

Minor Use and Minor Species Act of 2004 – meeting notes

- Meeting date:** 6 December 2004
- Location:** FDA – Center for Veterinary Medicine; Rockville, Maryland.
- Purpose of meeting:** To discuss the Minor Use and Minor Species (MUMS) Act in the context of providing input to CVM on potential content of forthcoming implementing Regulations to the MUMS Act.
- Attendees:** Andy Beaulieu (CVM – Director, Office of Minor Use and Minor Species), Meg Oeller (CVM – Deputy Director, Office of Minor Use and Minor Species), Jeff Punderson (CVM – Office of the Director, Policy and Regulations Team), Gerald Rushin (American Veterinary Medical Association), David Scarfe (AVMA), John Pitts (American Pet Products Manufacturers Association), Roz Schnick (National Coordinator for Aquaculture New Animal Drug Applications), Dave Erdahl (FWS Aquatic Animal Drug Approval Partnership) & Tom Bell (FWS-AADAP). On the phone: Randy MacMillan (MUMS Coalition & Clear Springs Foods, Inc.) and Gina Valeri (APPMA).
- General Background:** President Bush signed into law, on August 2, 2004, "The Minor Use and Minor Species Animal Health Act of 2004." The "MUMS Act" provides new means by which aquaculturists, and others involved in the rearing of minor species (i.e., any animal other than horses, cows, pigs, dogs, cats, chickens and turkeys), can legally gain access to new drugs. The Act also provides, for those involved in the rearing of major species, new means to gain access to drugs for minor uses in those major species. The MUMS Act contains provisions for: (a) the creation of the Office of Minor Use and Minor Species, (b) research funding incentives, (c) a special designation for drugs for minor uses and minor species (similar to an orphan drug designation for human drugs), (d) a "drug index" list for drugs that have been assessed by a non-FDA expert panel relative to efficacy and safety, allowing for their legal marketing even though not approved, and (e) a "conditional approval" whereby a drug can be legally marketed for a set period prior to all efficacy data being collected.
- Like many laws (Acts) passed by Congress, associated Federal Regulations must be written by the elected Federal agency, and reviewed by the public, before many parts of the law can go into effect. The MUMS Act follows this pattern; the Food and Drug Administration's Center for Veterinary Medicine (CVM) is mandated by the MUMS Act to draft Federal Regulations which will provide the necessary details to assist federal regulators and the public in implementing and complying (respectively) with the new law. To assist CVM in their regulation-writing task, the CVM has indicated their interest in receiving input from stakeholders with ties to minor species and minor uses in major species. The following notes are from just such a meeting (held on 6 December 2004) that had been requested by a group of minor species stakeholders.
- Notes prepared by:** Tom Bell; U.S. Fish & Wildlife Service on 28 January 2005

Meeting notes¹

Introductory comments from Dr. Beaulieu:

-  The MUMS Act, *per se*, carries with it no new funds, and there does not appear to be any designated funds coming in the near future; FY06 may offer even less potential for new funding.
-  The actual delegation of authority down to CVM (from FDA) is forthcoming.
-  All correspondence should be CC'd to Dr. Oeller; she will be Acting Office Director in Dr. Beaulieu's absence.
-  The Office of Minor Use and Minor Species (OMUMS) became "official," as of 28 November 2004, and is hoping to add two additional positions sometime in the future; Jeff Punderson (CVM's Policy and Regulations Team), although not assigned to the OMUMS, will be assisting for the time being in the actual regulation writing.
-  The OMUMS reports directly to the Director of CVM; OMUMS does not fall under CVM's Office of New Animal Drug Evaluation (i.e., the office responsible for the review of INAD and NADA submissions).
-  Time frames for the associated Regulations, as defined in the Act, are very aggressive but are conditional relative to availability of resources. CVM, in spite of not having the funds to add new staff to the OMUMS, is prepared to act on the required timeframes as if they do have the resources.

Statutorily Required* Completion Dates [#] for Specific MUMS Implementing Regulations			
Section Number	Section topic	Date for Proposed Regulations	Date for Final Regulations
573	Designated New Animal Drugs for Minor Use or Minor Species	August 2005	August 2006
572	Index for Legally Marketed Unapproved New Animal Drugs for Minor Species	February 2006	August 2007
571	Conditional Approval of New Animal Drugs for Minor Use and Minor Species	February 2007	February 2008
* requirement conditional relative to availability of resources			
[#] date for publication of regulation in the <i>Federal Register</i>			

Discussion on minor use in major species:

-  Background Information: "Minor use in a major species" pertains to the treatment of diseases that occur very rarely in a major species. The prevalence of the disease may be a function of it being generally rare over the entire population of the major species or it may be rare due to it occurring only within a subsector of the population (e.g., only within a certain strain or race of the population, or only within a small defined geographic area in which the major species is reared).
-  In general, minor use in major species will be more difficult to define in the Regulations than minor species use; CVM will be soliciting comments on how to define minor use in a major species (via the Federal Register and the public docket process).

¹ The following bullets represent paraphrased comments made by attendees of the meeting, except those bullets prefaced with the phrase "Background Information." The background information represents the FWS's interpretation of the MUMS Act and is meant to aid the reader in understanding the relevance of the meeting notes.

-  The minor use in major species “definitions” will likely be independent of human consumption rates.
-  The anticipated market that such a definition will create may indirectly factor into the development of the definition.
-  An essential component of the definition of a particular minor disease in a major species is the disease prevalence (or incidence) rates. Unfortunately, these are not as cut and dried as the definitions of specific rare diseases in humans (in the context of human orphan drugs).
-  Entities representing unique species-groups may be able to help establish disease prevalence rates for each species.
 -  The question was asked (by a stakeholder at the meeting) about the possibility of establishing a pilot period, at the outset of which no specific prevalence rates exist, but during which species industry groups would be required to establish their respective prevalence rates.
-  It appears that Congress had an expectation that economics would enter into the determination of whether a specific disease within a major species qualifies as a “minor disease in a major species.”

Discussion on the “Minor Use and Minor Species Designation:”

-  Background Information: In the Act, it is stated that a sponsor or manufacturer may request CVM to formally classify their drug, when used for a particular claim (e.g. the control of a specific disease in a certain animal species), as a “Designated MUMS Drug.” When CVM does such, that particular sponsor/drug/claim combination then becomes eligible for other benefits as stated within the MUMS Act. Of greatest potential importance, the existence of that particular Designated MUMS Drug essentially precludes any other drug from being “Designated.” The sponsor of any Designated MUMS Drug will be eligible for federal research and development funds and possible tax incentives. Additionally, once the sponsor completes and submits all the necessary studies to establish the drug’s effectiveness and safety, and receives from CVM either a full approval or conditional approval (see below), that drug will be granted 7 years of exclusivity during which time no other sponsor or manufacturer may seek an approval for the same drug/claim combination. The 7-year exclusivity is at least two years longer than the exclusivity provided to a new drug approved which has not been classified as a “Designated MUMS Drug” and the non-MUMS exclusivity applies only to generic copies of the drug. It should be understood that when a drug is classified as a “Designated MUMS Drug,” there is no automatic guarantee of it being approved or conditionally approved. The sponsor must still provide the data to support the drug’s safety and effectiveness, and the data requirements are no less stringent than if the drug were not a “Designated MUMS Drug.”
-  Drugs for all fish species, being minor species by definition, are eligible for “MUMS designation.”
-  All requests for “designation” will be handled sequentially as they are logged into the system (a queue). Individual drug assessments will begin as soon as official delegation of authority has been received by CVM. Actual granting of “designation” will be handled by OMUMS, with potential consultation with other CVM Offices.
-  Just because a drug/company has not received a “designated” MUMS status does not mean that it cannot “beat” a “designated” drug (for the same claim) in gaining a full or

conditional approval. They do not, however, receive the 7-year exclusivity, but instead receive either 5 years (if they submitted “new” data) or 3 years (without “new” data) and only with respect to generic copying.



A sponsor requesting and receiving “designation” for a particular drug/claim is not required to be the one to generate all data; i.e., a sponsor can use public data as in a Public Master File.



A MUMS designation for a drug includes specific label claims. Hence, to gain approval as a MUMS drug, all the label claims noted within the request for designation must be supported within the application for approval.



A request for MUMS designation will not be granted if there currently exists an approved or conditionally approved product for the same claim **or** the same drug for the same claim has already received MUMS designation.



For the time being, prospective applicants can seek guidance on submitting a request for MUMS designation by reviewing FDA’s Orphan Products Designation webpage, which is located at: <http://www.fda.gov/orphan/designat/index.htm>. CVM plans to use these guidance documents as a model for “MUMS designation” guidance.



If an entity is seeking an “all-species” claim under their designation request, and would like to use representative species, they will have to seek CVM’s definition of what species will be required as representatives. This can be accomplished via a Product Development Meeting with CVM.



CVM may allow the sponsoring entity to reduce its claim (spelled-out within their “designation” request) if it can be demonstrated that progress has been made on all other portions of the claim and that the outstanding portion cannot be completed for some unforeseen reason.



Designation will probably require an annual review, reports, etc. to establish progress and retain MUMS designation status. If progress is not deemed acceptable, designation status will be terminated. The determination of “lack of progress” will be made on a “case-by-case” basis.



The MUMS Act, as passed, does not include the tax incentives originally anticipated. All present at the meeting were in concurrence that these are a vital part of the incentive package and should be enacted as soon as possible. It was explained that tax incentives are best put in place by modifying the U.S. Tax Codes, and not the MUMS Act, and doing so would not in any way change any existing portion of the MUMS Act. Such tax incentives, once enacted, could possibly reduce the costs of development by as much as 50%.

Discussion on the Minor Use and Minor Species “Indexing:”



Background Information: The MUMS Act provides an additional means by which drugs may be legally obtained for use with minor species or for minor uses in major species. The Act states that a drug can be placed (by CVM) on a legally-marketed unapproved new animal drug index (MUMS Index). Any drug which has been placed on the “Index” can be legally marketed and used as per its CVM-reviewed label. It should be understood that an “Indexed” MUMS drug does not have an FDA approval of any kind. Hence, the data to support its safety and effectiveness will not have been reviewed in the same manner that it would be for a drug which has gained a full FDA approval or conditional FDA approval.

The assessment of the drug's safety and effectiveness will be accomplished by an FDA-approved expert panel.

 It was assumed, when the MUMS Act was drafted, that any product (i.e., drug) being requested to be included on the "Index" would already be "Drug Listed" with CVM and manufactured in a registered establishment as required by law, and as such, the product would be produced under GMPs (a condition of manufacturing a drug in a registered establishment). Hence, some of the MUMS Act's language may be unclear as to the manufacturing requirements for "Indexed" drugs. The associated Regulations should clarify this.

Index Drug "Expert Review Panel" Comments

 Background Information: as defined by the MUMS Act, an "Expert Review Panel" (comprising subject experts not employed by FDA) will make the judgment call as to whether or not a particular drug should be included on the "Drug Index." The "Expert Review Panel" will review the safety and effectiveness data submitted in defense of the drug's inclusion on the "Drug Index" and will provide their recommendation to FDA. FDA will decide which drugs are eligible to go forward for panel review and whether to accept or reject the recommendations of the "Expert Review Panel."

 The criteria for individual member selection and for panel composition will be in the Regulations.

 A minimum of three experts will likely be required per panel.

 Concern was expressed by a stakeholder in attendance at the meeting about the possibility that "experts" may be on the payroll of the drug's sponsor. CVM stated that Regulations would deal with this situation.

 CVM is considering the possibility that experts would be solicited to have their names placed on a standing list of CVM-recognized experts, from which individual panel members could be drawn for inclusion on a specific expert panel.

 The Regulations will clarify the Panel's responsibilities. It is presently unclear as to whether the Panel will do either the first or both of the following: 1) review and assess the appropriateness and adequacy of the safety and effectiveness data provided to them, and 2) collect the data for their review and assessment.

 The actual formulation (e.g., capsule, liquid) and packaging of the drug may be a consideration for eligibility to be "Indexed"

 At least for aquarium products, an initial assessment of eligibility for indexing will probably include an assessment of the likelihood of diversion of products to human use or food animal use. Examples of formulations for ornamental fish that would cause concern would be antibiotics in capsule form that could easily be diverted to human use or products in 55 gallon drums that could be diverted to food animal use.

 There will probably not be any drugs or drug groups expressly prohibited, via the Regulations, from being included in the "Index."

 CVM will probably not be able to make a generic statement in the Regulations regarding specific consideration for non-food lifestages of food animals.

 For fish reared by the public aquaculture sector (i.e., federal, state, tribal and local governmental resource agencies), the USFWS will develop a white paper for submission to CVM to propose specific sizes/life-stages for fish groups (taxonomic

groupings or whatever) under which size/life-stage animals will be considered non-food lifestages, regardless of whether or not they ultimately will legally enter the human food chain.

 Any combination product (several drugs intentionally mixed during production) intended by the sponsor to be “Indexed”, will probably need to have each drug “Indexed” separately.

 The Expert Panel will need to determine if a combination is more effective and as safe as each of the drugs administered separately but in close sequence.

 The same principles of review will likely apply to “Index” combination drugs as apply to combination products under an NADA, except for the requirement for “adequate and well-controlled studies.”

 As it pertains to environmental safety, aquarium products currently being used by home aquarists will probably not be able to gain categorical exclusion. An Abbreviated Environmental Assessment (EA) will probably be the method by which environmental safety will be demonstrated.

 New products by new manufacturers (those manufacturers with no previously approved products) will probably need a full EA for the manufacturing component of their request for “Indexing.”

 Full EAs may be required for pond-use of “indexed” drugs.

 The Expert Panel will need to recommend specific labeling for each “indexed drug.”

Discussion on the Minor Use and Minor Species “Conditionally-Approved New Animal Drugs:”

 Background Information: The MUMS Act provides for conditionally-approved new animal drugs (conditional approvals). A conditional approval is essentially the same as a full approval, except the submitted application does not contain a complete data set demonstrating the effectiveness of the drug for the intended claim. All other data sets (i.e., human food safety, environmental safety, target animal safety, manufacturing, etc.) are complete and have been accepted by CVM. Relative to the effectiveness data set submitted in a conditional approval, the sponsor/manufacturer needs only to submit sufficient data to demonstrate a reasonable expectation that the drug will be effective for the label claim. However, once the drug is conditionally-approved by CVM, the sponsor has up to 5 years to provide a complete effectiveness data set, representing “adequate and well-controlled studies.” Additionally, over the course of the 5 years, the sponsor must demonstrate progress toward completing the effectiveness data set.

 For the most part, very few new Regulations will be required for conditional approvals, because the process (with the exception of that for the effectiveness data set) is the same as for a full approval. The “standards for assessment” for all technical sections of a conditional approval are exactly the same as for an NADA.

 Once a conditional approval is gained (for a particular drug/claim), INADs for that drug will not necessarily be terminated, especially if the INADs are for different claims or if the INADs are for generating the efficacy data needed by the sponsor to complete the efficacy package (i.e., converting their conditional approval into a full approval).