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(2) *Airworthy Product*: For any requirement in this AD to obtain corrective actions from a manufacturer or other source, use these actions if they are FAA-approved. Corrective actions are considered FAA-approved if they are approved by the State of Design Authority (or their delegated agent). You are required to assure the product is airworthy before it is returned to service.

(3) *Reporting Requirements*: For any reporting requirement in this AD, under the provisions of the Paperwork Reduction Act, the Office of Management and Budget (OMB) has approved the information collection requirements and has assigned OMB Control Number 2120-0056.

#### Related Information

(h) Refer to MCAI Brazilian Airworthiness Directives 2007-11-01 and 2007-11-02, both effective December 12, 2007; and EMBRAER Service Bulletins 170-21-0032 and 190-21-0019, both dated August 10, 2007; for related information.

#### Material Incorporated by Reference

(i) You must use EMBRAER Service Bulletin 170-21-0032, dated August 10, 2007; or EMBRAER Service Bulletin 190-21-0019, dated August 10, 2007; as applicable; to do the actions required by this AD, unless the AD specifies otherwise.

(1) The Director of the Federal Register approved the incorporation by reference of this service information under 5 U.S.C. 552(a) and 1 CFR part 51.

(2) For service information identified in this AD, contact Empresa Brasileira de Aeronautica S.A. (EMBRAER), P.O. Box 343-CEP 12.225, Sao Jose dos Campos-SP, Brazil.

(3) You may review copies at the FAA, Transport Airplane Directorate, 1601 Lind Avenue, SW., Renton, Washington; or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call (202) 741-6030, or go to: <http://www.archives.gov/federal-register/cfr/ibr-locations.html>.

Issued in Renton, Washington, on August 18, 2008.

**Ali Bahrami,**

*Manager, Transport Airplane Directorate, Aircraft Certification Service.*

[FR Doc. E8-19850 Filed 9-5-08; 8:45 am]

**BILLING CODE 4910-13-P**

## DEPARTMENT OF TRANSPORTATION

### Federal Aviation Administration

#### 14 CFR Part 39

[Docket No. FAA-2007-0036; Directorate Identifier 2007-NE-22-AD; Amendment 39-15636; AD 2008-16-18]

RIN 2120-AA64

#### Airworthiness Directives; Rolls-Royce plc RB211-524 Series Turbofan Engines; Correction

**AGENCY:** Federal Aviation Administration, DOT.

**ACTION:** Final rule; correction.

**SUMMARY:** This document makes a correction to Airworthiness Directive (AD) 2008-16-18. That AD applies to Rolls-Royce (RR) RB211-524 series turbofan engines with certain high pressure (HP) turbine disks installed. That AD was published in the **Federal Register** on August 11, 2008 (73 FR 46550). Paragraph (c) in the regulatory section is incorrect. This document corrects that paragraph. In all other respects, the original document remains the same.

**DATES:** *Effective Date:* Effective September 8, 2008.

**FOR FURTHER INFORMATION CONTACT:** Jason Yang, Aerospace Engineer, Engine Certification Office, FAA, Engine & Propeller Directorate, 12 New England Executive Park, Burlington, MA 01803; e-mail: [jason.yang@faa.gov](mailto:jason.yang@faa.gov); telephone (781) 238-7747; fax (781) 238-7199.

**SUPPLEMENTARY INFORMATION:** On August 11, 2008 (73 FR 46550), we published a final rule AD, FR Doc. E8-18102, in the **Federal Register**. That AD applies to RR RB211-524 series turbofan engines. We need to make the following correction:

#### § 39.13 [Corrected]

On page 46551, in the first column, in the Regulatory Section, in the Applicability paragraph (c), in the second line, "with certain high pressure (HP) turbine discs installed" is corrected to read "with high pressure (HP) turbine discs, part numbers (P/Ns)-serial numbers (SNs) FK24651-LAQDY6061 and -LDRCZ10453 to -LDRCZ10720, and -LQDY9903, and -LQDY9924, FK24790-CRCZ6 to -CRCZ25 and -LDRCZ10717 to -LDRCZ14022, UL23166-LQDY6516 to -LQDY8718, UL24561-LQDY6389 to -LQDY6438, UL24994-LQDY6405 to -LQDY8727, UL29472-LAQDY6013 to -LAQDY6092 and -LDRCZ10029 to -LDRCZ10821 and -LDRCZ6000 to -LDRCZ6060 and -LQDY6592 to -LQDY9993, UL29473-CRCZ24 to

-CRCZ25 and -CZ12135 to -CZ12333 and -LAQDY6010 to -LAQDY6088 and -LDRCZ10003 to -LDRCZ15372 and -LDRCZ6001 to -LDRCZ9995 and -LQDY10001 and -LQDY9606 to -LQDY9989, installed".

Issued in Burlington, Massachusetts, on August 28, 2008.

**Marc Bouthillier,**

*Acting Manager, Engine and Propeller Directorate, Aircraft Certification Service.*

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**BILLING CODE 4910-13-P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food And Drug Administration

#### 21 CFR Parts 16 and 1240

[Docket No. FDA-2003-N-0427] (formerly Docket No. 2003N-0400)

#### Control of Communicable Diseases; Restrictions on African Rodents, Prairie Dogs, and Certain Other Animals

**AGENCY:** Food and Drug Administration (HHS).

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is removing its regulation that established restrictions on the capture, transport, sale, barter, exchange, distribution, and release of African rodents, prairie dogs, and certain other animals. We are removing the restrictions because we believe they are no longer needed to prevent the further introduction, transmission, or spread of monkeypox, a communicable and potentially fatal disease, in the United States.

**DATES:** Effective September 8, 2008.

**FOR FURTHER INFORMATION CONTACT:** Philip L. Chao, Office of Policy, Planning, and Preparedness (HF-23), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-0587.

#### SUPPLEMENTARY INFORMATION:

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## I. What Is Monkeypox, and How Did It Spread in the United States?

Monkeypox is a sporadic, zoonotic, viral disease that occurs primarily in the rain forest countries in central and west Africa. (A zoonotic disease is a disease of animals that can be transmitted to humans under natural conditions.) The illness was first noted in a monkey in 1958 (which explains its name), but, in Africa, serologic evidence of monkeypox infection has been found in many other species, including some species of primates, rodents, and lagomorphs. Lagomorphs include animals such as rabbits. African rodents are considered to be the most likely natural host of the monkeypox virus (Ref. 1). In Africa, however, direct viral evidence of monkeypox has been found in only one native African rodent species (a rope squirrel), but this may be due to the limited scope of the ecologic studies that have been done in Africa (Ref. 1).

In humans, monkeypox is marked by rashes that are similar to those seen in smallpox; other signs and symptoms include a temperature at or above 99.3 degrees, chills and/or sweats, headache, backache, lymphadenopathy (a disease of the lymph nodes), sore throat, cough, and shortness of breath (Ref. 2). The disease's incubation period in humans is approximately 12 days (Ref. 3). In Africa, monkeypox has a mortality (death) rate in humans ranging from 1 to 10 percent of the people who become infected, although higher mortality rates have been seen.

In May and June of 2003, public health officials identified an outbreak of human monkeypox in the United States. Epidemiological and traceback investigations by State and Federal agencies revealed that the patients became infected primarily as a result of contact with prairie dogs that had contracted monkeypox from diseased African rodents. The investigations indicated that a Texas animal distributor imported a shipment of approximately 800 small mammals from Ghana on April 9, 2003. This shipment contained 762 African rodents, including rope squirrels (*Funisciurus*

sp.), tree squirrels (*Heliosciurus* sp.), Gambian giant pouched rats (*Cricetomys* sp.), brushtail porcupines (*Atherurus* sp.), dormice (*Graphiurus* sp.), and striped mice (*Hybomys* sp.). Some of these African animals were infected with monkeypox, and laboratory testing confirmed the presence of monkeypox in several rodent species, including two Gambian giant pouched rats, nine dormice, and three rope squirrels (Ref. 23). Of the 762 rodents from the original shipment, 584 were traced to distributors in 6 states. A total of 178 African rodents could not be traced beyond the point of entry in Texas because records were not available (Ref. 4).

Some African rodents made their way to an animal distributor in Illinois who also sold prairie dogs (Ref. 5). The Illinois animal distributor had approximately 200 prairie dogs. Thirty-nine of these prairie dogs, along with one Gambian giant pouched rat, went to another animal distributor in Wisconsin in early May, 2003; it was at this time that several prairie dogs appeared to be ill, and several of the animals died (Ref. 5). By late May, the first human cases began to appear in Wisconsin (including the Wisconsin animal distributor), with other human cases appearing later in Kansas, Missouri, Illinois, Indiana, and Ohio (Refs. 5 and 6).

Of the 200 prairie dogs that were at the Illinois animal distributor, only 93 were able to be traced during the traceback investigation (Ref. 4).

The 2003 monkeypox outbreak in the United States eventually resulted in 72 human cases, with 37 of those cases being laboratory-confirmed (Ref. 7). Most patients had direct or close contact with prairie dogs. For example, 28 children at an Indiana day care center were exposed to 2 prairie dogs that later became ill and died. Twelve of these exposed children reported handling or petting the prairie dogs, and seven of these children later became ill with symptoms that were consistent with monkeypox infection (Ref. 7). In Wisconsin, more than half of the human monkeypox cases occurred through occupational exposure to infected prairie dogs, with veterinary staff being at greater risk of acquiring monkeypox than pet store employees (Ref. 21). The human cases in the United States included children as young as 3 years old, and 19 people were hospitalized, although some were hospitalized primarily for isolation purposes (Ref. 6). The initial signs or symptoms seen in some patients included skin lesions or fever with drenching sweats and severe chills (Ref. 5). Other signs and symptoms seen most often included:

- Headache;
  - Persistent cough;
  - Lymphadenopathy; and
  - Sore throat (Ref. 5).
- Less frequent signs and symptoms included:

- Pharyngitis;
- Tonsillar hypertrophy;
- Tonsillar erosions;
- Malaise;
- Mild chest tightness;
- Diarrhea;
- Myalgias;
- Back pain;
- Nasal congestion;
- Blepharitis; and
- Nausea (Ref. 5).

In general, the human cases in the United States were milder than those seen in Africa (Ref. 6), and patients who had been vaccinated against smallpox appeared to have milder cases compared to those who had not been vaccinated against smallpox. However, two children suffered serious clinical illnesses. One child had severe encephalitis that improved during a 14-day hospital stay, and another child had pox lesions on many parts of her body, including lesions inside her mouth and throat which created difficulty in breathing and swallowing (Refs. 6, 9, and 19). At least 5 patients (3 adults and 2 children) had temperatures greater than or equal to 38.3 °C (100.94 °F) and rashes comprised of 100 or more lesions (Ref. 9). One adult patient remained symptomatic for approximately 5 months; the patient became asymptomatic only after having a corneal transplant (Ref. 9).

## II. How Did We Respond to the Monkeypox Outbreak?

On June 11, 2003, the Director of the Centers for Disease Control and Prevention (CDC) and the Commissioner of Food and Drugs, under 42 CFR 70.2 and 21 CFR 1240.30 respectively, issued a joint order (Refs. 10 and 11) prohibiting, until further notice, the transportation or offering for transportation in interstate commerce, or the sale, offering for sale, or offering for any other type of commercial or public distribution, including release into the environment, of:

- Prairie dogs (*Cynomys* sp.);
- Tree squirrels (*Heliosciurus* sp.);
- Rope squirrels (*Funisciurus* sp.);
- Dormice (*Graphiurus* sp.);
- Gambian giant pouched rats (*Cricetomys* sp.);
- Brush-tailed porcupines (*Atherurus* sp.), and
- Striped mice (*Hybomys* sp.).

The June 11, 2003, order did not apply to the transport of listed animals to veterinarians or animal control

officials or other entities pursuant to guidance or instructions issued by Federal, State, or local government authorities. In addition, under 42 CFR 71.32(b), CDC implemented an immediate embargo on the importation of all rodents (order *Rodentia*) from Africa.

FDA and CDC issued the June 11, 2003, order to address quickly what was then a new and rapidly developing monkeypox outbreak (Ref. 11). As the two agencies became more experienced with the order and more knowledgeable about the monkeypox outbreak, it became apparent that we and CDC needed a regulatory approach to prevent the monkeypox virus from becoming established and spreading in the United States and to modify the June 11, 2003, order, such as creating exemption procedures to accommodate special circumstances. Consequently, on November 4, 2003 (68 FR 62353), FDA and CDC issued an interim final rule that superseded the June 11, 2003, order. The interim final rule created two complementary regulations. First, with respect to certain animals that are in the United States, the interim final rule added 21 CFR 1240.63 entitled "African rodents and other animals that may carry the monkeypox virus." Second, for African rodents that are being imported or offered for import to the United States, the interim final rule added 42 CFR 71.56 that is also entitled "African rodents and other animals that may carry the monkeypox virus." We are responsible for 21 CFR 1240.63, and CDC is responsible for 42 CFR 71.56; both sets of regulations are intended to prevent the further introduction, establishment, and spread of the monkeypox virus in the United States.

We also indicated that we would revoke or amend, as warranted, all or parts of 21 CFR 1240.63 if we concluded that monkeypox is eradicated or adequately controlled so that the virus does not become established in the United States (see 68 FR at 62359).

We issued the interim final rule under section 361 of the Public Health Service Act (PHS Act) (42 U.S.C. 264). Section 361 of the PHS Act gives the Secretary of Health and Human Services (the Secretary) the authority to make and enforce regulations to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or from one State to another State.

### III. What Other Actions Did the Department of Health and Human Services Take?

#### A. Why Did the Interim Final Rule Continue After January 20, 2004?

The preamble to the interim final rule stated that:

Monkeypox is endemic in parts of Africa. Therefore, we do not anticipate revoking the prohibition on import of African rodents and any other animals that the Director of CDC has specified under 42 CFR § 71.56(a)(1)(i). However, FDA will revoke or amend, as warranted, all or parts of 21 CFR § 1240.63 if FDA concludes that monkeypox is eradicated or adequately controlled so that the virus does not become established in the United States. FDA's decision would depend on scientific principles for controlling zoonotic diseases. For example, if the incubation period is known, then it would be prudent to continue the restrictions for a time period that is double the incubation period to ensure that there is little further risk of infection or restarting the monkeypox outbreak. CDC tests on some animals involved in the original April 9, 2003, shipment from Ghana suggest that, insofar as dormice are concerned, the incubation period may be as long as 2.5 months. If FDA rounds this time frame up to 3 months, and then doubles the incubation period, there would appear to be little further risk of infection after 6 months had passed with no further evidence of monkeypox identified, and FDA would be able to take actions to revoke or amend 21 CFR § 1240.63. The last infected animal from the April 9, 2003, shipment that died from monkeypox died on July 20, 2003. There have been no identified monkeypox cases in animals or people in the United States since that date. If no further monkeypox cases are identified in the United States, and if there is no new information warranting an extension of the 6-month time period, FDA intends to revoke or amend 21 CFR § 1240.63 as early as January 20, 2004, which will be six months after July 20, 2003. At that time, if FDA decided to revoke or amend 21 CFR § 1240.63, it would publish an appropriate document (such as a proposed rule or direct final rule) in the **Federal Register**. FDA invites comments on this approach.

(Id. at page 62359.) However, the preamble to the interim final rule also cautioned that:

We emphasize that any possible revocation or amendment of 21 CFR § 1240.63 may also depend on new data or new developments. For example, various animal studies are being conducted to learn more about the incubation period and transmission dynamics of monkeypox. If those studies suggest that the period for incubation and transmission may be longer than 2.5 months, FDA could decide to recalculate the date on which it might revoke or amend 21 CFR § 1240.63. Studies are also underway to determine whether certain species that may be infected with the virus, but not display any symptoms, can infect other species. To illustrate how the virus could spread from an asymptomatic animal, assume that an animal

can carry the monkeypox virus, but that the animal does not develop monkeypox. If that animal later comes into contact with prairie dogs, a species which is already known to be susceptible to monkeypox, then the prairie dogs could become infected, and another monkeypox outbreak in prairie dogs could erupt. Again, if the CDC studies suggest that species can be asymptomatic, but still infectious, those results could cause FDA to recalculate the date on which it could revoke or amend 21 CFR § 1240.63. (Id.)

After the interim final rule's publication in the **Federal Register** on November 4, 2003, CDC notified us that it had test information that warranted our continued application and enforcement of 21 CFR 1240.63. This information confirmed monkeypox virus infection in several prairie dogs and in a few animals from other species, including a Gambian giant pouched rat, dormice, rope squirrels, a ground hog, a South American opossum, and a chinchilla. Some of these infections were subclinical (the animal was infected with the virus, but did not appear to be ill). Some of this preliminary information subsequently appeared in peer-reviewed scientific journal articles, and, in a **Federal Register** notice dated February 21, 2007 (72 FR 7825), we announced the addition of those articles and other recent journal articles to the docket. However, follow-up investigations confirmed that the human monkeypox cases in the United States were not associated with exposure to any animals except prairie dogs.

CDC also was monitoring the progress of a human case where a patient had developed monkeypox in late June 2003, but still had symptoms 5 months later. Conjunctival swabs from this patient were positive (following polymerase chain reaction (PCR) analysis) at 139 days after onset and culture positive at 126 days after onset. This patient eventually required a corneal transplant (see Ref. 9 which discusses this case briefly).

We also note that, when we wrote the interim final rule, efforts were continuing to track down animals from the original African shipment as well as prairie dogs from the Illinois distributor. Ultimately, over 170 African rodents from that shipment and 103 prairie dogs from the Illinois distributor were never recovered or located.

#### B. Were the New Data Available to the Public?

In the **Federal Register** of April 14, 2004, the Department of Health and Human Services published a notice announcing that the Secretary's Council on Public Health Preparedness

(Secretary's Council) would hold a public meeting where one topic would be "Transport of Possibly Infected Exotic Animals" (see 69 FR 19854 (April 14, 2004)). The Secretary's Council invited FDA and CDC to make presentations regarding the interim final rule. FDA made a presentation to the Secretary's Council seeking its advice on assessing the risk of monkeypox in the United States so that we could determine the appropriate way to manage that risk. CDC presented information concerning the new data, thus making the data publicly available. The Secretary's Council did not assess the risk of monkeypox; it recommended instead that the interim final rule's restrictions on prairie dogs and certain African rodents remain in place, although it also recommended that we make minor clarifications or changes to the rule so that prairie dog owners could take their animals to receive veterinary care and to transport their animals in certain situations. The Secretary's Council did not issue its recommendations in writing.

#### *C. Is There a Risk That Monkeypox Still Exists in the United States?*

From mid-2004 through 2007, more information regarding the 2003 monkeypox outbreak appeared in the scientific and medical literature. For example, two scientific articles demonstrated that the monkeypox virus easily infected prairie dogs and that infection in prairie dogs could occur through contact or through inhalation (Refs. 13 and 17). Another article described the laboratory evaluation of animals associated with the monkeypox outbreak; the authors examined tissue samples from 249 animals of 26 different species and found the monkeypox virus in 33 animals (Ref. 23). These animals included three rope squirrels, two Gambian giant pouched rats, and nine dormice from the shipment of African rodents (Ref. 23). Additionally, 14 of 20 prairie dogs tested were PCR positive for the monkeypox virus deoxyribonucleic acid (DNA), and infectious virus was recovered from 9 of 11 prairie dogs (Ref. 23). In general, prairie dogs also had higher levels of monkeypox virus or monkeypox virus DNA than other animal species (Ref. 23). The authors also found monkeypox virus DNA in tissues of other animal species housed at the Illinois establishment; this suggested that monkeypox could infect several animal species (Ref. 23). The article also described the limited, live-trapping of wild animals that the United States Department of Agriculture's Wildlife Service and the United States

Geologic Survey's National Wildlife Health Center completed after the United States monkeypox outbreak. Trapping of 201 animals occurred at sites located near where six human monkeypox cases (and associated captive prairie dogs) in Wisconsin occurred. No evidence of orthopox virus infection in any of these animals was detected. (The term "orthopox virus" refers to a genus (a term used in biology to denote a type or group that is above that of a species) of poxviruses. Examples of orthopox viruses include monkeypox virus, cowpox virus, and the variola virus; the variola virus causes smallpox.) The Illinois Wildlife Services program conducted further trapping studies in Illinois at three locations linked by trash disposal routes to the Illinois animal distributor. Forty-three animals were trapped, and all were negative for evidence of orthopox virus infection (Ref. 23).

Other articles (Refs. 14, 15, and 9) shed more light as to why the 2003 outbreak in the United States was not as deadly as those seen in Africa; for example, there are two different strains (or "clades") of the monkeypox virus, and the virus that appeared in the United States was representative of the less virulent (and less transmissible between humans) strain insofar as humans are concerned (Refs. 14 and 20). The risk of infection in humans correlated with the type of exposure to infected prairie dogs, and most human cases in the United States were associated with direct contact to (specifically the handling of) infected prairie dogs (Refs. 16 and 22). Children (persons under 18 years old) who were infected were more likely to be hospitalized in intensive care compared to infected adults (Ref. 9). Additionally, while some adults had received smallpox vaccinations before 1972, it is unclear as to whether childhood smallpox vaccinations offer durable protection against monkeypox. Some articles indicated that there did not appear to be significant differences in serious clinical observations or complications between vaccinated and unvaccinated adults (Ref. 9 and 20), yet another suggested that an individual's history of smallpox vaccination might protect against monkeypox illness (Ref. 21). In brief, the recent publications validate and reinforce the facts that:

- Prairie dogs are easily infected with the monkeypox virus, and infected prairie dogs have higher levels of monkeypox virus than other infected animals;
- Human cases in the United States were linked to contact with infected prairie dogs; and

- Monkeypox is a serious disease, particularly in children, but the virus implicated in the United States was representative of the less virulent and less transmissible between humans strain.

More significantly, one recent article assessed the risk for monkeypox associated with domestic trade in certain animal species in the United States (Ref. 18). The authors evaluated the data and uncertainties concerning monkeypox and its potential spread to animal and human populations in the United States and characterized in a qualitative analysis the probability of harm based on that data. They concluded that the risk for further domestically acquired human infections is low with the restrictions that FDA and CDC had established. The authors noted that there have been no new cases in humans or animals in the United States since the outbreak, despite the likelihood that some surviving infected animals may have been kept alive by pet owners or dealers. However, there have been no prospective surveillance activities that would fully address this question.

#### **IV. Given Recent Evidence, Is FDA Action Still Necessary?**

##### *A. Are the Measures of the Interim Final Rule Needed Now to Prevent Disease Spread?*

As we explained in the preamble to the interim final rule, we issued the interim final rule under section 361 of the Public Health Service Act (PHS Act) (42 U.S.C. 264) (see 68 FR at 62360) to prevent the spread of communicable disease. Section 361 of the PHS Act authorizes the Secretary to make and enforce such regulations as judged necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or from one State to another State. We may regulate intrastate transactions under this authority as appropriate (see *State of Louisiana v. Mathews*, 427 F. Supp. 174 (E.D. La. 1977)).

We have invoked section 361 of the PHS Act to regulate various activities and articles. For example, we have invoked this authority to prevent the transmission of communicable disease through certain shellfish, turtles, certain birds, and human tissue intended for transplantation (see 21 CFR 1240.60 (molluscan shellfish), 1240.62 (turtles), 1240.65 (psittacine birds), and 1270.1 through 1270.43 (human tissue)).

Our regulations, at 21 CFR 1240.30, provide further insight as to when we will use our communicable disease

authority. The regulation, in relevant part, states that:

Whenever the Commissioner of Food and Drugs determines that the measures taken by health authorities of any State or possession (including political subdivisions thereof) are insufficient to prevent the spread of any of the communicable diseases from such State or possession to any other State or possession, he may take such measures to prevent such spread of the diseases as he deems reasonably necessary \* \* \*

Thus, when we issued the June 11, 2003, order and later issued the interim final rule, we acted because we determined that measures taken by State health authorities, in 2003, were insufficient to prevent the spread of monkeypox. We took those actions because infected and potentially infected animals were crossing State lines, and human cases were appearing in several States; the multi-state impact, as well as the then-rapidly developing outbreak, indicated that measures taken by individual States would be insufficient to prevent the spread of monkeypox.

The risk assessment published in 2006, however, suggests that the risk of further monkeypox transmission from the original events of 2003, particularly to humans, in the United States is low. Consequently, based on that low risk, we believe that the import controls of CDC's interim final rule in 42 CFR 71.56 and routine State surveillance and disease prevention measures should be sufficient to prevent further human and animal monkeypox cases. Therefore, we have concluded that the domestic controls in 21 CFR 1240.63 are no longer necessary, and we are removing our regulation.

Please note that this revocation pertains solely to FDA's provisions at 21 CFR 1240.63; the requirements imposed by the CDC at 42 CFR 71.56 remain in effect.

#### *B. How Many Comments Did We Receive?*

The interim final rule provided an opportunity for public comment; this comment period expired on January 20, 2004. We received over 570 comments on the interim final rule. We received comments from State government agencies or departments, zoos, zoological associations, animal interest groups, animal breeders, animal vendors, and individuals, including foreign citizens. The comments reflected a wide array of differing and sometimes conflicting opinions. For example, most, but not all, State agencies supported the rule. Most State agencies appreciated Federal efforts in responding to the monkeypox outbreak, but one State agency criticized the rule as interfering

with the State's wildlife management obligations, and another State agency commented that it, rather than FDA, should operate a permit system that would enable certain animals to move within a State. As another example, many individuals commenting on the rule either captured, sold, owned, or wanted to own prairie dogs and objected strongly to the rule's impact on the prairie dog trade and to continuing the rule. In contrast, a few individuals supported the rule and advocated more stringent measures regarding the pet trade, including animals that the interim final rule did not address.

The comments also varied in their complexity and familiarity with the rule. For example, the American Zoo and Aquarium Association (AZA) recommended a specific change in the rule for AZA-accredited zoological parks because of the quarantine protocols used by AZA-accredited zoos; the AZA included its detailed accreditation standards as part of its comment. In contrast, many comments simply expressed their strong objections to the rule, particularly as it applied to prairie dogs, without explaining the reasons for their objections, discussing any specific regulatory provision, or suggesting any alternative approaches. Some comments advocated defiance or violations of the rule. Several comments denied that monkeypox is a serious disease, although they offered no evidence to contradict the scientific or medical reference we had cited. Other comments criticized the rule or FDA harshly, yet some criticisms pertained to issues that were not in the interim final rule or to actions, statements, or positions that were mistakenly attributed to us. For example, some comments accused us of killing or conspiring to kill prairie dogs. Virtually none of these comments mentioned any other animal covered by the interim final rule, and none offered any evidence to support their accusations.

Additionally, we received over 120 more comments on a notice that appeared in the **Federal Register** on February 19, 2004 (69 FR 7752). The notice was a routine opportunity for public comment on the information collection provisions in a rule pursuant to the Paperwork Reduction Act of 1995. In this particular case, the notice pertained to the information we were requiring from persons who wanted our permission to capture, offer to capture, transport, offer to transport, sell, barter, or exchange, or offer to sell, barter, or exchange, distribute, offer to distribute, and/or release into the environment any animals covered by the rule. Specifically, the notice sought comment

on the numerical estimates pertaining to the permit information, such as the estimated number of persons who would request a permit, the number of hours they would spend in preparing a permit request, the frequency at which permit requests would be submitted, etc. Most comments either interpreted or treated the notice as either a new opportunity to comment on the interim final rule or as finalizing the interim final rule. As a result, almost all comments submitted in response to the Paperwork Reduction Act notice focused on whether the interim final rule should remain in effect and did not address the collection of information under the Paperwork Reduction Act or any of our Paperwork Reduction Act estimates. Even though most comments submitted in response to the February 19, 2004, notice were not relevant to the Paperwork Reduction Act and were submitted months after the interim final rule's comment period had expired, we considered those comments in addition to the comments that were submitted in response to the interim final rule.

Finally, we received seven comments in response to a **Federal Register** notice which we published on February 21, 2007 (72 FR 7825). The notice added new information, primarily in the form of peer-reviewed scientific literature, to the administrative record, and we invited comment on the information being added. Of the seven comments, only one addressed a specific new reference. (The comment challenged the risk assessment article discussed earlier in section III.C of this document. The comment opined that the article "may underestimate the potential disease transmission risk associated with wild-caught prairie dogs," but did not challenge the authors' methodology or the authors' conclusion that the risk of monkeypox associated with the 2003 introduction of the virus into the United States was low. Rather, the comment noted a risk of transfer or importation of infectious pathogens risk remains due to illegal importation of animals, as well as the risk that domestic wild animals, particularly prairie dogs, may be a source for diseases other than monkeypox, such as plague and tularemia. The comment argued that there is no way to estimate the degree of illegal importation of African rodents or the legal importation of other potentially infected species. We note that the article does address each of these points.) Most comments discussed issues that were outside the scope of the **Federal Register** notice of February 21, 2007, such as urging FDA to retain its regulation, discussing the invasive

species potential of a Gambian Giant Pouched Rat population located in Florida, discussing plague and tularemia in prairie dogs, or discussing the pet trade, zoonotic diseases generally, or gaps in Federal authority.

Given our decision to remove the regulation based on the current evidence and circumstances, we will not respond in detail to all of the comments that opposed the rule. However, we would like to clarify a few points as follows:

- Many individuals believed that the rule was unfair because the Federal Government did not act against other animals that are capable of transmitting disease to humans. These individuals often argued that the Federal Government did not “ban” cows despite bovine spongiform encephalopathy (BSE, or “mad cow disease”) disease; dogs despite rabies; birds due to West Nile virus; or other animals associated with zoonotic diseases. Some claimed that we were discriminating against prairie dogs because they believed a rabbit had been infected with monkeypox, yet we did not include rabbits in the rule.

As a preliminary matter, the existence of other zoonotic diseases does not, and cannot, mean that we must treat all diseases in the same manner and at the same time. We agree that BSE and several other diseases cited by the comments raise public health concerns, but that fact does not mean that we are compelled to promulgate regulations for other or all zoonotic diseases before we can issue regulations to deal with monkeypox. In addition, it is important to note that monkeypox, as we stated in the preamble to the interim final rule (see 68 FR at 62353), is a zoonotic disease that, until mid-2003, occurred in central and west Africa. The monkeypox virus’ appearance in the United States demanded our immediate attention because monkeypox is a potentially fatal disease in humans, so it was important to prevent the virus from becoming established in the United States. West Nile virus is an example of how a virus can become established in the United States and result in sickness and death. Before 1999, West Nile virus had not been recorded in the United States; in 2002 alone, more than 4,000 Americans had become ill, and 284 had died (see 68 FR at 62361). Many animal species also suffered as the West Nile virus became established in the United States (id.).

To put it another way, unlike most of the pathogens or factors responsible for the diseases cited by the comments, the monkeypox virus was new to the United States in 2003, and (unlike West Nile

virus) could be controlled through regulation of human activity; as a result, a regulatory approach was taken that we anticipated would prevent the virus from becoming established in the listed animal populations or in other domestic animal populations. To the best of our knowledge, the efforts undertaken in 2003 were fully successful.

We also wish to point out that, contrary to the comments’ assumptions, we have taken regulatory action regarding other animals and other diseases. Those regulatory actions varied depending on the risk presented. For example, we have issued regulations restricting the sale and commercial distribution of turtles (21 CFR 1240.62) and restricting the transportation of psittacine birds (21 CFR 1240.65) because of their potential to transmit certain diseases to humans. We prohibited the use of mammalian protein in ruminant feed (21 CFR 589.2000) and have taken a number of additional actions to reduce the potential risk of BSE in cattle (see, e.g., 72 FR 1582 (January 12, 2007) (proposed rule to prohibit the use of certain cattle material in or in the manufacture of drugs intended for use in ruminant animals); 70 FR 58570 (October 6, 2005) (proposed rule to prohibit the use of certain cattle origin materials in the food or feed of all animals); 69 FR 58448 (September 30, 2004) (notice of availability of a guidance titled “Use of Material from Bovine Spongiform Encephalopathy-Positive Cattle in Animal Feed”); 69 FR 42288 (July 14, 2004) (advance notice of proposed rulemaking inviting comment on Federal measures to mitigate BSE risks)). We also have taken action to prohibit the use of certain cattle material (such as brain, skull, eyes, spinal cord, and other material) in human food to minimize human exposure to materials that are highly likely to contain the BSE agent (see 69 FR 42256 (July 14, 2004); see also 69 FR 42275 (July 14, 2004) (proposed rule to require manufacturers and processors of human food and cosmetics that are manufactured from, processed with, or otherwise contain material from cattle to establish and maintain records sufficient to demonstrate that the food or cosmetic is not manufactured from, processed with, or does not otherwise contain prohibited cattle materials)). Thus, we have taken regulatory actions when necessary to protect the public health, and the nature of the risk presented shaped our regulatory response to that risk.

Finally, insofar as rabbits and monkeypox are concerned, we acknowledge that a report issued as the

2003 outbreak was unfolding (Ref. 24) suggested that a rabbit might have transmitted the monkeypox virus to a human. However, subsequent tests on the rabbit in question and the human patient proved negative. Consequently, there are no documented cases of monkeypox transmission from rabbits to humans in the United States (Ref. 22).

- The 2003 monkeypox outbreak was significant because it involved a potentially fatal disease that had never been seen within the United States. It was important to stop monkeypox from becoming established in the United States because, once established, the disease could become a greater public health problem. If the virus became established in the United States, the potential impact on humans and other animal species could have been significant. In brief, final analysis of the 2003 monkeypox outbreak showed the following: (1) Besides rope squirrels, additional native species of African rodents (Gambian giant pouched rats and dormice) are susceptible to monkeypox; (2) prairie dogs are susceptible to monkeypox; (3) infected prairie dogs can transmit the disease to humans; and (4) children may be affected more severely than adults. Additionally, laboratory experiments demonstrated that additional North American animal species are susceptible to monkeypox (Ref. 23). We did not know, in 2003, and, in many cases, still do not know, whether the virus had spread or could spread to other domestic animal species (such as rodents) which, in turn, could expose more humans to monkeypox. In short, when dealing with a novel communicable disease, trying to prevent the disease from spreading has both present effects (i.e., fewer individuals become sick or die) and future effects (i.e., the potential for more animals and humans to become infected decreases if prevention efforts are successful).

- With respect to the comments that supported the interim final rule, we agree that the risks of communicable disease spread justified the measures taken in the interim final rule. Because we have decided to remove the regulation, we will not address the details of the comments that suggested variations on the permit system or other modifications to the rule. Nor will we address the issues related to other diseases of prairie dogs or to zoonotic diseases in general, which are outside the scope of this rule.

- The circumstances being addressed by most of the comments supporting the interim final rule have changed significantly, in large part because of the success of the interim final rule. As

discussed in section III.C above, the current evidence supports the conclusion that the risk of further infections from the monkeypox virus in the United States is low. Only one comment challenged the risk assessment that concluded that the current risk is low, but that comment did not challenge the authors' methodology. Instead, the comment expressed concern about future illegal importation of African rodents or legal importation of other animals that could be infected with monkeypox. Although we agree that the risk of future importations of animals infected with the monkeypox virus is not zero, we believe that the restrictions in 42 CFR 71.56 have been successful, and will continue to be successful, in keeping this risk low. Together, the measures taken by FDA and CDC under 21 CFR 1240.63 and 42 CFR 71.56 have successfully brought the risk of further human or animal monkeypox infection in the United States associated with the 2003 outbreak to its current low level. Based on the evidence, we believe that the risk will remain low in the absence of the measures in FDA's interim final rule. Under these circumstances, including the fact that CDC's interim final rule at 42 CFR 71.56 remains in effect, we have decided to remove 21 CFR 1240.63 in its entirety.

#### V. Environmental Impact Analysis

We have determined under 21 CFR 25.32(g) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

#### VI. Analysis of Impacts

We have examined the impacts of this regulatory action under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We believe that the removal of the regulation is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the removal of FDA's

regulation would eliminate most of the small administrative costs imposed by the interim final rule, we certify that it will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before publishing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is \$127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. We do not expect the removal of FDA's regulation to result in any 1-year expenditure that would meet or exceed this amount.

We issued a regulation on November 4, 2003, that modified existing restrictions on the import, capture, transport, sale, barter, exchange, distribution and release of African rodents, prairie dogs and certain other animals in order to prevent the spread of monkeypox. The decision to remove the regulation pertaining to domestic trade in prairie dogs and certain African rodents will eliminate most of the costs of the regulation to the extent that they have been realized.

In the interim final rule, we stated that incomplete data precluded us from developing quantitative estimates of the economic costs and benefits of the rule. The analysis of the rule, however, did contain a discussion about the sale of prairie dogs prior to and immediately after the June 11, 2003, administrative order banning the sale of these animals in order to reduce the spread of monkeypox. In effect, the analysis described the loss of the market for these pets that resulted from the earlier administrative order restricting their further distribution. The removal of the regulation would reopen the domestic market for pet prairie dogs, which prior to 2003 was estimated at about 30,000 animals per year with a retail value of about \$4.5 million. The domestic markets for certain African rodents would also be reopened, but the CDC restrictions on the importation of African rodents would remain in effect. Although we do not have data to estimate the size of these markets in 2003, the analysis in the interim final rule concluded that they would be fairly small.

The interim final rule also allowed for exemptions from the rule's restrictions on trade in these animals by requesting written permission from FDA. The analysis estimated that individuals requesting these exemptions would incur annual administrative costs ranging from about \$3,500 to \$6,500. FDA's administrative costs to process these requests each year were estimated at \$13,300. These administrative costs will be eliminated with the removal of FDA's regulation.

The analysis of the interim final rule also concluded that the regulation may have a significant impact on a substantial number of small entities, including trappers and distributors of prairie dogs, other small animal distributors, and retail pet stores. Most of these impacts will be negated with the removal of FDA's regulation.

#### VII. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Khodakevich, L., Jezek, Z. and Messinger, D., "Monkeypox Virus: Ecology and Public Health Significance," *Bulletin of the World Health Organization*, 66: 747–752 (1988). This reference identifies several species of squirrels as playing a major role as a reservoir for the monkeypox virus.
2. Centers for Disease Control and Prevention, "Updated Interim Case Definition for Human Case of Monkeypox," dated July 2, 2003.
3. Centers for Disease Control and Prevention, "Questions and Answers About Monkeypox," dated July 7, 2003.
4. Centers for Disease Control and Prevention, "Update: Multistate Outbreak of Monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003," *Morbidity and Mortality Weekly Report*, 52: 642–646 (July 11, 2003).
5. Reed, K. D. et al., "The Detection of Monkeypox in Humans in the Western Hemisphere," *New England Journal of Medicine*, 350: 342–350 (January 22, 2004).
6. DiGiulio, D. B., and Eckburg, P. B., "Human Monkeypox: An Emerging Zoonosis," *The Lancet—Infectious Diseases* 4: 15–25 (2004).
7. Centers for Disease Control and Prevention, "Update: Multistate Outbreak of Monkeypox - Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003," *Morbidity and Mortality Weekly Report*, 52: 561–564 (June 20, 2003).
8. Reynolds, G., "Why Were Doctors Afraid to Treat Rebecca McLester?" *New York Times Magazine*, section 6, page 32, column 1 (April 18, 2004) (available at [www.nytimes.com/2004/04/18/magazine/18MONKEYPOX.html](http://www.nytimes.com/2004/04/18/magazine/18MONKEYPOX.html)).
9. Huhn, G.D., et al., "Clinical Characteristics of Human Monkeypox, and Risk Factors for Severe Disease," *Clinical Infectious Diseases* 41: 1742–1751 (2005).

10. Order dated June 11, 2003, signed by Julie Louise Gerberding, Director, Centers for Disease Control and Prevention, and Mark B. McClellan, Commissioner of Food and Drugs, titled "Joint Order of the Centers for Disease Control and Prevention and the Food and Drug Administration, Department of Health and Human Services."

11. 68 FR 36566 (June 18, 2003).

12. Fleischauer, A. T., et al., "Evaluation of Human-to-Human Transmission of Monkeypox from Infected Patients to Health Care Workers," *Clinical Infectious Diseases*, 40: 689–694 (2004).

13. Xiao, S.Y., et al., "Experimental Infection of Prairie Dogs with Monkeypox Virus," *Emerging Infectious Diseases* 11(4): 539–545 (2005).

14. Likos, A.M., et al., "A Tale of Two Clades: Monkeypox Viruses," *Journal of General Virology* 86: 2661–2672 (2005).

15. Nalca, A., Rimoin, A.W., Bavari, S. and Whitehouse, C.A., "Reemergence of Monkeypox: Prevalence, Diagnostics, and Countermeasures," *Clinical Infectious Diseases* 41: 1765–1771 (2005).

16. Kile, J.C., et al., "Transmission of Monkeypox Among Persons Exposed to Infected Prairie Dogs in Indiana in 2003," *Archives of Pediatric Adolescent Medicine* 159: 1022–1025 (2005).

17. Guarner, J. et al., "Monkeypox Transmission and Pathogenesis in Prairie Dogs," *Emerging Infectious Diseases*, 10: 426–431 (March 2004).

18. Bernard, S., and Anderson, S., "Qualitative Risk Assessment: Monkeypox in the United States Associated with Domestic Trade in Certain Animal Species," *Emerging Infectious Diseases*, 12: 1827–1833 (2006).

19. Anderson, M.G., et al., "A Case of Severe Monkeypox Virus Disease in an American Child: Emerging Infections and Changing Professional Values," *Pediatric Infectious Disease*, 22: 1093–1096 (2003).

20. Croft, D.R., et al., "Occupational Risks during a Monkeypox Outbreak, Wisconsin, 2003," *Emerging Infectious Diseases*, 13: 1150–1157 (2007).

21. Reynolds, M.G., et al., "Spectrum of Infection and Risk Factors for Human Monkeypox, United States, 2003," *Emerging Infectious Diseases*, 13: 1332–1339 (2007).

22. Reed, K. D., Davis, J. P., and Damon, I. K., "Monkeypox in the Western Hemisphere," (Response to a Letter to the Editor), *New England Journal of Medicine*, 350: 1791 (April 22, 2004).

23. Hutson, C.L., et al., "Monkeypox Zoonotic Associations: Insights from Laboratory Evaluation of Animals Associated with the Multi-State US Outbreak," *American Journal of Tropical Medicine and Hygiene*, 76: 757–767 (2007).

24. Centers for Disease Control and Prevention, "Multistate Outbreak of Monkeypox - Illinois, Indiana, and Wisconsin, 2003," *Morbidity and Mortality Weekly Report*, 52: 537–540 (June 13, 2003).

### VIII. Federalism

FDA has analyzed this rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial

direct effects on States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we have concluded that the rule does not contain policies that have federalism implications as defined in the Executive Order, and, consequently, a federalism summary impact statement is not required.

### List of Subjects

#### 21 CFR Part 16

Administrative practice and procedure.

#### 21 CFR Part 1240

Communicable diseases, Public health, Travel restrictions, Water supply.

■ Therefore, under the Public Health Service Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR 16 and 1240 are amended as follows:

### PART 16—REGULATORY HEARING BEFORE THE FOOD AND DRUG ADMINISTRATION

■ 1. The authority citation for 21 CFR part 16 continues to read as follows:

**Authority:** 15 U.S.C. 1451–1461; 21 U.S.C. 141–149, 321–394, 467f, 679, 821, 1034; 28 U.S.C. 2112; 42 U.S.C. 201–262, 263b, 364.

#### § 16.1 [Amended]

■ 2. Section 16.1 is amended in paragraph (b)(2) by removing the entry for "§ 1240.63(c)(3)".

### PART 1240—CONTROL OF COMMUNICABLE DISEASES

■ 3. The authority citation for 21 CFR part 1240 continues to read as follows:

**Authority:** 42 U.S.C. 216, 243, 264, 271.

#### § 1240.63 [Removed]

■ 4. Remove § 1240.63.

Dated: August 27, 2008.

**Jeffrey Shuren,**

*Associate Commissioner for Policy and Planning.*

[FR Doc. E8–20779 Filed 9–5–08; 8:45 am]

**BILLING CODE 4160–01–S**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Parts 210 and 211

[Docket No. FDA–2007–N–0379] (formerly Docket No. 2007N–0280)

### Amendments to the Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is amending certain of its regulations on current good manufacturing practice (CGMP) requirements for finished pharmaceuticals as the culmination of the first phase of an incremental approach to modifying the CGMP regulations for these products. This rule revises CGMP requirements primarily concerning aseptic processing, verification of performance of operations by a second individual, and the use of asbestos filters. We are amending the regulations to modernize or clarify some of the requirements as well as to harmonize them with other FDA regulations and international CGMP standards.

**DATES:** This rule is effective December 8, 2008.

#### FOR FURTHER INFORMATION CONTACT:

Mary Malarkey, Center for Biologics Evaluation and Research (HFV–600), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–6190; or

Dennis Bensley, Center for Veterinary Medicine (HFV–140), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240–276–8268; or

Brian Hasselbalch, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., rm. 4364, Silver Spring, MD 20993, 301–796–3279.

#### SUPPLEMENTARY INFORMATION:

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