REGULATED PRODUCTS SAFETY ASSESSMENT

Safety Assessment on the Safety and Efficacy of the Authorised Feed Additive Patent Blue V, for Its Use in All Non-Food Producing Animals

Food Standards Agency[1], Food Standards Scotland[2]

[1] Regulated Products Risk Assessment, Food Standards Agency, UK, [2] Risk Assessment, Food Standards Scotland, UK

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FSA Research and Evidence

Food Standards Agency (FSA) and Food Standards Scotland (FSS) assessed the authorised feed additive Patent Blue V (2a131) for use in non-food-producing animals under Article 12A(1) of assimilated Regulation (EC) No 1831/2003. A renewal application (July 2022) could not be fully supported by the current applicant following a change of ownership, and the renewal assessment ceased with the coming into force of the Food and Feed (Regulated Products) Regulations 2025. FSA and FSS noted that EFSA had published an unfavourable opinion on this product citing unresolved safety concerns. The FSA and FSS continued the assessment with the available information under Article 12A(1) of assimilated Regulation (EC) No 1831/2003.

To support the FSA and FSS in evaluating the application, the Advisory Committee on Animal Feedingstuffs (ACAF) was asked to review the dossier and the supplementary information from the applicant at the time.

The ACAF concluded that the additive was not equivalent to the additive originally authorised, and that due to insufficient information, the additive was not fully characterised. The ACAF could not discard the aneugenicity potential of the additive, and could therefore not conclude on the safety for the target species of Patent Blue V. It should be considered a potential skin and eye irritant, and a potential respiratory sensitiser.

No evaluation of safety for the consumer, safety for the environment or efficacy was required for an additive proposed for use in non-food producing animals.

FSA and FSS agree and accept ACAF's advice on the safety of the additive Patent Blue V.

This safety assessment represents the opinion of the FSA and FSS.

This is a joint FSA and FSS publication.

1. Introduction

The FSA and FSS have undertaken an assessment for the authorised feed additive Patent Blue V (2a131[1]), (Versele-Laga NV, Kapellestraat 79, 9800 Deinze, Belgium), under Article 12A(1) of assimilated Regulation (EC) No 1831/2003 (EC, 2003) in the category of 'sensory additives' and functional group 'colourants, substances that add or restore colour in feedingstuffs' for its use in all non-food producing animal species.

The application for Patent Blue V was submitted to the FSA and FSS in July 2022 for renewal of its authorisation. In December 2023, a request for further information was issued to the applicant, who responded in January 2024 with a consolidated dossier. The applicant also indicated that, owing to a change in ownership of the authorisation, they were unable to address some of the queries raised by risk assessors. In April 2024, EFSA issued an unfavourable opinion on the additive, highlighting concerns regarding its safety. The renewal application ceased as a result of the changes to renewal applications in the Food and Feed (Regulated Products) (Amendment, Revocation, Consequential and Transitional Provision) Regulations 2025) (UK, 2025). However, in the light of the EFSA 2024 opinion FSA and FSS continued to assess the product under Article 12A(1) of assimilated Regulation No 1831/2003 using the available information on Patent Blue V.

To support the FSA and FSS in evaluating the application, the Advisory Committee on Animal Feedingstuffs (ACAF) was asked to review the dossier and the supplementary information from the applicant at the time. The principles of assimilated Regulation (EC) No 1831/2003, assimilated Regulation (EC) No 429/2008, and the FSA/FSS guidance for the evaluation of feed additive applications, have formed the basis and structure for the assessment.

This safety assessment represents the opinion of the FSA and FSS.

1 Previously authorised without a time limit in accordance with Directive 74/181/EEC and assimilated Regulation (EC) No 358/2005 under the ID code E131.

Table 1. Table showing products included in this assessment

Title	Product type	Intended use/s	Intended species or categories of animals
Patent Blue V (2a131)	Feed additive	Sensory - Colourant	All non-food producing animals

2. Assessment

2.1. Previous assessments and authorisations

Under assimilated Regulation (EU) No 643/2013, the additive is currently authorised in GB for its use in all non-food producing animal species (EU, 2013).

In the EU, the additive's authorisation was repealed by Commission Implementing Regulation (EU) 2025/2543, adopted on 11 December 2025, which also denied the renewal of the additive's authorisation (EU, 2025).

The European Food Safety Authority (EFSA) published an opinion in 2024 as part of the process of renewal of authorisation of the additive (EFSA FEEDAP Panel, 2024). The FEEDAP panel could not conclude on the safety of the additive for the target species as its genotoxicity potential could not be ruled out. The additive did not require additional demonstration of efficacy.

2.2. Section II: Identity, characterisation and conditions of use

The additive consists of a single active substance, Patent Blue V, which is a calcium or sodium salt of [4-(α-(4-diethylaminophenyl)-5-hydroxy-2,4-disulfophenyl-methylidene)2,5-cyclohexadien-1-ylidene] diethylammonium hydroxide inner salt. It also contains subsidiary colouring matters and uncoloured components such as sodium chloride, sodium sulphate, and/or calcium sulphate.

Patent Blue V is produced by chemical synthesis in a single-step reaction. This involves condensation (using urea as a catalyst) and sulfonation of N,N-diethylaniline with 3-hydroxybenzaldehyde under acidic conditions (sulfuric acid) to form the leuco compound. The leuco form is then dissolved in ammonia and oxidised with manganese dioxide in phosphoric acid. The oxidised product is neutralised with sodium hydroxide and precipitated using hydrochloric acid combined with either sodium chloride (to obtain the sodium salt) or calcium chloride (to obtain the calcium salt).

The reaction is controlled by ultraviolet light. The resulting precipitate is filtered, and the wet press cake is dried at 180°C, yielding a dark blue powder.

The applicant stated the additive currently aligns with the authorised specification values of minimum 90% colouring matters (sodium, calcium or potassium salts) and a maximum of 1% leuco base. Data submitted from several batches showed a different specification, with a minimum of 86% and up to 4% leuco base. The Committee noted that this discrepancy shows the formulation of the product submitted as part of the application for renewal does not comply with currently approved specifications. Table 2 shows identification values for the product as provided by the authorisation holder.

Table 2. Identity table for solid formulation of Patent Blue V

Composition	
Pure dye content	86 – 89%
Chlorides, sulphates, moisture	10 – 11%
Leuco base	Up to 4%

Physicochemical properties	
Appearance	Dark blue powder
Dusting potential	Not provided
Particle size distribution	> 100 µm – 56.91% < 45 µm – 7.87% < 1 µm – Not provided
Max water solubility	50 g/L at 20^{O}C

No impurity testing was provided with the dossier. The ACAF noted it is required for additives produced through chemical synthesis to test for the presence of any chemicals used or intermediate products that may remain in the final product.

Particle size distribution was assessed by sieve analysis on one batch, and no dusting potential analysis was provided. The ACAF noted the use of laser diffraction in several batches would have been needed to fully characterise the particle size distribution of the additive. The Committee did not agree with the authorisation holder's claim that the percentage of particles under 45 µm (7.87%) exempted them from the requirement of providing data on dusting potential.

The conditions of use for Patent Blue V as proposed by the applicant are presented in Table 3. The Committee did not raise concern over the proposed conditions of use.

Table 3. Conditions of use of Patent Blue V proposed by the applicant

Patent Blue V			
Species or category of animal	Min. content in complete feed (12% moisture)	Max. content in complete feed (12% moisture)	Withdrawal period
All non-food producing animals	-	250 mg/kg	-

Other provisions and additional labelling considerations	
Directions for use	May be added directly to the feedingstuffs as a powder or dissolved in water.

2.2.1. Conclusions on identity, characterisation and conditions of use

The Committee concluded that the additive presented in the renewal application was not equivalent to the additive originally authorised. Insufficient information on impurities and physicochemical properties was presented, and therefore the additive was not fully characterised. Aside from those previously listed, the Committee raised no further concerns regarding the identity, characterisation and conditions of use.

As part of the assessment of the authorised additive Patent Blue V based on the available information, FSA and FSS accept the Committee's advice on the identity, characterisation and conditions of use.

2.3. Section III: Safety

2.3.1. Safety for the target species, consumer and the environment

No consideration of safety for the consumer and the environment is required for additives used in non-food producing animals.

In their 2024 opinion, EFSA reviewed the genotoxicity data previously assessed in 2013, considering the updated guidelines (2021; EFSA FEEDAP Panel, 2017)) and confirmed there is no concern regarding gene mutations or structural chromosomal aberrations. The Panel did highlight that the earlier dataset did not address the additive's potential to induce numerical chromosomal damage, and no new genotoxicity studies on the additive were submitted.

The applicant provided an extensive literature review, in which only three relevant studies were identified, including EFSA's 2013 opinion (EFSA FEEDAP Panel, 2013). The Committee agreed the literature review had been carried out following the general requirements listed in Guidance. One study, (Husunet et al., 2022) did not show mutagenicity in the in vitro micronucleus test and bacterial reverse mutation assays used, although

the latter used only strains TA98 and TA100, therefore not covering all recommended strains for all possible mutation types. However, a significant micronucleus formation at high doses and longer treatment was observed, suggesting the potential for aneugenicity remains.

To address these concerns, FSA and FSS asked the applicant to provide the original studies submitted during the initial authorisation process, however, the applicant was unable to supply these studies. ACAF reviewed the available evidence but without the original studies they advised that they were unable to reach a conclusion on the additives' safety to the target species due to the potential for aneugenicity.

FSA and FSS accept the ACAF advice and therefore cannot conclude on the safety of the additive for the target species, given the potential for aneugenicity cannot be resolved.

2.3.2. Safety for the user/worker

The applicant stated that no data are available for the additive regarding effects on the respiratory system, eyes and skin. The literature review did not reveal any new relevant data regarding the safety of the additive for users/workers. As a user of the product and not a manufacturer, the applicant provided a statement declaring that no adverse effects had been observed over the past 10 years.

In the absence of new data, the Committee advised that the original conclusions on safety for the user/worker are still relevant for Patent Blue V, and that the additive should therefore be considered to be a potential skin and eye irritant, and a potential respiratory sensitiser. Measures should be put in place to minimise exposure.

2.3.3. Conclusions on safety

The FSA/FSS cannot discard the aneugenicity potential of the additive, and therefore cannot conclude on the safety for the target species of Patent Blue V. The additive should be considered to be a potential skin and eye irritant, and a potential respiratory sensitiser. No safety evaluation for the consumer or the environment is required for additives intended to be used in non-food producing animals.

2.4. Section IV: Efficacy

In the context of an Article 12A(1) assessment of an additive already authorised, the FSA/FSS did not carry out a new evaluation of the efficacy of the product. Previous conclusions made on efficacy (EFSA FEEDAP Panel, 2013), are still relevant.

3. Analytical methods evaluation

Conclusions on the analytical methods are presented here as an extract from the Evaluation Report of the European Union Reference Laboratory (EURL) for Feed Additives on the Method(s) of the Analysis Patent Blue V (2a131) (EURL, 2012).

> "For the determination of total colouring matters content of Patent Blue V in the feed additive, the Applicant proposed the internationally recognised FAO JECFA monograph for food additives. Identification and quantification of total colouring matters content of Patent Blue V is based on spectrophotometry at 638 nm in aqueous solution at pH 5, as recommended by Commission Directive 2008/128/EC laying down specific purity criteria concerning colours for use in foodstuffs. The total colouring matters content is quantified using JECFA Procedure 1. The Applicant applied this JECFA method to quantify the total colouring matters content of Patent Blue V in the feed additive and reported acceptable performance characteristics.
>
> The Applicant applied the JECFA method mentioned above for the quantification of total colouring matters content of Patent Blue V in feedingstuffs. The following performance characteristics were reported for a Patent Blue V concentration in feedingstuffs ranging from 2 to 25 mg /kg:
>
> - RSDr ranging from 3.4 to 5.9 %;
>
> - a recovery rate (Rrec) ranging from 83 to 97 %.
>
> The lowest concentration analysed by the applicant was set by the EURL as the limit of quantification (LOQ), to derive a LOQ of 2 mg/kg feedingstuffs.
>
> Based on the experimental evidence and the performance characteristics provided by the Applicant, the EURL recommends for official control the JECFA monograph method - recommended by Commission Directive 2008/128/EC - based on spectrophotometry at 638 nm - for the quantification of total colouring matters content of Patent Blue V in the feed additive and feedingstuffs. However, other colouring substances present in the feedingstuffs may absorb/interfer in the 600-700 nm range, thus influencing the determination of total colouring matters content of Patent Blue V. Whenever the spectrophotometric reported values

> are above the maximum content, an additional chromatographic separation may be required for confirmation."

The FSA/FSS accepts the EURL analytical method evaluation reports. The FSA/FSS determined the analytical methods proposed as appropriate for official controls for this feed additive. The analytical methods were approved in 2012, at the time in which the UK was still an EU member.

4. Conclusions

The FSA and FSS assessed Patent Blue V under Article 12A(1) of assimilated Regulation (EC) No 1831/2003, due to a safety concern for aneugenicity. The ACAF was asked to provide advice on the dossier and supplementary information presented.

The ACAF advised that the additive presented in the original renewal application was not equivalent to the authorised additive, and that due to insufficient information, the additive was not fully characterised. The authorisation holder was given the opportunity to provide further information on safety to the target species, but was unable to submit the requested studies. The ACAF reviewed the available information, but could not discard the aneugenicity potential of the additive, and advised that they could not conclude on the safety for the target species of Patent Blue V. It should be considered a potential skin and eye irritant, and a potential respiratory sensitiser. No evaluation of safety for the consumer, safety for the environment or efficacy was required for an additive used in non-food producing animals.

FSA and FSS agree and accept ACAF's advice on the safety of the additive Patent Blue V.

The FSA and FSS accept the EURL analytical method evaluation reports. The FSA and FSS determined the analytical methods proposed as appropriate for official controls for this feed additive.

This safety assessment represents the opinion of the FSA and FSS.

Abbreviations

Abbreviation	Definition
ACAF	Advisory Committee on Animal Feedingstuffs
EC	European Commission
EFSA	European Food Safety Authority
EURL	European Union Reference Laboratory
FEEDAP	Scientific Panel on Feed Additives and Products or Substances Used in Animal Feed
FAO	Food and Agriculture Organization

Abbreviation	Definition
FSA	Food Standards Agency
FSS	Food Standards Scotland
JECFA	Joint Expert Committee on Food Additives
LOQ	Limit of quantification
Rrec	Recovery rate
RSDr	Relative standard deviation for repeatability

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