become available. Based upon the underlying algorithms, studies including 2-3 dose levels and the control group will be useful for the database and will e.g. allow addressing the assumption of non-thresholded versus thresholded MoAs.

Reality-check for risk numbers underlying the health risk assessment of carcinogenic substances [ECETOC WS, TF, TP, ExpG] Code HH 9

Peter Boogaard, Shell Health (Netherlands)

More than one genotoxicity event might be needed for cancer to occur, and risk assessment needs to consider the heterogeneity of carcinogenicity. There were diverging views on the scientific relevance of risk numbers as well as on the opportunities to replace use of the very conservative assessment factors by more realistic risk estimates. However, there was consensus that improved communication of the risk assessment of carcinogenic substances is desirable; an objective that is also addressed in proposed activity HH 14 *(Awareness of benefits of chemicals and acceptance of exposures).*

Tracking chemicals in supply chains to reduce uncertainty in chemical risk assessment [WS] Code HH 13

Tatsiana Dudzina, ExxonMobil (Belgium); on behalf of the ECETOC Human Exposure TF

The Day 1 Q&A section did not provide additional information on this proposed activity. During the World Café discussions, it was confirmed that mining, tracking, and communicating information on substances in products along the supply chain is a prevailing challenge for industry that needs to be addressed. Such information would facilitate substance life cycle assessments and thus may also reduce uncertainty in exposure assessments.

A new tool for risk assessment: The Quantitative Genetic Toxicology [LRI] Code HH 17

Guy Steiblen, Solvay (France); George Johnson, University of Swansea (UK); presented by Guy Steiblen

How many case studies are needed to derive general principles, and are the case studies substance-specific so that one case study would be needed per substance (further considering that the number of data-rich substances is limited)? – It is planned to use reference tests, e.g. the *in vivo* micronucleus and transgenic mouse genotoxicity studies, to create a comprehensive database in order to experimentally determine thresholds and to identify benchmark substances.

The proposed tool shall both be useful for prospective as well as for retrospective risk assessment (following accidental exposures). The applicability of the tool will be enhanced by demonstrating its usefulness in a regulatory setting (including examples showing the scientific limitations of the traditional risk assessment approaches) and by initiatives to promote its regulatory acceptance.

This proposed activity may have some overlap (or synergies) with proposed activity HH 7 *(Improved interpretation of toxicological potential of chemical substances through mathematical modelling)* presented in Session 1 *(Hazard assessment and NAMs).*

Refinement of interspecies default assessment factor based on REACH data [LRI] Code HH 18

Blandine Doornaert, Solvay; presented by Jacques Aurélien Sergent, Solvay (Belgium)

This proposed activity is in an early stage of development and is presented at the 2020 Scoping Meeting to initiate the discussion with the relevant stakeholders. Generally, it is recommendable

that the proposed project makes best possible use of existing (curated) databases from different EU and non-EU agencies and that it is not restricted to the data from the ECHA dissemination portal. Usefulness of data from the RepDose database (https://repdose.item.fraunhofer.de) may merit consideration.

Further preparatory work is required to determine the specific species to be included in the assessments and relevant sources for high-quality human data. In this regard, the criteria to determine the quality of the data and to address uncertainties remain to be defined. Further, tools to import the relevant data into common database need to be established.

A consensus generic kinetic model for in vitro to in vivo extrapolation [ECETOC WS] Code HH 2

Aldert Piersma, RIVM (Netherlands)

As compared to the simplistic approach to validate NAMs by determining the numbers of true and false positives and negatives, the proposed work shall aim at translating potency into *in vitro* to *in vivo* extrapolations. The proposed activity is suggested as WS, i.e. to provide a platform for stakeholders and experts to share their experiences in developing and applying kinetic models, rather than to perform specific research work.

Since *in vitro* to *in vivo* extrapolations depend on many variables, it is unlikely that one single kinetic model will be applicable for all types of substances, all toxicological endpoints and all concentration ranges. Rather than using the outcome of the suggested WS to advance or merge available models, it should be used to draw up general guidance on how to develop a kinetic model and which standards it should meet (also to be able to address uncertainty). Drawing up general guidance will enhance flexibility while ensuring common standards.

'Omics thresholds of non-adversity [ECETOC WS/LRI] Code HH 20

Tewes Tralau, BfR - German Federal Institute for Risk Assessment (Germany)

While the 2016 ECETOC 'Omics WS confirmed the usefulness of 'omics for chemical risk assessment, such data are still hardly, if at all, being used for regulatory purposes. Several reasons are accountable for this including knowledge gaps in linking 'omics alterations to phenotypic alterations (i.e. health consequences) and in using 'omics quantitatively. This is closely related to the questions of 'what are background effects', 'what is normal'? Background effects can be determined for each specific study individually, but between-study comparability will be enhanced by establishing a generic background, that will be species- and tissue-specific. Even though a generic background will be less sensitive than a study-specific background, a deviation from the generic background, will clearly indicate a deviation from the healthy state. Establishment of species- and tissue-specific generic background levels will also serve to enhance the biological understanding of 'omics data which will further facilitate their acceptability in a regulatory context.

Voting session

After the plenary session in which the outcomes of the World Café sessions were summarised, all meeting participants were invited to take part in an indicative vote to prioritise the proposed activities for recommendation as potential ECETOC actions and/or Cefic LRI research projects. Apart from the hosts of the meeting, all represented affiliations were granted six votes each.

Participants interested to be involved in the development of any of the proposed activities were asked to please write their name on the corresponding A3 sheet of proposed activity title.

Figure 1 presents the outcome of the indicative vote, distinguishing between representatives from industry, academia, regulators / authorities, and consultancies, further indicating the suggested form of LRI or ECETOC activity.

Close of the meeting

In closing the ECETOC and Cefic LRI 2020 Human Health and Exposure Sciences Scoping Meeting, Olivier de Matos (ECETOC Secretary General) thanked all participants for their valuable contributions. The outcome of the meeting will enable ECETOC and Cefic LRI to define areas where specific action would be most important. The proposed activities that were prioritised during the meeting will be presented to the ECETOC Scientific Committee and the Cefic LRI Issue Team for evaluation and decisions on further progression as ECETOC action and/or Cefic LRI research projects.
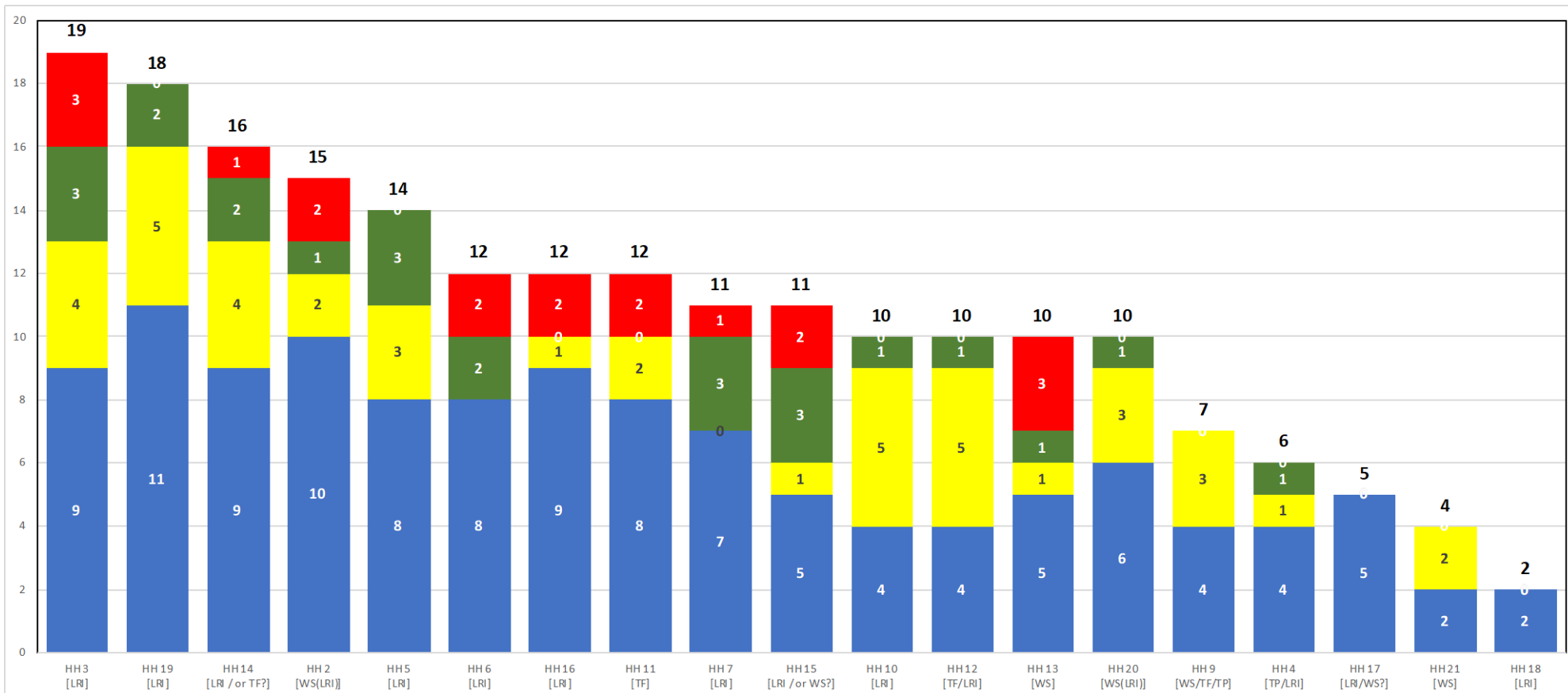
Figure 1: 2020 ECETOC and Cefic LRI Human Health and Exposure Sciences Scoping Meeting: Outcome of the indicative vote (see next page for list of HH codes of proposed activities) Blue = Industry; Yellow = Academia; Green = Regulator; Red = Consultant

Footnote to Figure 1: List of HH Codes of 2020 Human Health and Exposure Sciences proposed activities in numerical order

HH 2: A consensus generic kinetic model for *in vitro* to *in vivo* extrapolation [WS]

HH 3: Mining the developmental toxicity biomarker genome in the zebrafish embryo test [LRI]

HH 4: Building a database of dose-response data as a basis for gaining generic information on dose-response behaviour [TP/LRI]

HH 5: Inflammation as the key player in the development of an integrated AOP network for lung toxicity and disease [LRI]

HH 6: Prediction of carcinogenic potential of agrochemicals using mechanistic information: exploration of quantitative approaches [LRI]

HH 7: Improved interpretation of toxicological potential of chemical substances through mathematical modelling [LRI]

HH 9: Reality-check for risk numbers underlying the health risk assessment of carcinogenic substances [WS, TF, TP, ExpG]

HH 10: Control of exposure to SVHCs in a connected workplace [LRI]

HH 11: Building a common template for reporting the uncertainty in tiered exposure assessment [TF]

HH 12: Grouping of (multiple) chemicals for co-exposure assessment [TF/LRI]

HH 13: Tracking chemicals in supply chains to reduce uncertainty in chemical risk assessment [WS]

HH 14: Awareness of benefits of chemicals and acceptance of exposures [LRI / or TF?]

HH 15: The challenge of exposure estimation of substances in plastic articles under REACH: use the FCM experience to enable and improve exposure estimation methods [LRI / or WS?]

HH 16: Use of the fish embryo model as a screening tool for early human toxicity assessment: exposure methodologies and applicability domains [LRI]

HH 17: A new tool for risk assessment: The Quantitative Genetic Toxicology [LRI]

HH 18: Refinement of interspecies default assessment factor based on REACH data [LRI]

HH 19: Expansion of a regulatory accepted *in vitro* testing battery for DNT evaluation [LRI]

HH 20: 'Omics thresholds of non-adversity [WS/LRI]

HH 21: Maximising the value of new toxicity screening models to better inform both ecological and health endpoints [WS]