PROCEDURE FOR ALLOCATION OF NEW INSECTICIDAL MATERIALS TO THE MOA CLASSIFICATION

IRAC

Insecticide Resistance Action Committee

IRAC maintains the MoA Classification scheme as the definitive, globally recognised, ultimate authority on insecticide modes of action. In order to provide the best possible information for resistance management purposes, IRAC also issues regular updates of the scheme, in which newly introduced insecticides are allocated to an appropriate MoA classification group and structural sub-group, and in which re-classification or the correction of errors or anomalies for specific insecticidal agents is undertaken considering definitive new information. This document details how these processes are administered by IRAC.

Who is responsible for the process within IRAC?

The IRAC MoA Team comprises technical representatives of the member companies with expertise in insect toxicology, pharmacology or biochemistry. All IRAC companies are eligible to contribute technical expertise to the group. The group meets regularly to consider the content and detail of the MoA scheme and makes proposals on significant additions, deletions or reallocations of insecticidal agents within the scheme for consideration by the IRAC Executive.

Why and how often is the scheme updated?

New versions of the scheme are issued periodically as necessary, as a result of the MoA Team's consideration of new information. The introduction of major new MoA groups or the reallocation of insecticidal agents or groups would merit the issue of a new version (vN). Minor changes or corrections that do not significantly impact the scheme are undertaken automatically at intervals as necessary, and sub-versions are issued (vN.n). New sub-versions may be issued up to several times per year as required, while new full versions are not anticipated more than once per year. The potential impact of proposed significant changes on derived versions of the scheme around the world is fully appreciated, especially in countries where MoA labelling of products is used. The MoA team is cognisant of these impacts and revisions are only proposed when the evidence for change is scientifically compelling.

What evidence is needed to support MoA classification of an insecticidal agent?

Proposals for additions to the MoA scheme or for amendments to the current scheme should be submitted to the IRAC MoA team (details below). These proposals will be considered by the Team and a decision on the outcome will be provided to the proposer in due course. Published material in high quality, front line, peer-reviewed, scientific journals is especially useful as a source of information for consideration by the team, and those companies, bodies or individuals submitting proposals for consideration by the team are strongly encouraged to provide such information wherever possible. Corroborating information is also especially welcome. Unpublished material may be submitted in evidence, and the MoA team will interpret this appropriately.

Several types of data can be used to establish MoA (including the activation of pro-insecticides to their actives). Convincing evidence to support the MoA hypothesis is needed. This includes the demonstration of a clear target effect (activation, inhibition, or modulation) at concentrations

that can reasonably be expected in the intoxicated organism. Preferably, these data may be corroborated by physiological and/or symptomology studies to link insect mortality to the effect on the target site. A positive structure-activity correlation of *in vitro* efficacy with insecticidal potency, and/or target site mutations conferring resistance are required to further substantiate the proposed MoA.

What are the criteria for establishing MoA Sub-groups?

Sub-groups represent distinct chemical classes that are believed to have the same MoA but are different enough in chemical structure or mode of interaction with the target protein that the chance of selection for either metabolic or target-site cross-resistance is reduced compared to close analogs. Sub-groups may also distinguish insecticidal agents that are structurally similar but known to bind differently within the target or to have differential selectivity among multiple targets. Evidence supporting lack of cross-resistance between existing compounds within the Group and the new active ingredient submission must be provided to support sub-grouping. This should include bioassay based studies and provide quantifiable resistance ratios between susceptible and resistant strains.

The cross-resistance potential between sub-groups is higher than that between different groups, so rotation between sub-groups should be avoided. In exceptional circumstances (i.e., where effective registered insecticides from other mode of action groups are unavailable) rotation may be considered following consultation with local expert advice and where cross-resistance does not exist. These exceptions should not be considered sustainable resistance management strategies, and alternative options should be sought to maintain pest susceptibility.

How are decisions made by the MoA Team?

Given the definitive nature of the IRAC MoA scheme, the MoA Team regards it as an absolute priority that the highest levels of scientific integrity are always employed in the consideration and discussion of allocation of insecticidal agents. In general, agreement on allocation of an insecticidal agent is usually arrived at through consensus within the Team, following detailed discussion. Major decisions, for example the introduction of new MoA classes or sub-classes are proposed to the IRAC Executive for ratification. If the Team cannot agree it may choose to place the case with a panel of external MoA experts to gain their written opinion before reconsidering the case. The composition of the expert panel is agreed in advance by the Team. If after reconsidering the particular case the team is still in disagreement, the matter will be passed to the IRAC Executive for further consideration. Where individual members of the Team are subject to a conflict of interests through company affiliation or other interests, they may choose to withdraw from discussion of particular insecticidal agents as they consider appropriate.

How long does this process take?

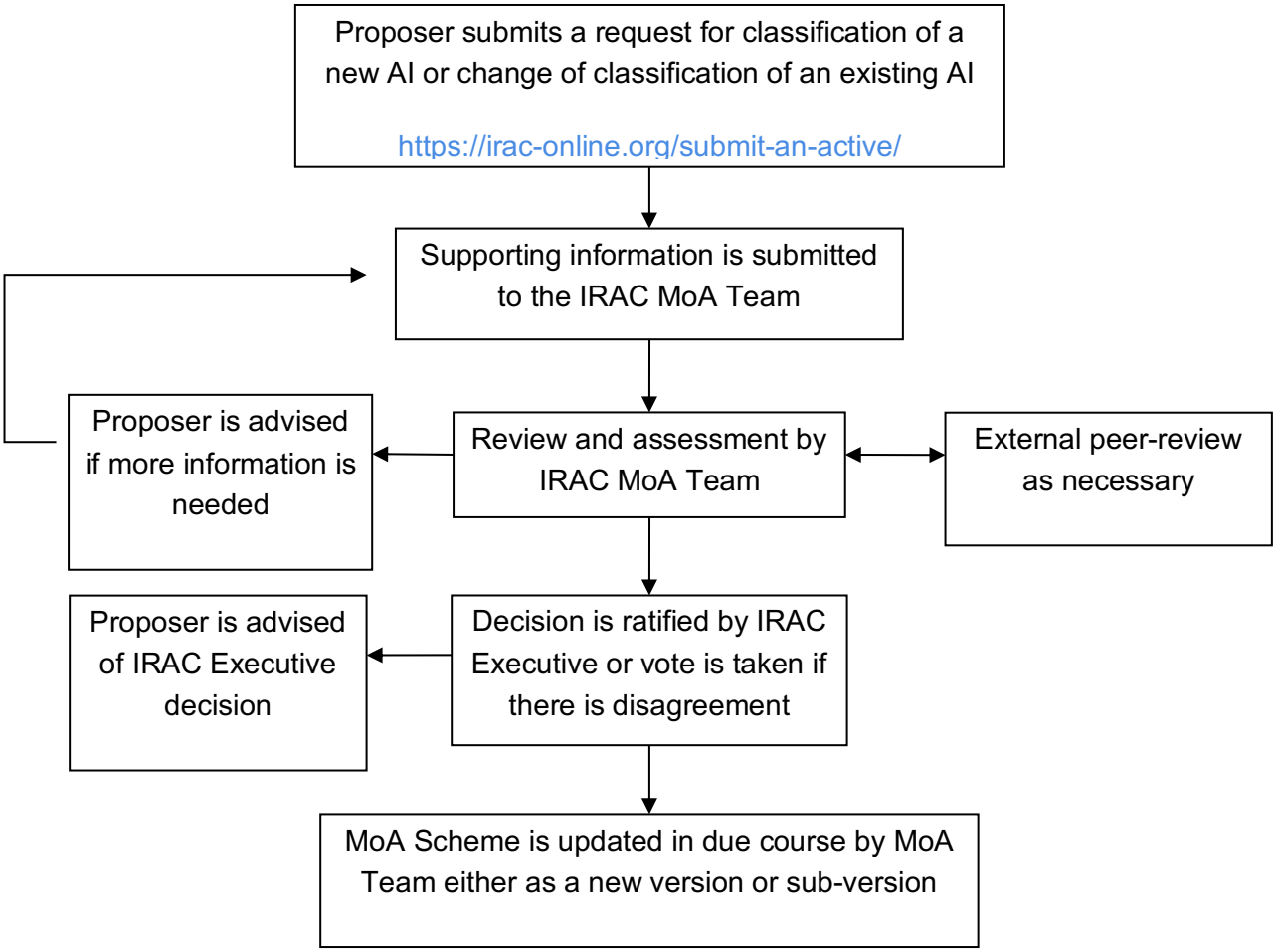
The MoA Team has a duty to make a definitive decision on allocation of an insecticidal agent as quickly as possible following receipt of appropriate supporting evidence. For straightforward

cases that do not require external consultation it should generally be expected that the Team could provide feedback to proposers within 3 months. The need for external consultants may extend the process to 6 months.

To whom should proposals be sent?

Proposals for new insecticidal agents or for changes to the current IRAC MoA scheme should be submitted to the IRAC MoA Team via the IRAC International Coordinator. A link to the coordinator is provided on the IRAC website (www.irac-online.org) at the bottom of each page under 'Contact'. Alternatively, the online request can be completed at http://www.irac-online.org/submit-an-active/

Procedure for updates to IRAC MoA Classification Scheme



MoA Classification Guidance Matrix

Supporting Evidence for Classification	Links
1. Existing Group	
a. Existing Subgroup / no Subgroup	
• Demonstration of a clear effect (activation, inhibition, or modulation) on the target / signal transduction pathway at concentrations that can reasonably be expected in the intoxicated organism	
• A positive structure-activity correlation of *in vitro* efficacy with insecticidal potency and/or • Target site mutation(s) supporting the proposed MoA	https://irac-online.org/documents/established-insecticide-target-site-mutations/?ext=xls
• Physiological and/or symptomology studies to link insect mortality to the effect on the target site / signal transduction pathway	
b. New Subgroup (additional evidence required)	
• Distinct chemical / biological class*	
Evidence supporting lack of cross-resistance between existing compounds within the Group and the new active ingredient: • Quantifiable resistance ratios between field-relevant susceptible and resistant strains • *In vitro* studies (optional)	resistance profiles of relevant pests incl. references https://irac-online.org/pests/
* Sub-groups may also distinguish insecticidal agents that are structurally similar but known to bind differently within the target or to have differential selectivity among multiple targets.	
2. New Group	
• New chemical / biological class	
• Demonstration of a clear effect (activation, inhibition, or modulation) on the target / signal transduction pathway at concentrations that can reasonably be expected in the intoxicated organism	
• A positive structure-activity correlation of *in vitro* efficacy with insecticidal potency and/or • Target site mutation(s) supporting the proposed MoA	
• Physiological and/or symptomology studies to link insect mortality to the effect on the target site / signal transduction pathway	
• Clear differentiation from existing sites in a known target / signal transduction pathway is required if activity on a new site in an existing target / signal transduction pathway is claimed: this might include experimental evidence that the insecticidal agent binds to a unique site of an existing target which is not impacted by mutations conferring resistance to the existing target	searchable online version of the MoA Classification https://www.irac-online.org/modes-of-action/
3. Unknown Mode of Action	
If there is insufficient evidence supporting a defined Mode of Action, insecticidal / acaricidal agents can be included in the classification scheme in the Unknown Mode of Action category they fall under: compounds, UN; bacterial agents, UNB; extracts and crude oils, UNE; fungal agents, UNF; mechanical and physical disruptors, UNM; peptides, UNP; viruses UNV	

Taken from the MoA Classification v10.1

https://www.irac-online.org/modes-of-action/