PQT/VCP Executive Summary of Prequalification Decision

Fludora Co-Max

(Flupyradifurone and Transfluthrin Space Spray – Indoors and Outdoors)

Prequalification Unit – Vector Control Products Assessment (PQT/VCP)

Regulation and Prequalification Department (RPQ)

Access to Medicines and Health Products (MHP)

World Health Organization (WHO)

1 Introduction

WHO's Prequalification Unit, Vector Control Product Assessment team (PQT/VCP) assesses vector control products and public health pesticide active ingredients to determine their acceptability and that they can be used safely, effectively and are manufactured to a high-quality standard. This is done by assessing product dossiers, inspecting manufacturing sites, and supporting quality-control testing of products. Products that meet prequalification requirements are added to the WHO list of vector control products.

WHO prequalification of vector control products primarily benefits populations most affected by vector-borne diseases by facilitating access to these prevention focused tools. The vector-borne diseases include malaria, and neglected tropical diseases such as Dengue, Chikungunya, Zika, Chagas, Lymphatic filariasis, Leishmaniasis, Human African trypanosomiasis, Onchocerciasis and Schistosomiasis.

This Executive Summary document conveys the decision for prequalification of the product Fludora Co-Max manufactured by Bayer SAS (PQ Ref# 008-007) in conjunction with the Letter of Prequalification. The PQT/VCP Decision Document presents the complete assessment. In some cases, the PQT/VCP Executive Summary may be published in advance of the PQT/VCP Decision Document.

2 Product Identification

Fludora Co-Max, is formulated as an emulsion oil in water (EW) and contains the active ingredients Flupyradifurone (26.3 g/L) and Transfluthrin (52.5 g/L). The product is packaged in 1L (or 5L) polyethylene bottles and is intended to be used for space spray applications (indoors and outdoors) in the course of *Aedes spp.* and *Culex spp.* mosquito vector control programs. The product is intended to be applied at a target application rate of 2.5 g/ha flupyradifurone + 5 g/ha transfluthrin for outdoor uses and 131 mg/1000 m^3 flupyradifurone + 263 mg/1000 m^3 transfluthrin for indoor uses.

Fludora Co-Max may be applied using hand-held, backpack, portable & truck mounted Ultra Low Volume Application (ULV) sprayers and portable and vehicle mounted thermal fogger.

3 Assessment of Quality

3.1 Chemical and Physical Properties

Data on the chemical and physical properties of the active ingredients and the product Fludora Co-Max were provided. These data were obtained from studies conducted according to established standards and/or Good Laboratory Practices (GLP) and are considered complete. Product specific properties are summarized in Table 1. The WHO Specification 987+741 EW (September 2019) is available for use in support of QA/QC testing.

The sources of active ingredients are supported by existing WHO specifications.

Data on the manufacturing process and product composition for Fludora Co-Max have been provided and are adequate. The product is formulated in Barranquilla, Colombia and Samutprakarn, Thailand.

The identified reference methods in Table 2 are appropriate for the determination of the active ingredient content in the product.

The quality component of the dossier is considered complete, and the assessment of the submitted information on quality supports the prequalification of the product.

Table 1 Chemical and Physical Properties for Fludora Co-Max			
Data Requirement	Study Number	Test Method ID	Result
Active ingredient	Mo6043 GLP Study	MV 156 validated analytical method (Validation study: Mo6044)	flupyradifurone concentration: initial: 26.75 g/L after 2 weeks at 54 °C: 26.19 g/L certified limits: 23.7 g/L – 28.9 g/L transfluthrin concentration: initial: 54.79 g/L after 2 weeks at 54 °C: 53.75 g/L certified limits: 47.3 g/L – 57.8 g/L One batch was analysed in three replicates and two parallel injections.
pH (1% aqueous dilution and undiluted formulation, initial and after 2 weeks at 54 °C)	Mo6043 GLP Study	SOP-PR-005 in compliance with CIPAC MT 75.3	1% aqueous dilution measured pH values: initial: 6.4 after 2 weeks at 54 °C: 6.1 undiluted formulation measured pH values: initial: 6.1 after 2 weeks at 54 °C: 6.1 pH range 5 to 9
Emulsion stability	Mo6043 GLP Study	CIPAC MT 36.3	Emulsion stability was tested at concentrations of 0.5 and 10 % v/v using CIPAC water A and D. Tests were carried out under normal conditions, after 1 week at 0 °C and after 2 weeks at 54 °C. A milky, turbid emulsion was obtained without sediment and oil at almost each testing time. In case of testing after 1 week at 0 °C and after 2 weeks at 54 °C, after 24 h some re-emulsifiable separation was observed. Requirement: no cream after 30 min. and re-emulsification should be complete after 24 h.
Pourability	Mo6043 GLP Study	CIPAC MT 148	Measured values: • Initial: o before rinsing : 2.23% o after 1st rinsing : 0.26 % o after 2nd rinsing : 0.16% • After 2 weeks at 54 °C: o before rinsing : 4.14%

Table 1 Chemical and Physical Properties for Fludora Co-Max			
			o after 1st rinsing : 0.28 % o after 2nd rinsing : 0.22% Acceptable limit max. 5% residue
Persistent foam	Mo6043 GLP Study	CIPAC MT 47.2	Persistent foam was tested at 10 % v/v concentration using CIPAC Water D. The test was carried out on initial samples and on samples kept for 2 weeks at 54 °C. In both cases the following result was obtained: after 10 sec 2 ml of foam after 1 min 2 ml of foam after 3 min 0 ml of foam after 12 min 0 ml of foam Acceptable limits: max. 30ml foam after 1 minute
Storage stability for 1 week at 0 °C	Mo6043 GLP Study	CIPAC MT 39.3	No significant changes for the test item were observed after storage for 1 week at 0 °C.
Storage stability for 2 weeks at 54 °C	Mo6043 GLP Study	CIPAC MT 46.3	No significant changes for the test item were observed after storage for 2 weeks at 54 °C. flupyradifurone concentration: initial: 26.75 g/L after 2 weeks at 54 °C: 26.19 g/L (-2.1%) transfluthrin concentration: initial: 54.79 g/L after 2 weeks at 54 °C: 53.75 g/L (-1.9%) Requirement: after storage at 54 ± 2 °C for 2 weeks the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage.

Table 2. Details of the analytical method used to determine flupyradifurone and transfluthrin in Fludora Co-Max	
Single Method Quantification of Flupyradifurone and Transfluthrin	For the analysis of flupyradifurone and transfluthrin content the company used a fully validated HPLC method (GLP Study number Mo6044). Determination by HPLC with UV detection according to the analytical method MV156.
Quantification of Flupyradifurone	987/EW/M/3
Quantification of Transfluthrin	741/VL/M/3, CIPAC Handbook L, p.130

4 Assessment of Safety

The applicant submitted an exposure and risk assessment for Fludora Co-Max. The submitted risk assessment was conducted according to the WHO "Generic risk assessment model for indoor and outdoor space spraying of insecticides; second edition, 2018".

PQT/VCP conducted its own hazard, exposure and risk assessments of Fludora Co-Max and the active ingredients flupyradifurone and transfluthrin using the WHO "Generic risk assessment model for indoor and outdoor space spraying of insecticides; second edition, 2018".

4.1 Acute Toxicity

Acute toxicity conducted with the formulated product Flupyradifurone + Transfluthrin EW 78.7 (26.3+52.5 g/L) are summarized below in Table 3. Fludora Co-Max is practically non-toxic via the oral, dermal and inhalation routes of exposure. It is neither an eye nor a skin irritant and is not a dermal sensitizer.

Table 3. Acute Toxicity of Fludora Co-Max.				
Route of Exposure	**Species**	**Toxicity**	**GHS [a] Category**	**Reference**
Oral	Rat	LD_{50} = 2000 mg/kg	5	Weisz, 2016
Dermal	Rat	LD_{50} = >2000 mg/kg	5	Weisz, 2016
Inhalation	Rat	LC_{50} = > 3.55 mg/L	3	Rosos-Matting, 2016
Dermal irritation	Rabbit	Non-irritant	None	Weisz, 2016
Eye irritation	Rabbit	Mild irritant	2B	Weisz, 2016
Dermal sensitization	Mouse	Non-sensitizer	Not applicable	Weisz, 2016

[a] GHS (Globally Harmonized System)

4.2 Safety Conclusions

The use of Fludora® Co-Max as space spray (indoors and outdoors) for vector control does not present any unacceptable risk for operators, residents, residents working as operators, or to newborn, children and toddlers.

The risk ratios are below 1 for all operator's exposure scenarios (mixing/loading, spray applications and washing and maintenance of spray equipment) under the guideline scenario where workers wear appropriate personal

protective equipment (PPE). Under the lax scenario where workers do not wear appropriate PPEs, risk ratios are also below 1 for all operator exposure scenarios, except for operators exposed to one of the active ingredients (transfluthrin) when using handheld equipment indoor (risk ratio= 1.8) and outdoor (risk ratio = 4.6).

The risk ratios are below 1 for all residential exposure scenarios via dermal (touching contaminated surfaces), oral (ingestion of contaminated food stuff) for adults, children, toddlers, and infants and hand-to-mouth activity for toddlers as well as via breast milk for infants and newborns. The risk ratios are also below 1 for residential exposure scenarios for bystanders (via inhalation exposure to spray outdoors), adults, children, toddlers and infants.

It is highly recommended that label instructions are strictly followed, and personal protective equipment is worn accordingly.

The safety assessment of the submitted information supports the prequalification of the product.

5 Assessment of Efficacy

5.1 Background

The primary purpose for the use of a pesticide is the control of a pest, including disease transmitting vector. Vector control tools, including formulated pesticides, which provide effective management/control of vectors, may be used as part of a resistance management program. Vector control products for use in public health are a component of Integrated Vector Management (IVM), which is a program that relies on a suite of diverse interventions and implementation of best practices to manage the vector and chemical/behavioral resistance.

5.2 Efficacy Conclusions

Assessment of all the submitted efficacy studies performed in lab, semi-field, and field settings revealed that there is sufficient evidence to demonstrate that Fludora Co-Max meets the efficacy requirements for prequalification. These efficacy studies were performed according to recommended protocols using different mosquito species and strains from different countries.

6 Labelling

The proposed Declaration of Labelling has been reviewed by PQT/VCP and found to be consistent with the supporting information.

7 Post-Prequalification Commitments

There are no additional post-prequalification commitments associated with this decision of prequalification.

8 Pre-Qualification Listing Decision

The review of the dossier submitted for the product Fludora Co-Max has been completed by PQT/VCP. The results of the assessments show the product is safe and effective when used according to the directions for use on the label. The product is allowed inclusion on the list of prequalified vector control products.